CHPA

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February 2, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2009-D-0322

Dear Sir or Madam:

Enclosed herein are comments on "Guidance for Industry; Dosage Delivery Devices for OTC Liquid Drug Products", published as *Draft Guidance*[1]. The Consumer Healthcare Products Association (CHPA) is the national trade association representing the leading manufacturers and distributors of over-the-counter (OTC) medicines and dietary supplements in the United States. CHPA and its member companies have an interest and expertise in dosage delivery devices and support FDA's efforts to develop guidance for industry on this important topic. CHPA member companies have made several commitments in this area. In October 2008, manufacturers of pediatric liquid drug products committed to provide dosing devices with all products and to ensure doses marked on the product label were also marked on the device. Recently, in collaboration with the CDC and other interested stakeholders, including FDA, CHPA members developed and adopted Voluntary Guidelines to simplify and standardize volumetric measures used in labeling of OTC oral liquid drug products intended for administration to children and their respective dosing devices[2]. CHPA's Voluntary Guidelines are generally consistent with, and in some cases more specific than, FDA's Draft Guidance.

CHPA's comments on the *Draft Guidance* are organized into General Comments and Detailed Comments by Section (Attachment 1).

1. General Comments

    a. Compared to FDA's *Draft Guidance*, the CHPA Voluntary Guidelines are more specific in terms of 1) recommending the metric unit mL, with or without teaspoonful (tsp) as the preferred unit of liquid measure and 2) recommending against use of other liquid units such as cubic centimeter, fluid ounce and dropper(ful). Since FDA's *Draft Guidance* intends to also include

[1] **Federal Register**, Vol. 74, No. 213, pp 57319, November 5, 2009.
[2] Voluntary Guidelines can be viewed at *www.CHPA-info.org*, or see Attachment 2.

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adult oral liquid drug products, use of either tea- or tablespoonful liquid measure should be allowed together with milliliter. We suggest FDA consider these additional comments for inclusion in the Draft Guidance.

b. Reports[3][4], research [5][6][7][8] and consumer information[9][10] suggest that a significant source of consumer misunderstanding related to measuring liquid medicines is associated with spoons: household vs. measuring spoon, amount of liquid held by a spoon, "teaspoon(ful)" vs. "tablespoon(ful)", either written as full text or as abbreviations. It is therefore preferable to use only one of these "spoonful" units on any product label or dosing device. We suggest FDA consider this additional evidence and recommendation.

c. Due to unique physicochemical properties of liquid formulations, dosing devices for liquids must be formulation-specific to accurately measure and deliver the labeled dose of medicine. Dosing devices provided with liquid medicine products are calibrated to deliver the appropriate dose[11]. We recommend against advising consumers to purchase or use any device other than that supplied with the products, since other devices are not calibrated for use with a specific formulation.

CHPA and its members look forward to working with FDA to further develop this guidance.

Respectfully submitted,

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Vice President, Regulatory Affairs

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[3] Litovitz, T. Implication of dispensing cups in dosing errors and pediatric poisonings: a report from the American Association of Poison Control Centers. Annals of Pharmacotherapy. 26: 917-18. 1992.
[4] Abbreviations can lead to medication errors! USP Quality Review. 80: 1-7. July 2004.
[5] Bailey S. et. al. Predictors of misunderstanding pediatric liquid medication instructions. Family Medicine. 41 (10): 715-21. 2009.
[6] Madlon-Kay, D. and Mosch F. Liquid medication dosing errors. Journal of Family Practice. 49(8): 741-744. 2000.
[7] Wansink, B. and van Ittersum, K. Spoons systematically bias dosing of liquid medicine. Annals of Internal Medicine. 152(1): 66-67. 2010.
[8] Davis, T.C. et. al. Literacy and misunderstanding prescription drug labels. Annals of Internal Medicine. 145(12): 887-894. 2006.
[9] FDA Consumer Health Information. Giving medication to children: Q&A with Dianne Murphy, M.D. June 2009.
[10] Parenting Corner Q&A: Medicine. American Academy of Pediatrics. Published online February 2009.
[11] United States Pharmacopeia 32-National Formulary 27, Chapter 1101, page 604; Chapter 1221, page 728.

