U.S. Food and Drug Administration

Proposed Administrative Order (OTC000037):

Over-the-Counter Monograph Condition B001: Single-Unit or Unit-Dose Containers for Over-the-Counter Monograph Drugs in Orally Disintegrating Tablet and Film Dosage Forms

(Issued June 5, 2025)

Pursuant to section 505G(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355h(b)), the U.S. Food and Drug Administration (FDA) is issuing a proposed administrative order (proposed order) as described herein and set forth in section IX below.

I. Introduction

FDA is issuing this proposed order to establish requirements for the packaging of certain over-the-counter (OTC) monograph drugs.[1]

The proposed order, if finalized, will set forth "Over-the-Counter Monograph Condition B001: Single-Unit or Unit-Dose Containers for Over-the-Counter Monograph Drugs in Orally Disintegrating Tablet and Film Dosage Forms" (hereinafter "B001"). As described below and detailed in proposed B001, this proposed order, if finalized, will require OTC monograph drugs that are 1) in an orally disintegrating tablet (ODT) or film dosage form and 2) subject to an OTC monograph identified in proposed § B001.1, "Scope," to be packaged in single-unit or unit-dose containers to be considered generally recognized as safe and effective (GRASE).

II. Public Comments

A. Dates

Submit electronic comments on the proposed order by 11:59 p.m. Eastern Time at the end of August 4, 2025. Comments submitted after this time will not be considered.

B. Instructions

Comments must be submitted electronically. The Federal eRulemaking Portal https://www.regulations.gov will accept comments at any time until 11:59 p.m. Eastern Time at the end of August 4, 2025.

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[1] This proposed order uses the term "OTC monograph drug" as it has been defined in section 744L(5) of the FD&C Act: "a nonprescription drug without an approved new drug application which is governed by the provisions of section 505G."

Submit electronic comments to Proposed Order ID OTC000037 as follows:

Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. All comments received must include the Proposed Order ID OTC000037 and the Docket No. FDA-2025-N-1359 for "Over-the-Counter Monograph Condition B001: Single-Unit or Unit-Dose Containers for Over-the-Counter Monograph Drugs in Orally Disintegrating Tablet and Film Dosage Forms."

- Comments, including attachments, must be submitted electronically to https://www.regulations.gov and will generally be posted in the docket unchanged, subject to any FDA redactions of confidential information as discussed below and subject to FDA's review of content that may have copyright protections.

- Confidential information will be identified and redacted by FDA: Submissions should not contain any redactions for claimed confidential information. FDA will review submissions to determine whether they contain information that, pursuant to section 505G(d) of the FD&C Act (21 U.S.C. 355h(d)) and any other applicable disclosure law, will not be made public. FDA will redact any such information prior to the comment being publicly viewable.

- Under section 505G(d) of the FD&C Act, FDA must make any information submitted by any person with respect to this proposed order available to the public upon submission, with limited exceptions. FDA will not make public any information pertaining to pharmaceutical quality information unless such information is necessary to establish standards under which a drug is GRASE under section 201(p)(1) of the FD&C Act (21 U.S.C. 321(p)(1)) (see section 505G(d)(2)(B)(i) of the FD&C Act). FDA will also not make public information that is of the type contained in raw datasets (see section 505G(d)(2)(B)(iv) of the FD&C Act).

- Additionally, for information not subject to any FDA redactions of confidential information and not subject to FDA's review of content that may have copyright protections, your comment should not include any information that you or a third party may not wish to be publicly posted, such as medical information or your or anyone else's Social Security number. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.

- Comments that are submitted in a timely manner (see Dates and Instructions) will be placed in the docket and will be publicly viewable on https://www.regulations.gov after FDA's review and redaction for confidential information.

C. Contact Information

For further information, contact: Shannon Liu, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-002, 240-402-2484.

III. Background

FDA is issuing this proposed order pursuant to section 505G(b)(2) of the FD&C Act, which authorizes the Agency to issue an administrative order at its initiative. Section 505G(b)(7) of the FD&C Act explicitly permits an administrative order issued under section 505G(b)(2) to include requirements for the packaging of a drug to encourage use in accordance with labeling, such as through requirements for unit-dose packaging, requirements for products intended for use by pediatric populations, and requirements to reduce risk of harm from unsupervised ingestion.

