⟨ 1178 ⟩ GOOD REPACKAGING PRACTICES

This chapter is intended to provide guidance to those engaged in repackaging of drug products in accordance with 21 CFR 10.90. A pharmacist who repackages under the state law needs to apply (1) the principal information provided in the USP general information chapter *Packaging Practice—Repackaging a Single Solid Oral Drug Product Into a Unit-Dose Container* ⟨ 1146 ⟩ and (2) other beyond-use date references in the *Expiration Date and Beyond-Use Date* section under *General Notices and Requirements*.

This chapter provides information to any person who removes drugs from their original manufacturer's container and repacks them into a different container–closure system for resale or for distribution to hospitals or other pharmacies. It does not apply to repackaging of any *radioactive* drug products, including oral solids.

A repackager referred to here may also be a contract packager or a contract repackager. The words "repackager" and "repacker" are the same in this text and may be used interchangeably. These functions are beyond the regular practice of a pharmacist. A repackager is required to register with the FDA and comply with current Good Manufacturing Practices (cGMPs) regulations in 21 CFR 210 and 211.

A repackager is expected to meet the requirements of packaging practice under 21 CFR 210 through 226. Because the packaging practice relates to packaging, processing, or holding a drug product intended for administration to humans or animals, the repackager is expected to comply with regulations such as those relating to the sections pertaining to quality control, personnel qualifications, building and facilities, equipment, production and process controls, packaging and labeling controls, laboratory controls, master production record, batch records and reprints, distribution records, storage control records, and complaint files.

DEFINITIONS

For the purposes of this chapter, repackager, contract packager, and contract repackager are defined as follows.

A REPACKAGER is one who purchases and removes a drug product from the manufacturer's market container or bulk dosage container and places the product into a different container for distribution for human or animal use. A repackager may or may not take ownership from the manufacturer. A repackager is engaged in the repackaging of drugs (see also *Packaging Practice—Repackaging a Single Solid Oral Drug Product Into a Unit-Dose Container* ⟨ 1146 ⟩ for more definitions of a repackager).

A CONTRACT PACKAGER is one who is contracted by original drug manufacturers to package or repackage their product into a single- or multi-unit container chosen by the manufacturer. These containers should meet all the applicable requirements in this chapter, pertinent sections in general test chapters *Containers* ⟨ 661 ⟩ and *Containers—Permeation* ⟨ 671 ⟩, and comply with 21 CFR food additive requirements.

AN EQUIVALENT CONTAINER–CLOSURE SYSTEM refers to a container–closure system that yields the same, or better, moisture vapor transmission rate (MVTR), oxygen transmission, and light transmission as the original market container. These values may be determined by the repackager, or they may be obtained from the container–closure vendor for the specific container–closure system under consideration.

BEYOND-USE DATE (BUD) AND DISCARD-AFTER DATE are equivalent and are assigned using the criteria stated in the relevant section below.

EXPIRATION DATE is determined using stability studies and is not the same as beyond-use date or discard-after date.

FACILITIES

The facility in which repackaging is practiced should be operated in conformity with cGMPs. The environmental conditions during the packaging and storage operation of the drug product should comply with the *controlled room temperature* (see *General Notices*), storage in a *dry place,* and other requirements as directed by the manufacturer or supplier, especially if the drug requires storage at special temperature and humidity conditions (see *Good Storage and Shipping Practices* ⟨ 1079 ⟩).

ACQUISITION PROCESS

The repackager is expected to perform appropriate analytical testing for all pertinent specifications, such as identity and strength of each active ingredient, and any other finished product tests to establish valid analytical data. The repackager is expected to maintain records of such analyses on a batch-by-batch basis for the repackaged product that is either transferred to the repackager by the manufacturer or independently maintained by the repackager.

