
Guidance for Industry

Dosage Delivery Devices for OTC Liquid Drug Products

DRAFT GUIDANCE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)
November 2009**

Compliance

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Dosage Delivery Devices for OTC Liquid Drug Products

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Guidance for Industry¹

Dosage Delivery Devices for OTC Liquid Drug Products

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You may use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This document is intended to provide guidance to firms that are manufacturing, marketing, or distributing over-the-counter (OTC) liquid drug products (e.g., elixirs, suspensions, solutions, syrups) that are packaged with dosage delivery devices (e.g., calibrated cups, droppers, syringes, spoons).² Because written, printed, or graphic matter appearing on dosage delivery devices packaged with OTC liquid drug products is considered labeling, such markings on these devices must not be false or misleading and must be clear and consistent with the drug product's directions for use. (See Sections 201(m), 502(a) and 502(f)(1) of the Federal Food, Drug, and Cosmetic Act).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents 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.

¹ This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

² This guidance is not intended to address the adequacy of dosage delivery devices to deliver the labeled dosage. It is the responsibility of the manufacturers, packers, and distributors of these liquid drug products packaged with dosage delivery devices to ensure that the accompanying dosage delivery devices accurately deliver the doses identified by the measurements. FDA may issue additional guidance regarding the adequacy of dosage delivery devices to deliver the labeled dosage and to ensure that consumers can properly use dosage delivery devices that accompany OTC liquid drug products.

II. BACKGROUND

Many OTC liquid drug products are packaged with dosage delivery devices intended to facilitate proper dispensing of the product by the patient, parent, or caregiver. In most cases, these devices have calibrated units of measure marked on the device (e.g., teaspoon, tablespoon, or milliliter) that are intended to ensure proper measurement of the appropriate dose. However, in many cases, OTC liquid drug products in the marketplace are packaged with dosage delivery devices that bear markings that are inconsistent with the labeled dosage directions. For example, some may contain superfluous markings or may be missing necessary markings. The Agency also is aware that some people typically do not use dosage delivery devices provided with OTC drug products, and consumers have reported some difficulties measuring OTC liquid medications for their children with provided dosage delivery devices. These difficulties may lead to consumers using less accurate means to give their children analgesics, cough and cold, and other common OTC liquid medications, e.g., household spoons.

There have been numerous reports of accidental overdose that were attributed, in part, to markings on measured dosage cups for OTC liquid drug products that were misleading or incompatible with the labeled dosage directions for use.

FDA is issuing this guidance because of ongoing safety concerns about the serious potential for accidental drug overdoses of OTC liquid drug products that can result from the use of dosage delivery devices with markings that are inconsistent or incompatible with the labeled dosage directions for OTC drug products. FDA is especially concerned because OTC liquid drug products are frequently intended to be used with pediatric populations.

III. REGULATORY/POLICY DISCUSSION

A. Statutory Requirements and Regulatory History

Section 502 of the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C 352) states that a drug is considered to be misbranded:

- (a) if its labeling is false or misleading in any particular [or] . . .
- (f) unless its labeling bears (1) adequate directions for use

Section 201(m) of the FFDCA further defines labeling as “all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article” (21 U.S.C 321(m)). The Agency considers any written, printed, or graphic matter, including measurements on dosage delivery devices, packaged with OTC liquid drug products to be labeling. FDA has issued notices and Warning Letters that cite misbranding violations under section 502(a) of the FFDCA (21 U.S.C. 352(a)) when markings on dosage delivery devices are inconsistent with the labeled dosage directions. Examples include the following:

- On December 9, 1991, FDA issued a Compliance Notice to alert all drug establishments that were registered with the Agency to review the labeling of all drug products marketed with an

83 accompanying dosage delivery device to determine if the product's labeling was compatible
84 with the markings on the dosage device, and make corrections where necessary.