Accordingly, this proposed order, if finalized, will explicitly require that certain OTC monograph drugs in ODT and film dosage forms be packaged in single-use or unit-dose containers to be GRASE. This result accords with FDA's view that absent such packaging, ODT and film dosage forms of such drugs are not GRASE and thus cannot be legally marketed under section 505G of the FD&C Act.

Relatedly, under section 505G(c) of the FD&C Act, FDA is issuing "Proposed Administration Order OTC000038: Over-the-Counter Monograph Procedure for Minor Changes C001: Minor Changes to Solid Oral Dosage Forms for Certain Over-the-Counter Monograph Drugs"[2] (hereinafter "C001"). If the proposed order setting forth C001 is finalized, C001 would permit, pursuant to section 505G(c)(1) of the FD&C Act, minor changes in the dosage form of certain OTC monograph drugs from tablets and capsules to chewable tablets, ODTs, and films, without the issuance of a separate order under section 505G(b) of the FD&C Act (i.e., to amend an applicable OTC monograph to add chewable tablets, ODTs, and films or otherwise find such dosage forms to be GRASE). Among the requirements in C001, if finalized, would be that requestors of drugs subject to C001 must maintain information demonstrating that the packaging of such drugs is consistent with the requirements described in B001, as finalized and in effect, if applicable.

IV. Statement of Reasons for Issuance of Proposed Order

FDA is issuing this proposed order to explicitly require that ODT and film dosage forms of certain OTC monograph drugs, i.e., those subject to an OTC monograph identified in proposed § B001.1, be packaged in single-unit or unit-dose containers to be considered GRASE. In the agency's view, single-unit or unit-dose containers are needed to ensure the safe and effective use of these OTC monograph drugs in such dosage forms.

If this proposed order is finalized, to be considered GRASE, OTC monograph drugs subject to this order would need to be packaged in single-unit or unit-dose containers, in addition to meeting other applicable requirements under section 505G of the FD&C Act, including the conditions of an applicable OTC monograph identified in § B001.1, and the general conditions in 21 CFR 330.1. An OTC monograph drug in an ODT or film dosage form subject to this order that is not packaged in a single-unit or unit-dose container may be considered an unapproved new drug whose distribution violates sections 505(a) and 301(d) of the FD&C Act, and

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[2] FDA's Proposed Administrative Order (OTC000038) is available via the OTC Monographs@FDA portal at https://dps.fda.gov/omuf.

misbranded under sections 502(ee) and violates section 301(a) of the FD&C Act (21 U.S.C. 352(ee)).

In Sections IV.A through IV.C of this document, FDA describes the major provisions of the proposed order and provides details on the reasons for proposing the requirements set forth in Section IX.

A. Scope (Proposed § B001.1)

This proposed order, if finalized, will apply to any OTC monograph drug in an ODT or film dosage form that is subject to an OTC monograph identified in proposed § B001.1 that allows for ingestion via oral administration.

B. Definitions (Proposed § B001.2)

FDA proposes defining *orally disintegrating tablet* (see proposed § B001.2(a)) and *film* (see proposed § B001.2 (b)). These dosage form definitions are intended to align with United States Pharmacopeia (USP) nomenclature. USP General Chapter <1151> *Pharmaceutical Dosage Forms* provides general descriptions of and definitions for dosage forms commonly used to administer the active pharmaceutical ingredient.[3]

FDA proposes definitions for *single-unit container* (see proposed §B001.2(c)) and *unit-dose container* (see proposed § B001.2 (d)) that are intended to align with the definitions for these types of containers in USP General Chapter <659> *Packaging and Storage Requirements*[4].

These proposed definitions (see proposed § B001.2), if finalized, will apply only for purposes of this order.

C. Packaging (Proposed § B001.10)

FDA proposes that OTC monograph drugs subject to this order that are in an ODT or film dosage form must be packaged in single-unit or unit-dose containers (see proposed § B001.10) to address potential safety and efficacy concerns posed, in part, because these dosage forms dissolve quickly in the mouth.