Attachment 1
CHPA Detailed Comments on Draft Guidance for Industry on Dosage Delivery Devices for OTC Liquid Drug Products

Line Numbers	Section Title
I.	**Introduction**
	No comments
II.	**Background**
42	We disagree with the statement that "in many cases", delivery devices bear markings that are inconsistent with labeled dosage directions, and recommend this phrase be deleted.
52	CHPA member experience suggests it would be more accurate to say that there have been "some" reports of accidental overdose that were attributed in some way to dosage cups, rather than "numerous".
58-59	We recommend changing "markings" to "liquid measure markings" to clearly refer to the markings associated with doses of medicine. We recommend changing "labeled dosage directions" to "liquid measures used in the labeled dosage directions".
III.A.	**Regulatory/Policy Discussion** **Statutory Requirements and Regulatory History**
	No comments
III.B	**Recommendations**
General	The *Draft Guidance* does not recommend a preferred standard unit of liquid measurement for dosing directions. CHPA members have voluntarily adopted the metric unit of milliliters (abbreviated "mL") as the preferred primary unit of liquid measure, and recommend FDA do the same.
120	We recommend changing "calibrated units of measure" to "calibrated units of liquid measure". We recommend an additional statement in the Guidance that liquid measure markings for doses consistent with professional labeling should also be included on the device. We recommend that FDA allow the full text spelling for teaspoon to be "teaspoonful" and for tablespoon to be "tablespoonful", per USP-NF (see footnote 11).
129	The *Draft Guidance* does not specify what "less common or nonstandard used abbreviations" should be avoided. We recommend avoiding use of cubic centimeters, cc, dram, fluid ounce, dropper(ful) and dessertspoon(ful) liquid measure units. We further recommend avoiding use of tablespoon(ful) and teaspoon(ful) on the same product label or device.
130	Space on a dosing device is extremely limited. It is potentially confusing to the consumer to define abbreviations on a dosing device. We agree that liquid measure abbreviations used in labeling should be defined on the product label.
139	We recommend deleting this statement, as the relevant liquid measure information to be included on a dosing device is covered in lines120-123. Also, as written in the *Draft Guidance*, this statement is vague and open to interpretation. For example, markings required for optical readers (manufacturing equipment) or to identify the product are examples of markings that should be allowed on the device. This statement could also be interpreted to mean that a unique dosing device should be specifically manufactured for each product, with only those

	markings on the product label appearing on the device. There is no evidence that this is necessary and doing so would increase cost of products and could increase the probability of dosing device mix-ups.
143	It is not feasible to add a lengthy statement to the dosing device stating that only the device that comes with the product should be used with the product. Such a lengthy statement adds significant extra text and risks obscuring important liquid measure markings on the device. Such a statement is more appropriately included in the Drug Facts panel, as space is available, on the carton or immediate container label.
149	We recommend that FDA delete the phrase "should not be significantly larger" since there are legitimate and important reasons for the dosage delivery device to have a physical capacity larger than the largest labeled dose, including 1) for technical functionality of the device, 2) to facilitate consumer handling of the device, 3) to minimize liquid spillage, 4) to facilitate measurement and delivery of the liquid, 5) to allow adequate size to secure onto the product bottle.
154	We recommend FDA delete this recommendation. It is outside the stated scope of this *Draft Guidance*, which focuses on consistency of the units of measure on the dosing device and label. Also, no information is provided by FDA characterizing potential concerns/root cause related to consumer usability. As FDA notes in their footnote 4, this *Draft Guidance* is not intended to address the adequacy of dosage delivery devices to deliver the labeled dosage. Devices are calibrated using existing guidance to assure accuracy (see CHPA footnote 11).
191	Use of the statement "consult a physician" is appropriate for some drugs. We recommend deleting the statement that "FDA is concerned", as no basis for concern is stated. If a basis for concern is stated, data supporting the concern should be referenced.
196	We recommend deleting this statement about consulting a pharmacist or healthcare provider for any appropriate additional dosage delivery device…". As noted in our General Comments (1.c.), consumers should not be encouraged to use dosing devices other than those supplied with the product. Markings for doses currently recommended by professional labeling should be included on the device (as noted in comment 120 above).
Footnote 3	We recommend inserting "As an example" at the beginning of this sentence, since acetaminophen infant drops are only one example of commonly used dosages communicated to consumers by professionals. There are other OTC pediatric medicines with professional labeling.

