Inspections, Compliance, Enforcement, and Criminal Investigations

CPG Sec 430.100 Unit Dose Labeling for Solid and Liquid Oral Dosage Forms (CPG 7132b.10)

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BACKGROUND:

In recent years the pharmaceutical industry has responded to an increased demand for drug products which are packaged for "unit dose" dispensing, i.e. the delivery of a single dose of a drug to the patient at the time of administration for institutional use, e.g., hospitals. The drug product is dispensed in a unit dose container--a non-reusable container designed to hold a quantity of drug intended for administration (other than the parenteral route) as a single dose, directly from the container, employed generally in a hospital unit dose system. The advantages of unit dose dispensing are that the drug is fully identifiable and the integrity of the dosage form is protected until the actual moment of administration. If the drug is not used and the container is intact, the drug may be retrieved and redispensed without compromising its integrity.

In view of the intended use of unit dose packaging, each unit dose container is regarded as a drug in package form subject to all requirements of the Act and implementing regulations. However, the pertinent labeling regulations [21 CFR 201.10(i) and 201.100] present problems in interpretation in that they are inconsistent with respect to exemptions for containers too small or otherwise unable to accommodate a label with sufficient space to bear all mandatory information. As a result of several recent regulatory actions emphasizing these inconsistencies, the regulations will be rewritten in the future to clarify the requirements.

Because of the general lack of uniformity in the labeling for unit dose containers due to inconsistent interpretations of the regulations, or to a lack of knowledge of unit dose labeling requirements, we are issuing this Compliance Policy Guide (CPG).

This CPG does not encompass "Unit of Use" packaging which is defined as a method of preparing a legend medication in an original container, sealed and labeled, prelabeled by the manufacturer, and containing sufficient medication for one normal course of therapy. (Reference: Proceedings Unit of Use Packaging Conference, January 24-26, 1979).

POLICY:

Until the regulations are revised, the attached document describes the labeling requirements for oral solid and liquid dosage forms packaged in unit dose containers. The requirements apply to all firms which package drugs into unit dose containers.

Since unit dosage forms are primarily intended for institutional use rather than sale to the general public, we will not require the warnings described in 21 CFR, Part 369 or the statements described under item 6.b. (Section I and II) of Attachment A to be on the label; however, this information must appear elsewhere in the labeling.

Where unit dose repacking is performed by a single facility for a closed membership or group (e.g. "shared services") a current package insert, bearing adequate directions for use, located on the premises of each member to whom the repacked goods are shipped is regarded as satisfying this requirement. The absence of such a current package insert on the premises of a member to which a drug product is shipped will cause that drug product to be misbranded.

Solid and liquid oral dosage forms in unit dose containers shall be deemed misbranded under Section 502 of the Act if they deviate from the attached list of requirements.

Other unit dose forms, e.g., topical ointments/creams, ophthalmic, etc. are not included in this document. They will be considered at a future date should circumstances warrant.

ATTACHMENT A

UNIT DOSE LABELING

I. PRESCRIPTION DRUGS (Solid and Liquid Oral Dosage Forms, e.g., Capsules, Tablets, Solutions, Elixirs, Suspensions, etc.)

The label of the actual unit dose container must bear all of the following information (except item 9).

NOTE: A firm may not claim an exemption on the basis that the label is too small to accommodate all mandatory information if all available space is not utilized or the label size can readily be made larger, or if the type size on the label can readily be made smaller without affecting the legibility of the information.

1. The established name of the drug and the quantity of the active ingredient per dosage unit, if a single active ingredient product; if a combination drug, the established name and quantity of each active ingredient per dosage unit. In each case, the label must bear the established name and quantity or proportion of any ingredient named in Section 502(e) whether active or not. For solid dosage forms, a declaration of potency per tablet/capsule will suffice; for liquid

dosage forms, the total volume shall be declared as well as the quantity or proportion of active ingredient contained therein, e.g., Cimetadine HCL Liquid 5 ml, 300 mg/5 ml or 300 mg per 5 ml; or Septra/Bactrim Suspension 5 ml, contains Trimethoprim 40 mg and Sulfamethoxazole 200 mg per 5 ml; or each 5 ml. contains...

2. The expiration date (see Attachment B). (Ref. 21 CFR 201.17, 211.137).

3. The lot or control number. [Ref. 21 CFR 201.100(b), 211.130].

4. The name and place of business of the manufacturer, packer, or distributor as provided for in 21 CFR 201.1.

5. For a drug recognized in an official compendium, the subject of an approved new drug application (NDA/ANDA) or as provided by regulation:

A. Required statements such as "Refrigerate", "Protect From Light", "Dilute Before Using", etc., [Ref.: FD&C Act 502(f)(1), 502(g), and 505].

B. Any pertinent Statement bearing on the special characteristics of the dosage form, e.g., sustained release, enteric coated, chewable, suspension, etc.; [Ref. FD&C Act 502(e), 502(a), 201(n)].

6. For any drug product, not subject to 5:

A. Any pertinent statement bearing on special characteristics of the dosage form, e.g., sustained release, enteric coated, sublingual, chewable, solution, elixir, suspension, etc.; [Ref. FD&C Act 502(e), 502(a), 201(n)].

B. While not required to be on the label per se, it is strongly recommended that:

(1) Any pertinent statement bearing on the need for special storage conditions, e.g., "Refrigerate", "Do not Refrigerate", "Protect from Light", etc., [Ref. FD&C Act 502(f)(1)] appear on the label, and

(2) Any information needed to alert the health professional that a procedure(s) is necessary prior to patient administration to prepare the product as a finished dosage form, e.g., "Shake Before Using" [Ref: FD&C Act 502(f)(1)].