85
86 In this notice, FDA said that dosage delivery devices that had markings inconsistent with the
87 product's labeling rendered the drug product misbranded under 21 U.S.C. 352(a).
88

- 89 • On January 21, 1992, FDA issued a Public Health Announcement warning parents against
90 the inadvertent overdosing of children with liquid OTC medications for colds and flu.
- 91 • Between November 1991 and January 1992, FDA issued Warning Letters to five firms that
92 were marketing OTC liquid drug products with dosage delivery devices that were not
93 compatible with the products' labeled dosage directions. Those letters cited violations of
94 section 502(a) of the FFDCA (21 U.S.C. 352(a)) because the markings on the dosage cups
95 packaged with the products were misleading within the context of the labeled directions for
96 use. Additionally, eight firms initiated recalls of over 980,000 retail units nationwide of
97 OTC oral liquid drug products that had misleading or incompatible dosage delivery devices
98 during the same time period. Since January 1992, several other firms have conducted large-
99 scale recalls of OTC oral liquid drug products with misleading or incompatible dosage
100 delivery devices.
- 101 • On January 17, 2008, FDA issued a Public Health Advisory recommending that when giving
102 OTC cough and cold medicines to children ages two years and older, parents and caregivers
103 use only the measuring spoons or cups that come with the medicine or those made specially
104 for measuring drugs.

105 Despite these efforts, through routine monitoring and surveillance programs, FDA has become
106 aware that an increasing number of OTC liquid drug products have dosage delivery devices that
107 are incompatible with labeled product dosage directions.
108

109 In addition to misbranding under section 502(a) of the FFDCA (21 U.S.C. 352(a)), when dosage
110 delivery devices packaged with OTC liquid drug products fail to bear a mark or markings
111 consistent with the labeled dosage directions, the products also lack adequate directions for use
112 and are misbranded under section 502(f)(1) of the FFDCA (21 U.S.C. 352(f)(1)).
113

114 **B. Recommendations**

115

116 The Agency makes the following recommendations for OTC liquid drug products:
117

- 118 • Dosage delivery devices should be included for all OTC drug products that are liquid
119 formulations.
- 120 • These devices should have calibrated units of measure marked on the device (e.g. teaspoon,
121 tablespoon, or milliliter) that are the same as the units of measure specified in the labeled
122 dosage directions on any outside packaging (carton labeling), bottle, and any accompanying
123 written instructions.
- 124 • If units of measure are abbreviated on the dosage delivery device, the abbreviation used on
125 the device should be the same abbreviation used in the labeled dosage directions, outside
126 packaging (carton labeling), bottle, and any accompanying written instructions.

- International or national standards for abbreviations should be used. For example, milliliters should be abbreviated as “mL” and teaspoons abbreviated as “tsp,” and less common or nonstandard used abbreviations should be avoided.
- Abbreviations should be defined on the dosing device (e.g., tsp = teaspoon) and, if they are not, should be defined in the labeled dosage directions, outside packaging (carton labeling), bottle, and any accompanying written instructions.
- Any decimals or fractions included on dosage delivery devices should be listed as clearly as possible.
 - Use leading zeroes before decimal points (“0.4” not “.4”) to avoid 10-fold dosing errors.
 - Use smaller font size for numerals in fractions (“½” not “1/2”) to avoid interpreting “1/2” as “1 or 2.”
- Dosage delivery devices should not bear extraneous or unnecessary markings that may be confusing.
- Manufactures should try to ensure that the dosage delivery devices are used only with the products with which they are included. Possible ways of accomplishing this are to either:
 - Include a statement on the dosage delivery device and the drug product’s bottle and/or carton labeling that only the provided dosage delivery device is to be used with the particular OTC drug product with which it is included. This information can also be included under the Directions Section of the product’s Drug Facts panel
 - Devise a mechanism to secure the dosage delivery device to the drug product, such as creating an integrated dosing device.
- Dosage delivery devices should not be significantly larger than the largest dose described in the labeled dosage directions and should permit clear measurement and delivery of the smallest labeled dosage.³
- The markings on dosage delivery devices should be clearly visible and not be obscured when the product is added to the device.

