Guidance

Expiration Dating of Unit-Dose Repackaged Drugs: Compliance Policy Guide

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Compliance

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Sec. 480.200 (CPG 7132b.11)

I. INTRODUCTION

Many companies repackage solid and liquid oral dosage form drug products into unit-dose containers. This guidance states the circumstances under which the Food and Drug Administration (FDA) intends to exercise its enforcement discretion and does not intend to take enforcement action against such repackagers for failure to conduct stability studies to support expiration dates for these unit-dose repackaged products.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Unit-dose packaging systems are widespread in health care. Some unit-dose containers are available directly from manufacturers and repackagers; some drug products are repackaged into unit-dose containers by hospital or community pharmacies or shared service establishments. A shared service repackaging operation is one that exclusively serves one or more hospitals and/or related institutions, each having separate or no pharmacy services and each having responsibility for restricting distribution of the drug products received from the shared service establishment.

[1] This guidance has been prepared by the Office of Compliance in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

The nature of drug dispensing within hospitals in particular has made such unit-dose packaging useful and convenient in helping to ensure that medications are properly administered to patients. However, questions have arisen concerning the appropriate expiration dating for drug products repackaged into unit-dose containers.

FDA's current good manufacturing practice (CGMP) regulations for finished pharmaceuticals, 21 CFR Part 211, include § 211.137 on "Expiration dating." Section 211.137(a) requires that each drug product bear an expiration date determined by appropriate stability testing, as described in § 211.166. Under § 211.137(b), a drug product's expiration date must be related to any storage conditions stated on the labeling, as determined by stability studies described in § 211.166. Samples used for stability testing must be in the same container-closure system as that in which the drug product is marketed (§ 211.166(a)(4)). This is to ensure the drugs' safety and efficacy over their intended shelf life.

The U.S. Pharmacopeia (USP) contains standards on expiration dating and beyond-use dating in its General Notices and Requirements section.[2] The USP directs dispensers of prescription drug products to place on the label of the prescription container a suitable beyond-use date to limit the patient's use of the product. The beyond-use date cannot be later than the expiration date on the manufacturer's container. The USP states:

> For nonsterile solid and liquid dosage forms that are packaged in single-unit and unit-dose containers, the beyond-use date shall be one year from the date the drug is packaged into the single-unit or unit-dose container or the expiration date on the manufacturer's container, whichever is earlier, unless stability data or the manufacturer's labeling indicates otherwise.[3]

III. DISCUSSION

FDA has considered the USP beyond-use standard and believes that similar conditions are appropriate for FDA's CPG 7132b.11 for expiration dating. FDA believes that under certain specified conditions, it may be possible to assign appropriate expiration dating without conducting new stability studies on the nonsterile solid and liquid oral dosage forms repackaged into unit-dose containers. Therefore, FDA does not intend to take action against any nonsterile unit-dose repackaging firm (including shared services repackaging operations) or drug product in a unit-dose container solely on the basis of the failure of the repackaging firm to have stability studies supporting the expiration dates used, provided that the repackager meets all other regulations applicable to repackaged drug products and:

1. The expiration date does not exceed (a) 1 year from the date of repackaging or (b) the expiration date on the container of the original manufacturer's product, whichever is earlier, unless stability data or the original manufacturer's product labeling indicates otherwise.

[2] USP 27 (2004) at 11.
[3] Id.

2. If the drug product repackaged is in solid oral dosage form, the formed unit-dose container complies with the Class A standard described in the USP, General Chapter <671> Containers—Permeation, "Single-Unit Containers and Unit-Dose Containers for Capsules and Tablets."

3. The original bulk container of drug product has not been opened previously and the entire contents are repackaged in one operation.

4. The repackaging and storage of the drug product are accomplished in a controlled environment that is consistent with the conditions described in the labeling for the original drug product and the repackaged drug product. Where no temperature is specified in the labeling of the original drug product, a controlled room temperature (as defined in the General Notices and Requirements section of the USP) should be maintained during repackaging and storage of both solid and liquid oral dosage form drug products. Where no humidity is specified in the labeling of the original drug product, the relative humidity should not exceed 75 percent at 23 degrees Celsius for the repackaging and storage of solid oral dosage forms.

This CPG applies only to nonsterile solid and liquid oral dosage forms in unit-dose containers. Sterile products and other types of dosage forms and packages pose sterility and/or stability concerns that this CPG would not adequately address. Thus, this CPG does not apply to sterile products, other dosage forms, and other types of packages.

Liquid oral dosage forms should not be repackaged unless suitable materials are used and precautions are taken to prevent evaporation or solvent loss.

This CPG does not apply to nitroglycerin sublingual tablets or any other solid or liquid oral dosage form drug product known to have stability problems that preclude the product from being repackaged. This group of products generally would include any drug known to be oxygen sensitive or that exhibits extreme moisture or light sensitivity. In deciding whether a particular drug product is suitable for repackaging, the repackager should take into consideration any available information from the manufacturer, published literature, the USP, and FDA.

FDA's intent to exercise enforcement discretion concerning stability studies for repackaged products does not apply to any other requirements of Parts 210 and 211.