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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-1473]

Over-the-Counter Pediatric Oral Liquid Drug Products Containing Acetaminophen; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the availability of a guidance for industry entitled "Over-the-Counter Pediatric Oral Liquid Drug Products Containing Acetaminophen." The guidance is intended to help drug manufacturers, packagers, and labelers minimize the risk to consumers of acetaminophen-related liver damage associated with the use of nonprescription, also known as over-the-counter or OTC, pediatric oral liquid acetaminophen drug products. This guidance provides recommendations regarding acetaminophen concentration, container labels, carton labeling, and packaging of such products, as well as for any associated delivery devices. FDA's recommendations are designed to encourage safer use of these products by minimizing the potential for acetaminophen overdosing due to medication errors or accidental ingestion.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: Submit written requests for single copies of the guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001

New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

Submit electronic comments on the guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Alice Tu, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4325, Silver Spring, MD 20993-0002, 301-796-7586.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Over-the-Counter Pediatric Oral Liquid Drug Products Containing Acetaminophen." Acetaminophen is marketed in many OTC drug products as a pain reliever and fever reducer. Most OTC acetaminophen products are marketed under FDA's ongoing rulemaking to establish a final monograph for OTC internal analgesic, antipyretic, and antirheumatic (IAAA) drug products. These products must conform to the conditions described in FDA's Tentative Final Monograph for Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter (OTC) Human Use (the IAAA TFM)[1] and FDA's general regulations for OTC drug marketing (21 CFR 330.1) and labeling (21 CFR 330.10 and part 201). They also must be labeled with acetaminophen-related warnings and other information as specified in 21 CFR 201.326. However, OTC pediatric oral

[1] "Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use; Tentative Final Monograph," 53 FR 46204 (November 16, 1988). Available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Over-the-CounterOTCDrugs/StatusofOTCRulemakings/UCM078460.pdf.

liquid drug products containing acetaminophen have been associated with overdoses due to medication errors that resulted in serious adverse events, including severe liver damage and death. In particular, there have been reports of overdose attributed to confusion between concentrated acetaminophen drops (80 milligrams (mg)/0.8 milliliters (mL) and 80 mg/mL) and acetaminophen oral liquid (160 mg/5 mL).

This guidance document is part of FDA's ongoing initiative to reduce the risk of acetaminophen-related liver injury associated with all OTC and prescription acetaminophen-containing products. As part of that initiative, in June 2009, three FDA committees, the Drug Safety and Risk Management Advisory Committee, the Nonprescription Drugs Advisory Committee, and the Anesthetic and Life Support Drugs Advisory Committee, met jointly to consider a range of risk reduction measures. Among other measures, these Advisory Committees recommended moving to a single, standardized acetaminophen concentration for OTC pediatric oral liquid drug products because the availability of multiple concentrations causes confusion and errors among both consumers and health care professionals. In May 2011, FDA convened a joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee to discuss the use of acetaminophen in children. Shortly before the meeting, the Consumer Healthcare Products Association (CHPA) proposed to voluntarily phase out all of the existing single-ingredient concentrated drop formulations of the OTC, pediatric , oral, liquid acetaminophen drug products and market only the 160 mg/5 mL. At the Advisory Committee meeting, FDA took note of CHPA's voluntary transition to a single concentration of pediatric oral liquid acetaminophen.

In response to CHPA's voluntary transition to a single concentration of OTC oral liquid acetaminophen products, FDA published a Drug Safety Communication on December 22, 2011,

to inform the public of the 160 mg/5 mL concentration now marketed for children ages 2 to 3 years and to recommend that end users of the product read the Drug Facts label to identify the concentration of the oral liquid acetaminophen, dosage, and directions for use.

FDA issued the draft guidance on October 8, 2014 (79 FR 60854), to address ongoing concerns about the potential for acetaminophen overdose associated with these products and to encourage safer use. Comments on the draft guidance were considered while finalizing this guidance, which has been revised and clarified in some respects.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on addressing safety achieved through drug product design and labeling to minimize medication errors. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

III. Paperwork Reduction Act of 1995

This guidance refers to a previously approved collection of information found in FDA regulations. The collection of information is subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3520). The

collection of information referenced in this guidance that pertain to the format and content requirements for OTC drug product labeling (§ 201.66) have been approved under OMB control number 0910-0340. The labeling requirements in § 201.326 are not subject to review by OMB because they do not constitute a "collection of information" under the PRA. Rather, the labeling statements are a "public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public" (5 CFR 1320.3(c)(2)).

IV. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or http://www.regulations.gov.

Dated: July 30, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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