The Agency also recommends that firms conduct usability studies to ensure that dosage delivery devices are easily understood and accurately used by consumers.⁴

Because the Agency regards the markings on these delivery devices as labeling, FDA considers their failure to bear markings consistent with the labeled dosage directions to cause the drug product to be misbranded. For example, if the bottle and/or carton labeling for a drug product contains dosage directions that are written exclusively in terms of a specific unit of measure, the accompanying dosage delivery device should contain markings in the same unit of measure. The following examples illustrate situations that would render the products misbranded:

³ For concentrated acetaminophen infant drops, the Agency recommends that dosage delivery devices should also permit clear measurement and delivery of the smallest intended dosage consistent with professional labeling for infants under 2 years of age.

⁴ Although this Guidance is not intended to address the adequacy of dosage delivery devices to deliver the labeled dosage, the Agency may consider issuing future guidance to industry that addresses topics such as: age, weight, solubility, viscosity, patient populations, and instructions for cleaning, reuse, and storage.

Example 1: The directions for use on the bottle and/or carton specify teaspoon measures to describe the dosing amount; the dosage cup that is supplied with the product bears three different graduated scales (one is a combined scale of teaspoonfuls/dessertspoonfuls/tablespoonfuls; the second provides metric measurements (cc/ml); and, the third is a combined scale of fluid ounces and drams) (see Appendix A, Illustration #1).

Example 2: The directions for use on the bottle and/or carton specify teaspoon measures to describe the dosing amount; the dosage cup provided with the product bears two different graduated scales (one is a combined scale of teaspoonfuls/tablespoonfuls with juxtaposed conversions to milliliters (Note: the illustration also has a dessertspoon marking); the second is a combined scale of milliliters and fluid ounces) (see Appendix A, Illustration #2).

The Agency also recommends that the dosage delivery device for a drug product provide markings that can readily measure the dosage indicated by the directions on the bottle and/or carton labeling. Again, the following examples illustrate situations that would render the products misbranded:

Example 3: The directions for use on the drug product's bottle and/or carton specify a 2-teaspoonful dose (see Appendix A, Illustration #3); the dosage cup does not bear a corresponding 2-teaspoonful graduation (See Appendix A, Illustration #1).

Example 4: The directions for use on the drug product's bottle and/or carton specify 1/2-teaspoonful dose (see Appendix A, Illustration #3); the dosage cup does not bear a corresponding 1/2-teaspoonful graduation (see Appendix A, Illustration #4).

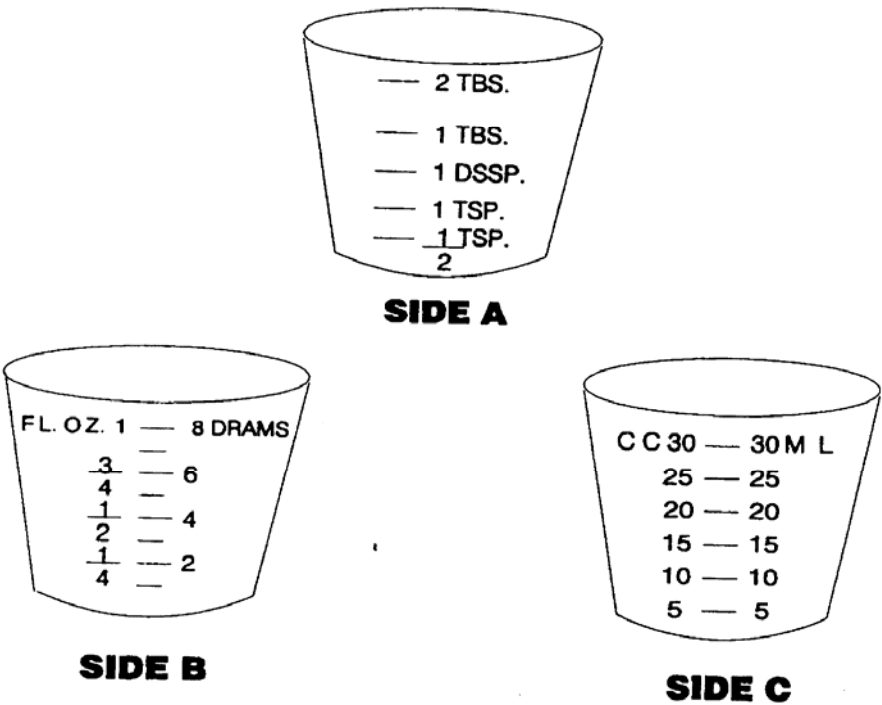
In addition to the scenarios described above, FDA is concerned about products that include a dosage delivery device and provide directions for use that state:

Under 2 [or 6, etc.] years of age: consult a physician

The Agency recommends that the labeling for these types of products include a prominent statement that directs consumers to consult their pharmacist or healthcare provider for any appropriate additional dosage delivery device necessary for use when a physician recommends a dose that is different than the doses that appear on the dosage delivery device that accompanies the product.

