

ASHP Technical Assistance Bulletin on Single Unit and Unit Dose Packages of Drugs

Drug packages must fulfill four basic functions:

1. Identify their contents completely and precisely.
2. Protect their contents from deleterious environmental effects (e.g., photodecomposition).
3. Protect their contents from deterioration due to handling (e.g., breakage and contamination).
4. Permit their contents to be used quickly, easily, and safely.

Modern drug distribution systems use single unit packages to a great extent and, in fact, such packages are central to the operation of unit dose systems, intravenous admixture services, and other important aspects of pharmacy practice. These guidelines have been prepared to assist pharmaceutical manufacturers and pharmacists in the development and production of single unit and unit dose packages, the use of which has been shown to have substantial benefits.

A *single unit* package is one that contains one discrete pharmaceutical dosage form, i.e., one tablet, one 2-ml volume of liquid, one 2-g mass of ointment, etc. A *unit dose* package is one that contains the particular dose of the drug ordered for the patient. A single unit package is also a *unit dose* or *single dose* package if it contains the particular dose of the drug ordered for the patient. A unit dose package could, for example, contain two tablets of a drug product.

General Considerations

Packaging Materials. Packaging materials (and the package itself) must possess the physical characteristics required to protect the contents from (as required) light, moisture, temperature, air, and handling. The material should not deteriorate during the shelf life of the contents. Packages should be of lightweight, nonbulky materials that do not produce toxic fumes when incinerated. Materials that may be recycled or that are biodegradable, or both, are to be preferred over those that are not. Packaging materials should not absorb, adsorb, or otherwise deleteriously affect their contents. Information should be available to practitioners indicating the stability and compatibility of drugs with various packaging materials.

Shape and Form. Packages should be constructed so that they do not deteriorate with normal handling. They should be easy to open and use, and their use should require little or no special training or experience. Unless the package contains a drug to be added to a parenteral fluid or otherwise used in compounding a finished dosage form, it should allow the contents to be administered directly to the patient (or IPPB apparatus or fluid administration set) without any need for repackaging into another container or device (except for ampuls).

Label Copy. Current federal labeling requirements must be adhered to, with attention also given to the items at right. The desired copy and format are as follows:

**Nonproprietary Name
(and proprietary name if to be shown)
Dosage Form (if special or other than oral)
Strength
Strength of Dose and Total Contents Delivered
(e.g., number of tablets and their total dose)
Special Notes (e.g., refrigerate)
Expiration Date
Control Number**

1. *Nonproprietary and proprietary names.* The nonproprietary name and the strength should be the most prominent part of the package label. It is not necessary to include the proprietary name, if any, on the package. The name of the manufacturer or distributor should appear on the package. In addition, the name of the manufacturer of the finished dosage form should be included in the product labeling. The style of type should be chosen to provide maximum legibility, contrast, and permanence.
2. *Dosage form.* Special characteristics of the dosage form should be a part of the label, e.g., extended release. Packages should be labeled as to the route of administration if other than oral, e.g., topical use. In a package containing an injection, the acceptable injectable route(s) of administration should be stated on both outer and inner packages, i.e., both on the syringe unit and carton (if any).
3. *Strength.* Strength should be stated in accordance with terminology in the *American Hospital Formulary Service*. The metric system should be used, with dosage forms formulated to provide the rounded-off figures in the *USP* table of approximate equivalents and expressed in the smallest whole number. Micrograms should be used through 999, then milligrams through 999, then grams. Thus, 300 mg, *not* 5 gr, nor 325 mg, nor 0.3 g; 60 mg, *not* 1 gr, nor 0.06 g, nor 64.5 mg, nor 65 mg; 400 mcg, *not* 1/150 gr, nor 0.4 mg, nor 0.0004 g; ml (milliliters) should be used instead of cc (cubic centimeters).
4. *Strength of dose and total contents delivered.* The total contents and total dose of the package should be indicated. Thus, a unit dose package containing a 600-mg dose as two 300-mg tablets should be labeled "600 mg (as two 300-mg tablets)." Likewise, a 500-mg dose of a drug in a liquid containing 100 mg/ml should be labeled "Delivers 500 mg (as 5 ml of 100 mg/ml)."
5. *Special notes.* Special notes such as conditions of storage (e.g., refrigerate), preparation (e.g., shake well or moisten), and administration (e.g., not to be chewed) that are not obvious from the dosage form designation are to be included on the label.
6. *Expiration date.* The expiration date should be prominently visible on the package. If the contents must be reconstituted prior to use, the shelf life of the final product should be indicated. Unless stability data warrant otherwise, expiration dates should fall during January and July to simplify recall procedures.