"Bulk" in this text refers to the quantity of either drug product or dosage form. The following criteria should be considered by the repackager upon receipt of bulk prior to repackaging.

a. The bulk article should be distributed to the repackager by the manufacturer in accordance with all regulatory requirements and accompanied by appropriate labeling and a valid expiration date. The repackager should also receive Material Safety Data Sheets (MSDS), Certificates of Analysis, and sample market labeling, including inserts from the drug product manufacturer.

b. The bulk article should be received intact and undamaged and in properly labeled containers with the Certificate of Analysis.

c. The bulk article should undergo definitive organoleptic evaluations to confirm its identity (e.g., physical appearance, marking, color, and odor) and to confirm the labeling as described by the manufacturer.

d. Records should be maintained to verify the identity and quantity of each shipment received and to verify the lot number and bar coded information for each article of the bulk shipment received. This record should also include the name of the manufacturer or supplier and its lot numbers and the date of receipt.

e. The repackager should store and maintain the bulk under storage conditions specified by the manufacturer, and/or as directed under *Controlled Room Temperature* (see *General Notices*).

REPACKAGING PROCESS

The following criteria should be observed.

a. The repackaging operations should be conducted under conditions that meet specified storage temperature definitions (see *General Notices*). Conditions of operation include maintenance of *controlled room temperature* in the area where the repackaging operation is conducted or other conditions as instructed by the manufacturer.

b. The manufacturer should include, in the package insert or in other appropriate literature supplied to the repackager, the following information about the packaging: materials of construction of the market package, its MVTR (see *Containers—Permeation* ⟨ 671 ⟩), as well as oxygen transmission and light transmission characteristics in order to enable the repackager to properly select an equivalent container–closure system. If the repackager does not use a

container–closure system equivalent to the manufacturer's market package, then the repackager must generate stability data for the drug product in the new container–closure system to justify the expiration date assigned.

c. The repackaging containers are labeled with the same labeling information as the market label that is used by the manufacturer. The conditions on the labeling should meet those required under 21 CFR 201, 211.122, 211.125, and 211.130.

d. Written procedures should be maintained to ensure that correct labels, labeling, and packaging materials are used for drug products.

e. All requirements for repackaging of bulk products should meet 21 CFR 211.

f. The packaging materials should comply with 21 CFR food additives regulations and all applicable requirements in USP general chapters ⟨ 661 ⟩, ⟨ 671 ⟩, and ⟨ 1146 ⟩.

LABELING

A repackager should provide appropriate labeling of the product identical to the manufacturer's approved market container. All repackaged products should be labeled with an appropriate BUD in the absence of stability data, or with an expiration date in cases where suitable stability studies, determined in CFR 211.166 (for recommended conditions see *International Conference on Harmonization ICH Q1A Stability Testing of New Drug Substances and Products*), have been performed on the product using the repackager's container. The expiration date will ensure that the products meet applicable standards of identity, strength, quality, and purity at the time of use.

EXPIRATION DATE/BEYOND-USE DATE

Expiration Date

Stability studies are performed on the drug product in the original manufacturer's containers to establish an expiration date. When a drug is repackaged into a different container, the product's expiration date is altered or interrupted.

a. The repackager may perform stability studies on the repackaged products to establish an expiration date for the product based on scientific evaluation of the drug product in the container–closure system in which it is to be marketed.

b. A repackager may use the manufacturer's original expiration date without additional stability testing if the drug product is repackaged into an equivalent container–closure system that is at least as protective as, or more protective than, the original system and complies with criteria established for equivalency. Establishment of system equivalency means (1) that the requirements of USP general test chapters ⟨ 661 ⟩ and ⟨ 671 ⟩ are met and (2) that the specifications such as light transmission, seals, or desiccants associated with the original container–closure system, or special protective materials in which the drug product is marketed, are the same. Comparison of container–closure systems may be done through stress testing of the product after storage under exaggerated conditions of temperature and humidity. If the repackager does not use a container–closure system equivalent to the manufacturer's market package, then the repackager must generate stability data for the drug product in the new container–closure system to justify the expiration date or BUD assigned.

c. A repackager should not use the equivalency container–closure system criteria to repackage drug products where such products have been identified by the manufacturer to have stability problems or if the manufacturer specifically states that the product should not be repackaged using the equivalency container–closure system criteria. For example, "This product is labile (e.g., moisture sensitive) and therefore should be dispensed only in the original manufacturer's container". In this case, a repackager needs to demonstrate the stability of the drug product in the repackager's container–closure system.