Because ODTs and films are intended to dissolve in the mouth, they are designed to be more palatable than other oral dosage forms, such as tablets and capsules, in order to ensure proper administration and adherence by consumers. This attribute also makes them more attractive to young children. The rapid dissolution of these dosage forms may also pose greater risks of

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[3] United States Pharmacopeia (USP) General Chapter <1151> Pharmaceutical Dosage Forms. See also USP General Chapter <1121> Nomenclature, USP Nomenclature Guidelines (available at https://www.usp.org/health-quality-safety/compendial-nomenclature), and draft guidance for industry *Statement of Identity and Strength — Content and Format of Labeling for Human Nonprescription Drug Products* (September 2022) for information on selecting the established name for a drug as defined in section 502(e)(3) of the FD&C Act and 21 CFR 299.4. When final, this guidance will represent the FDA's current thinking on this topic.

[4] United States Pharmacopeia (USP) General Chapter <659> Packing and Storage Requirements.

adverse outcomes in the event of accidental ingestion by young children. If a child were to open a multiple-unit container (e.g., a bottle) of drugs in an ODT or film dosage form, those dosage forms' ability to rapidly dissolve in the mouth could allow the child to ingest a large amount of drug in a short amount of time. For some OTC monograph drugs, even a small difference in the amount of a drug taken can have a significant adverse effect on safety and efficacy for an individual, especially in children.[5]

Moreover, films packaged in a multiple-unit container have the potential to stick together, making it easy for a consumer to inadvertently dose more than one film at the same time. ODTs may also break apart when handled or stored in high humidity, which could result in underdosing from a multiple-unit container. Due to these potential safety and efficacy concerns, FDA has generally required nonprescription drug products in ODT and film dosage forms approved in a new drug application to be packaged in single-unit or unit-dose containers. In the context of OTC monograph drugs, these same concerns are likewise mitigated by single-unit or unit-dose containers, which would help ensure the safe and effective use of OTC monograph drugs in ODT and film dosage forms subject to this order.

Although some OTC monograph drugs are required to be in special packaging[6] (referred herein as child-resistant packaging), this requirement does not apply to many OTC monograph drugs. Even if the drug is packaged in a multiple-unit container that meets special packaging requirements, this packaging is only helpful if the child-resistant feature is fully engaged, making multiple-unit child-resistant packaging alone inadequate to fully mitigate risk of accidental ingestion for ODTs and films in the nonprescription setting. FDA recommends that all drugs, irrespective of the type of packaging, be stored safely out of reach and sight of children to further the overall public health efforts to address accidental pediatric ingestion of drugs.[7]

V. Exclusivity

This proposed order, if finalized, will not have the effect of authorizing marketing exclusivity under section 505G(b)(5)(C) of the FD&C Act for any entity or with respect to any drug.

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[5] See, e.g., Wang GS et al., 2020, Medication Errors From Over-the-Counter Cough and Cold Medications in Children, Acad Pediatr, 20(3): 327–332.

[6] *Special packaging* means "packaging that is designed or constructed to be significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly, but does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time" (16 CFR 1700.1(b)(4)). The list of substances requiring special packaging and the relevant packaging standards and testing procedures can be found in 16 CFR 1700.

[7] FDA also encourages single-unit and unit-dose containers to include child-resistant packaging features, such as puncture-resistant and peel-push blisters, to further help impede access to and reduce the risk of poisoning in children who come into possession of a drug in an ODT or film dosage form.

VI. Effective Date

This proposed order, if finalized, shall take effect—

(a) 60 calendar days after the date on which notice of the final order is published in the Federal Register; or

(b) if the final order is disputed under section 505G(b) of the FD&C Act, in accordance with section 505G(b)(2)(A)(iv)(I) of such Act.

VII. Analysis of Environmental Impact

FDA has carefully considered the potential environmental effects of this proposed order. FDA has concluded, under 21 CFR 25.31(a), that this action does not increase the use of the active moieties and thus does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. References

For references that support this proposed order, see the Federal eRulemaking Portal: https:/www.regulations.gov.

Literature

Wang, GS, KM Reynolds, W Banner, GR Bond, RE Kauffman, RB Palmer, IM Paul, M Rapp-Olsson, JL Green, and RC Dart, 2020, Medication Errors From Over-the-Counter Cough and Cold Medications in Children, Acad Pediatr, 20(3):327-332.