7. *Control number (lot number).* The control number should appear on the package.

Product Identification Codes. The use of product identification codes, appearing directly on the dosage form, is encouraged.

Evidence of Entry. The package should be so designed that it is evident, when the package is still intact, that it has never been entered or opened.

Specific Considerations

Oral Solids

1. *Blister package.* A blister package should
 - a. Have an opaque and nonreflective backing (flat upper surface of package) for printing.
 - b. Have a blister (dome or bubble) of a transparent material that is, preferably, flat bottomed.
 - c. Be easily peelable.
 - d. If it contains a controlled substance, be numbered sequentially for accountability purposes.
2. *Pouch package.* A pouch package should
 - a. Have one side opaque and nonreflective for printing.
 - b. Be easily deliverable, i.e., large tablets in large pouches, small tablets in small pouches.
 - c. Tear from any point or from multiple locations.
 - d. If it contains a controlled substance, be numbered sequentially for accountability purposes.
3. The packages should be such that contents can be delivered directly to the patient's mouth or hand.

Oral Liquids

1. The packages should be filled to deliver the labeled contents. It is recognized that overfilling will be necessary, depending on the shape of the container, the container material, and the formulation of the dosage form.
2. The label should state the contents as follows: Delivers ____mg (or g or mcg) in ____ml.
3. If reconstitution is required, the amount of vehicle to be added should be indicated. These directions may take the form of "fill to mark on container" in lieu of stating a specific volume.
4. Syringe-type containers for oral administration should not accept a needle and should be labeled "For Oral Use Only."
5. Containers should be designed to permit administration of contents directly from the package.

Injectables

1. The device should be appropriately calibrated in milliliters and scaled from the tip to the fill line. Calibrated space may be built into the device to permit addition of other drugs. The label should state the contents as follows: Delivers ____mg (or g or mcg) in ____ml.

2. An appropriate size needle may be an integral part of the device. The needle sheath should not be the plunger. The plunger should be mechanically stable in the barrel of the syringe.
3. The device should be of such a design that it is patient ready and assembly instructions are not necessary.
4. The sheath protecting the needle should be a non-penetrable, preferably rigid material, to protect personnel from injury. The size of the needle should be indicated.
5. The device should be of such a design that easy and visible aspiration is possible. It should be as compact as possible and of such a size that it can be easily handled.

Parenteral Solutions and Additives

1. The approximate pH and osmolarity of parenteral solutions should be stated on the label. The amount of overfill also should be noted. Electrolyte solutions should be labeled in both mEq (or millimole) and mg concentrations. Solutions commonly labeled in terms of percent concentration, e.g., dextrose, should also be labeled in w/v terms.
2. Parenteral fluid container labels should be readable when hanging and when upright or in the normal manipulative position.
3. Drugs to be mixed with parenteral infusion solutions should be packaged into convenient sizes that minimize the need for solution transfers and other manipulations.
4. Partially filled piggyback-type containers should
 - a. Be recappable with a tamperproof closure.
 - b. Have a hanger.
 - c. Have volume markings.
 - d. Be designed to minimize the potential for contamination during use.
 - e. Contain a partial vacuum for ease of reconstitution.
5. If an administration set is included with the container, it should be compatible with all large volume parenteral delivery systems.

Other Dosage Forms—Ophthalmics, Suppositories, Ointments, etc. Dosage forms other than those specifically discussed above should be adequately labeled to indicate their use and route of administration and should adhere to the above and other required package labeling and design criteria.

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