Attachment 2

CHPA VOLUNTARY GUIDELINES

CDC Stakeholder Initiative: Preventing Unsupervised Medication Ingestions and Overdoses in Children

CDC Working Group #2: Volumetric Measures for Dosing of Over-the-Counter Oral Liquid Drug Products for Children ≤ 12 years of Age

Approved by CHPA Board of Directors November 17, 2009

Table of Contents

1. Introduction

As part of multiple stakeholder efforts to help prevent accidental, unsupervised medication ingestions and overdoses in children, this document suggests ways to improve the consistency and standard format of volumetric measures within the dosing directions on the outer packaging and immediate container label, as well as on the dosing device for OTC oral liquid drug products with dosing directions for children, defined as ≤12 years of age (both covered under the monograph system as well as an approved NDA/ANDA). While research evidence is limited, the recommendations made herein do represent the integration of stakeholder communications and standards, including those from authoritative bodies and professional organizations, as well as knowledge gained from consumer experience and research with OTC medicine products.

Although similar principles may apply, this does not address other oral liquid medicines such as those for only adults, prescription medicines or dietary supplements whose special packaging may require additional considerations. Neither does this document address the packaging nor directions for products with children's dosing intended for topical use such as crèmes, pastes or sprays.

2. Background

One of the principle objectives of OTC Drug Facts Labeling regulation was to establish a standardized format and content of certain OTC labeling information so as to assist consumers in reading and understanding the OTC labeling. While the OTC Drug Facts regulation lays out specific labeling format and content information which is required for the ingredients, uses, warnings, directions and other information, the OTC Drug Facts regulation does not specify standard dose-related volumetric measures.

Communications exist for parents and caregivers about the best ways to give medicines to children, especially the proper use of oral liquid medicines (1,2,3,4,5). Key points to parents and caregivers are to always read the label carefully, use the dosing device that comes with the product and to understand the types of liquid measure units for dosing liquid medicines. Some have suggested preferred volumetric measure terms, units and abbreviations, as well as potential areas to avoid (6,7,8,9,10,11,12).

Findings from an industry-wide survey (April 2009) of OTC oral liquid drug products with dosing directions for children suggest potential areas to improve the consistency and standard format of volumetric measures:

- Dosing Directions
    - Representation in a dosing chart versus running text
    - Volumetric measures: unit types and standards; abbreviations, formats and style
    - Decimals and fractions
- Dosing device accompanying the product; consistency with labeling dosing directions

3. Proposal Objectives

To identify and support consistent terminology, format, and text for volumetric measures within the context of OTC Drug Facts dosing directions for OTC oral liquid drug products with dosing directions for children.

4. Proposal

The following recommendations are suggested for the labeling dosing directions on the outer packaging and immediate container label, as well as on the dosing device for OTC oral liquid drug products with dosing directions for children (includes products marketed under the OTC monograph system and those marketed under an approved NDA/ANDA).

4.1 OTC Drug Facts Dosing Directions: Outer Package and Immediate Container Labeling

A. Dosing Directions: Statement(s)

1) Provide a statement(s) that 1) encourages a consumer to select the right dose, 2) use the dosing device that accompanies the product, 3) keep dosing device with product/do not discard dosing device (see Appendix for examples of possible statements)

2) Provide a definition of any volumetric unit of measure specified in the product's dosing directions using the following abbreviations and full text exactly:
    a) "mL = milliliter"
    b) "tsp = teaspoonful"

B. Dosing Directions: Guidelines for Volumetric Measures

1) If space permits, use a dosing table format to provide dosing directions
2) Use milliliter as the preferred unit of measure in the dosing directions
    a) use a milliliter unit alone (e.g. "5 milliliter or 5 mL")
    b) or, alternatively, use a milliliter unit together with a "teaspoonful" unit equivalent (e.g. 5 mL (1 tsp))
3) Avoid use of a "teaspoonful" unit alone
4) Use the following abbreviation and text exactly:
    a) Abbreviations: "mL"; "tsp" (preferable to use only one unit of measure)
    b) Full text: "teaspoonful"
5) Avoid use within labeling dosing directions of the following: tablespoon, cubic centimeters, cc, dram, fluid ounce, Fl. Oz., and dropper(ful).
6) Use a format and style for expressing fractions that is consistent with the type of measure unit (i.e metric or English/Imperial)
    a) for metric units, use a decimal; if <1 mL volume, use decimal with a leading zero (e.g. 0.5).
    b) for English/Imperial units (i.e. teaspoonful), use a mathematical notation (e.g. lower case ½, but not upper case 1/2).