7. If more than one dosage unit is contained within the unit dose container (solid dosage form), the number of dosage units per container and the strength per dosage unit should be specified (e.g., two capsules; each capsule contains 300 mg. Rifampin).

8. The statement "Warning: May be habit forming" where applicable, the controlled drug substances symbol required by Drug Enforcement Administration (DEA), and the name and quantity or proportion of any substance as required by Section 502(d).
9. The National Drug Code designation is recommended, although this is not

mandatory.

In addition to all of the above (except item 9), the following information must appear on the outer package from which the unit dose container is dispensed:

1. The number of unit dose containers in the package, e.g., 100 unit doses. If more than one dosage unit is within each unit dose container this should also be stated (e.g., "100 packets; each packet contains two tablets," or "100 packets of two tablets each.").

2. Full disclosure information, as detailed in 21 CFR 201.100. Where unit dose repacking is performed by a single facility for a closed membership or group (e.g., "shared services") a current package insert bearing adequate directions for use, located on the premises of each member to whom the repacked goods are shipped is sufficient to satisfy this requirement. The absence of such a current package insert on the premises of a member to which a drug is shipped will cause that drug to be misbranded.

3. The prescription legend.

II. OVER THE COUNTER DRUGS (Solid and Liquid Oral Dosage Forms, e.g. Capsules, Tablets, Elixirs, Suspension, etc.)

The label of the actual unit dose container must bear all of the following information (except item 9).

NOTE: A firm may not claim an exemption on the basis that the label is too small to accommodate all mandatory information if all available space is not utilized, the label size can be made larger, or if the type size on the label can readily be made smaller without affecting the legibility of the information.

1. The established name of the drug if it contains a single active ingredient; if a combination drug, the established name of each active ingredient. If a compendial drug, the label must express the quantity of each therapeutically active ingredient contained in each dosage unit, e.g., Aspirin Tablets, 325 mg., (USP -General Notices), and the quantity or proportion of any ingredient, whether active or not, as required by Section 502(e).

2. The expiration date (see attachment B).

3. The lot or control number.

4. The name and place of business of the manufacturer, packer, or distributor as provided for in 21 CFR 201.1.

5. For a drug recognized in an official compendium, the subject of an approved new drug application (NDA/ANDA) or as provided by regulation:

A. Required statements such as "Refrigerate", "Protect from Light", "Dilute Before Using", etc.; [Ref. FD&C Act 502(f)(1), 502(g), and 505].

B. Any pertinent statement bearing on special characteristics of the dosage form, e.g., sustained release, enteric coated, chewable, suspension, etc.; [Ref. FD&C Act 502(e), 502(a), 201(n)].

6. For any drug product not subject to 5:

A. Any pertinent statement bearing on special characteristics of the dosage form, e.g., sustained release, enteric coated, sublingual, chewable, solution, elixir, suspension, etc.; [Ref. FD&C Act 502(e), 502(a), 201(n)].

B. While not required to be on the label per se, it is strongly recommended that:

(1) Any pertinent statement bearing on the need for special storage conditions, e.g., "Refrigerate", "Do not Refrigerate", "Protect from Light", etc., [Ref. FD&C Act 502(f)(1)], appear on the label, and
(2) Any information needed to alert the user that a procedure(s) is necessary prior to patient administration to prepare the product for use, e.g., "Shake Well", "Dilute Before Using" [Ref: FD&C Act 502(f)(1), 21 CFR 201.5].

7. If more than one dosage unit is contained within the unit dose container, the number of dosage units per container should be specified (e.g., two tablets aspirin; each tablet contains 325 mg).

8. The statement "Warning: May be habit forming" where applicable, the controlled drug substances symbol required by DEA, and the name and quantity or proportion of any substance required by Section 502(d).

9. The National Drug Code designation is recommended, although this is not mandatory.

In addition to all of the above (except item 9), the following information must appear on the outer package from which the unit dose container is dispensed:

1. The number of unit dose containers in the package. If more than one dosage unit is within each unit dose container this should also be stated (e.g., "100 packets; each packet contains two tablets," or "100 packets of two tablets each.")

2. The labeling, i.e., the outer carton or a leaflet enclosed within the package must bear adequate directions for use as specified in 21 CFR 201.5 and should include:

A. Statement of all conditions, purposes, or uses for which the drug product is intended.

B. Quantity of dose, including usual quantities for each of the uses for which it is intended and usual quantities for persons of different ages and conditions.

C. Frequency of administration.

D. Duration of administration.

E. Time of administration (in relation to time of meals, time of onset of symptoms, or other time factors).

ATTACHMENT B

EXPIRATION DATING OF SOLID AND LIQUID ORAL DOSAGE FORMS IN UNIT DOSE CONTAINERS. (See CPG 7132b.11).

No action will be initiated against any unit dose repackaging firm, including shared services, or drug product in unit dose container meeting all other conditions of FDA's repackaging requirements, solely on the basis of the failure of the repacking firm to have stability studies supporting the expiration dates used provided:

1. The unit dose container complies with the Class A or Class B standard described in the Twentieth Edition of the United States Pharmacopeia, General Tests, Single-Unit Containers and Unit-Dose Containers for Capsules and Tablets (page 955); and

2. The expiration date does not exceed six months; and

3. The six month expiration period does not exceed 25 per cent of the remaining time between the date of repackaging and the expiration date shown on the original manufacturer's bulk container of the drug repackaged, and the bulk container has not been previously opened.

This policy does not apply to antibiotics or to nitroglycerin sublingual tablets which are known to have stability problems that preclude them from being repackaged.

Issued: 2/1/84