Other

United States Pharmacopeia (USP) *General Chapter <659> Packing and Storage Requirements.*
United States Pharmacopeia (USP) *General Chapter <1151> Pharmaceutical Dosage Forms.*

IX. Proposed Administrative Order (OTC000037)

For the reasons stated above, FDA is issuing the Proposed Administrative Order (OTC000037) to establish "Over-the-Counter Monograph Condition B001: Single-Unit or Unit-Dose Containers for Over-the-Counter Monograph Drugs in Orally Disintegrating Tablet and Film Dosage Forms."

If this proposed order is finalized, OTC monograph drugs in an ODT or film dosage form subject to this order must be packaged in single-unit or unit-dose containers, in addition to meeting other applicable requirements under section 505G of the FD&C Act, to be considered GRASE under section 201(p) of the FD&C Act, not misbranded under section 502(ee) of the FD&C Act, and not subject to section 503(b)(1) of the FD&C Act.

Upon effective date of this order, if finalized, OTC Monograph Condition B001 would read, in its entirety, as follows:

U.S. Food and Drug Administration

Over-the-Counter Monograph Condition B001: Single-Unit or Unit-Dose Containers for Over-the-Counter Monograph Drugs in Orally Disintegrating Tablet and Film Dosage Forms

Part A—General Provisions

Part A—General Provisions

§ B001.1 Scope

This order applies to any over-the-counter (OTC) monograph drug in an orally disintegrating tablet or film dosage form that is subject to one or more of the following OTC monographs:[8]

(a) OTC Monograph M001: Antacid Products for Over-the-Counter Human Use

(b) OTC Monograph M002: Antiflatulent Products for Over-the-Counter Human Use

(c) OTC Monograph M007: Laxative Drug Products for Over-the-Counter Human Use

(d) OTC Monograph M008: Antidiarrheal Drug Products for Over-the-Counter Human Use

(e) OTC Monograph M009: Antiemetic Drug Products for Over-the-Counter Human Use

(f) OTC Monograph M010: Nighttime Sleep-Aid Drug Products for Over-the-Counter Human Use

(g) OTC Monograph M011: Stimulant Drug Products for Over-the-Counter Human Use

(h) OTC Monograph M012: Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use

(i) OTC Monograph M013: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use

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[8] The listed OTC monographs reflect OTC monograph conditions for each specified therapeutic category as set forth by relevant final administrative order(s) established and in effect under section 505G of the FD&C Act.

(j) OTC Monograph M023: Poison Treatment Drug Products for Over-the-Counter Human Use

(k) OTC Monograph M024: Anthelmintic Drug Products for Over-the-Counter Human Use

(l) OTC Monograph M025: Cholecystokinetic Drug Products for Over-the-Counter Human Use

(m) OTC Monograph M026: Deodorant Drug Products for Internal Use for Over-the-Counter Human Use

(n) OTC Monograph M027: Orally Administered Menstrual Drug Products for Over-the-Counter Human Use

§ B001.2 Definitions

As used in this order:

(a) Orally disintegrating tablet. A solid dosage form composed of active and inactive ingredients that is intended to be ingested by placing on the tongue and designed to disintegrate rapidly on contact with saliva, not including buccal or sublingual tablets.

(b) Film. A solid dosage form consisting of a thin sheet composed of active and inactive ingredients that is placed on the tongue where it rapidly dissolves before being swallowed, not including buccal or sublingual films.

(c) Single-unit container. A container closure system that holds a quantity of an article intended for administration by other than the parenteral route as a single dose intended for use promptly after the packaging system is opened.

(d) Unit-dose container. A single-unit container closure system for an article intended for administration by other than the parenteral route as a single dose.

Part B—Packaging

§ B001.10 Single-unit or unit-dose containers

Drugs in an orally disintegrating tablet or film dosage form that are subject to an OTC monograph identified in § B001.1 must be packaged in single-unit or unit-dose containers.

Theresa M. Michele, MD

Office of Nonprescription Drugs

Center for Drug Evaluation and Research

June 2, 2025

Theresa M. Michele -S

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