4.2 Dosing Device Accompanying the Product

A. Guidelines for Volumetric Measures
1) Provide a calibrated dosing device with all products
2) Provide graduated markings on the dosing device that include dosage(s) specified in the dosing directions
3) Use only the volumetric unit(s) of measure provided in the dosing directions; if using abbreviations, define abbreviations in the labeling dosing directions
4) Use contrasting graduated markings (e.g. etched or printed) so as to aid the readability of the measured liquid
5) Use only the fraction format and style (i.e decimal or mathematical) provided in the dosing directions

5. Appendix: Examples

5.1 Examples: Dosing Directions Statement(s)

Example A:
"Measure the dose correctly using the enclosed [insert specific name of product's dosing device, e.g. dosing cup, dropper, oral syringe] "

Example B:
"For accurate dosing, use the enclosed [insert specific name of product's dosing device, e.g. dosing cup, dropper, oral syringe] to measure a dose"

Example C: Label statement using only mL (infant acetaminophen drops)
"Find right dose on chart below"
"Use only enclosed [insert specific name of product's dosing device, e.g. dosing cup, dropper, oral syringe] designed for use with this product. Do not use any other dosing device."

5.2 Examples: OTC Drug Facts Directions

Example A

Drug Facts

Directions

- for accurate dosing, use the enclosed [insert specific name of product's dosing device, e.g. dosing cup, dropper, oral syringe] to measure a dose
- mL = milliliter; tsp = teaspoon

adults and children 6 years and over	10 mL (2 tsp) once daily; do not take more than 10 mL (2 tsp) in 24 hours.
adults 65 years and over	5 mL (1 tsp) once daily; do not take more than 5 mL (1 tsp) in 24 hours.
children 2 to under 6 years of age	2.5 mL (½ tsp) once daily. do not give more than 2.5 mL (½ tsp) in 24 hours.
children under 2 years of age	do not use

Example B

Drug Facts

Directions

- shake well before using
- use only enclosed dosing device
- mL = milliliter; tsp = teaspoon

adults and children 6 years and over	30 mL (6 tsp) once daily; do not take more than 30 mL (6 tsp) in 24 hours.
adults 65 years and over	15 mL (3 tsp) once daily; do not take more than 15 mL (3 tsp) in 24 hours.
children 2 to under 6 years of age	7.5 mL (1 ½ tsp) once daily. do not give more than 7.5 mL (1 ½ tsp) in 24 hours.
children under 2 years of age	do not use

Example C

Drug Facts

Directions

- shake well before using
- use only with enclosed dosing device
- find right dose on chart below. If possible, use weight to dose; otherwise, use age.
- fill to dose level
- dispense liquid slowly into child's mouth, toward inner cheek
- if needed, repeat dose every 4 hours
- do not use more than 5 times in 24 hours
- use dropper to close bottle and maintain child resistance

Weight (lb)	**Age (yr)**	**Dose (mL)**
Under 24	Under 2	Call a doctor
24-35	2-3	1.6 mL (0.8 + 0.8 mL)

Attention: specifically designed for use with enclosed dosing device. Do not use any other dosing device with this product.

1 United States Food and Drug Administration. Medicines in My Home. URL: http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm093965.pdf

2 American Academy of Pediatrics. What is the best way to give my child medicine? URL: http://www.aap.org/publiced/BR_Medicine.htm

3 FamilyDoctor.Org. OTC Drugs: Special Groups at Risk of Adverse Effects. URL: http://familydoctor.org/online/famdocen/home/otc-center/basics/853.html

4 United States Food and Drug Administration. Giving Medication to Children: Q&A with Dianne Murphy, M.D. URL: http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM164439.pdf

5 Consumer Products Healthcare Products. Treat with care – Kids and OTC cough and cold medicines. http://www.otcsafety.org/Media/128696932677584054.pdf

6 United States Pharmacopeia. USP Quality Review. July 2004; No.80. URL: http://www.usp.org/pdf/EN/patientSafety/qr802004-07-01.pdf

7 Institute for Safe Medication Practices. List of Error-Prone Abbreviations, Symbols, and Dose Designations. 2007. URL: http://www.ismp.org/Tools/errorproneabbreviations.pdf

8 USP-NF Online – 8.240. Weights and Measures and 1221 General Information

9 FDA Consumer Magazine. Avoiding Problems: Liquid Medicines and Dosing Devices. October 1994

10 Litovitz T. Implication of Dispensing Cups in Dosing Errors and Pediatric Poisonings: a report from AAPCC. Annals of Pharmacotherapy 1992:26;917-18.

11 FDA Guidance for Industry Labeling OTC Human Drug Products — Questions and Answers. December 2008 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm078792.pdf

12 Federal register 21 CFR 201. FDA Over-The-Counter Human Drugs; Labeling Requirements. Final Rule. March 17, 1999 64:51. Example 2 and 3. Pg 13298 and 13299. http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Over-the-CounterOTCDrugs/StatusofOTCRulemakings/UCM106781.pdf