



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-D-0829]

Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products; Revised Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a revised draft guidance for industry entitled "Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products." The last few decades have seen an increasing demand in various health care settings for solid oral dosage form drug products repackaged into unit-dose containers, which hold a quantity of drug for administration as a single dose. The increase in unit-dose repackaging has led to questions regarding stability studies and appropriate expiration dates for these repackaged products. This revised draft guidance describes the conditions under which FDA does not intend to take action regarding required stability studies for these repackaged products and the expiration date to assign under those conditions. Through this notice, FDA is hoping to decrease the regulatory burdens of drug regulations on manufacturers of these products, while at the same time ensuring patient safety. Since FDA's guidance documents do not bind the public or FDA to any requirements, they have not been considered to be subject to Executive Order 12866.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this revised draft guidance before it begins

work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. 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>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2017-D-0829 for "Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential."

Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the revised draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the revised draft guidance document.

FOR FURTHER INFORMATION CONTACT: Bill Harvey, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave. Bldg. 51, rm. 4214, Silver Spring, MD 20993-0002, 240-402-4180.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled "Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products." FDA's

current good manufacturing practice (CGMP) regulations for finished pharmaceuticals require that each drug product bear an expiration date determined by appropriate stability testing and that the date must be related to any storage conditions stated on the labeling, as determined by stability studies (21 CFR 211.137(a) and (b)). Samples used for stability testing must be in the same container-closure system as that in which the drug product is marketed (21 CFR 211.166(a)(4)). For unit-dose repackaged products, U.S. Pharmacopeial Convention (USP) General Chapter <1178> recommends that the expiration date "not exceed (1) 6 months from the date of repackaging; or (2) the manufacturer's expiration date; or (3) 25% of the time between the date of repackaging and the expiration date shown on the manufacturer's bulk article container of the drug being repackaged, whichever is earlier."

For solid oral dosage forms repackaged in unit-dose containers, the revised draft guidance states that FDA does not intend to take action regarding the requirements of §§ 211.137 and 211.166 (i.e., expiration dating determined by stability studies) under certain conditions. This revised draft guidance describes these conditions.

This draft guidance revises an earlier draft guidance for industry, "Expiration Dating of Unit-Dose Repackaged Drugs: Compliance Policy Guide." Changes include the following:

- Shortens the expiration date to be used under certain conditions for solid oral dosage forms repackaged in unit-dose containers from 12 months to 6 months or 25 percent of the time remaining until the expiration date on the container of the original manufacturer's product, whichever time period is shorter.
- Provides for an expiration date exceeding 6 months if supportive data from appropriate studies are available and other conditions are met.

- Excludes from the scope of the guidance products repackaged by State-licensed pharmacies, Federal facilities, and outsourcing facilities as defined under section 503B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353b).
- Excludes from the scope of the guidance all dosage forms other than solid oral dosage forms.
- Provides for the use of containers meeting USP <671> Class B standards if certain conditions are met.

This revised draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The revised draft guidance, when finalized, will represent the current thinking of FDA on expiration dating of unit-dose repackaged solid oral dosage form drug products. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

The current Compliance Policy Guide 480.200, "Expiration Dating of Unit-Dose Repackaged Drugs," issued February 1, 1984, revised March 1995, will be withdrawn when the revised draft guidance is finalized.

II. The Paperwork Reduction Act of 1995

This revised draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR parts 210 and 211 have been approved under OMB control number 0910-0139.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either
<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>
or <https://www.regulations.gov>.

Dated: August 3, 2017.

Anna K. Abram,

Deputy Commissioner for Policy, Planning, Legislation, and Analysis.

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