APPENDIX A: EXAMPLES OF DOSAGE CUPS THAT DO NOT CORRESPOND TO
DOSING DIRECTIONS

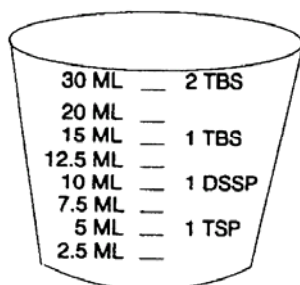
DOSAGE CUP
ILLUSTRATION #1



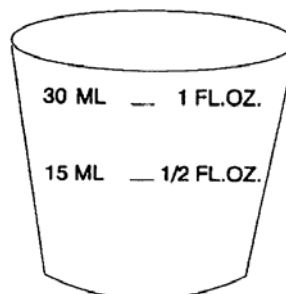
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DOSAGE CUP

ILLUSTRATION #2



SIDE A



SIDE B

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BOTTLE AND/OR CARTON LABELING

ILLUSTRATION # 3

I

Drug Facts (continued)

Directions

- do not take more than **6 doses** in any 24 hour period
- use only with enclosed measuring cup. Do not use with any other device
- dose as follows

adults and children 12 years of age and older	2 teaspoons every 4 hours
---	---------------------------

children 6 to 12 years of age	1 teaspoon every 4 hours
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children 2 years to 6 years of age	1/2 teaspoon every 4 hours.
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children under 2 years of age	do not use
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Other information

- store at 20 - 25°C (68 - 77°F)
- alcohol free

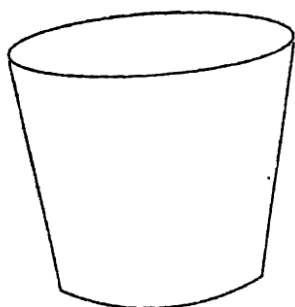
Inactive ingredients: (established names of each inactive ingredient listed in alphabetic order)

Questions? call weekdays 9 AM to 5 PM EST at **1-800-XXX-XXXX**

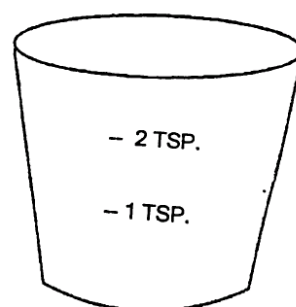
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DOSAGE CUP

ILLUSTRATION # 4



SIDE A



SIDE B

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APPENDIX B: EXAMPLE OF DOSAGE CUP THAT CORRESPONDS TO DOSING DIRECTIONS

The example below illustrates a dosage cup that corresponds to the dosing directions described in the drug facts panel below.

BOTTLE AND/OR CARTON LABELING

<i>Drug Facts (continued)</i>	
<i>Directions</i>	
<ul style="list-style-type: none"> do not take more than 6 doses in any 24 hour period use only with enclosed measuring cup. Do not use with any other device dose as follows 	
adults and children 12 years of age and older	2 teaspoons (tsp) every 4 hours
children 6 to 12 years of age	1 teaspoon (tsp) every 4 hours
children 2 years to 6 years of age	½ teaspoon (tsp) every 4 hours.
children under 2 years of age	do not use
<i>Other information</i>	
<ul style="list-style-type: none"> store at 20 - 25°C (68 - 77°F) alcohol free 	
<i>Inactive ingredients:</i> (established names of each inactive ingredient listed in alphabetic order)	
<i>Questions?</i> call weekdays 9 AM to 5 PM EST at 1-800-XXX-XXXX	

