

Submitted electronically via www.regulations.gov

January 27, 2015

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

Re: Comments on the Draft Guidance for Industry - “Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions”. 79 Fed. Reg. 70879-70880 (November 28, 2014). Docket No. FDA-2014-D-1862

The Consumer Healthcare Products Association (CHPA¹) appreciates the opportunity to provide comments to the FDA in response to the November 28, 2014 Federal Register notice announcing the availability of draft guidance for industry “Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions”. CHPA and its member companies have an interest and expertise in acetaminophen-containing over-the-counter (OTC) products and support FDA’s efforts to improve the safe use of acetaminophen including efforts to enhance awareness of these rare but serious reactions.

In August 2013, following a review of adverse events in the FDA Adverse Event Reporting System database and the medical literature, FDA released a Drug Safety Communication noting that acetaminophen had been associated with a risk of rare but serious skin reactions. In late fall 2013 FDA required that manufacturers of OTC acetaminophen products marketed under a New Drug Application add a warning regarding serious skin reactions and noted that they would be encouraging manufacturers of drug products marketed under the monograph to do the same.

In a February 21, 2014 letter to FDA, CHPA noted that some members marketing acetaminophen-containing OTC products intended to add a warning regarding serious skin reactions to the *Drug Facts* panel. The Allergy alert warning proposed by CHPA at that time is identical to that provided in the current Draft Guidance.

CHPA’s comments on the Draft Guidance are organized into General Comments and more detailed comments on Section IV of the Draft Guidance.

¹ CHPA, founded in 1881, is a national trade association representing manufacturers and distributors of over-the-counter medicines and dietary supplements (chpa.org).

1. General Comment

- a) While we applaud FDA efforts to enhance the safe use of all OTC products, including those containing acetaminophen, we strongly encourage the agency to adopt the suggested changes through the rulemaking process. CHPA has previously submitted detailed comments supporting FDA's efforts to modernize the monograph system² and remains committed to working with the agency to ensure finalization of rulemaking proceedings on the remaining tentative final monographs.

CHPA and its members remain committed to providing adequate labeling on our OTC products to facilitate their safe and effective use. Since FDA has proposed specific new labeling outside of the conventional rule making, we interpret the Guidance as FDA's intention to exercise enforcement discretion regarding compliance to the relevant sections of the OTC drug labeling regulations.

2. Comments on Section IV (Example OTC Drug Facts Label With Recommended Warning)

- a) FDA notes in the Draft Guidance that the recommended Allergy alert warning should directly follow the Liver warning (21 CFR 201.326) (lines 87-89).³ This sequence appears to be inconsistent with the order set forth in 21 CFR 201.66(c)(5)(ii)(B) and (E) (Allergy alert followed by Liver warning). As such, we will proceed under the assumption that, for acetaminophen-containing products that do not contain aspirin, either approach to ordering the Liver warning and Allergy alert will be acceptable. CHPA members request clarification from the FDA on this approach to ordering under Warnings.

CHPA members also request that FDA provide an additional example of *Drug Facts* labeling for a product containing both acetaminophen and aspirin in order to highlight the difference in ordering of the "Allergy alert" and "Liver warning" statements for single ingredient acetaminophen products versus products containing both acetaminophen and aspirin.

- b) In the current Draft Guidance FDA has proposed the following formatting for the Allergy alert warning:

"Allergy alert: acetaminophen" (*lower case "a" in acetaminophen*)

This formatting is consistent with that provided in a 2013 FDA correspondence to holders of New Drug Applications for OTC acetaminophen-containing products. In contrast, FDA has previously provided a formatting example for an 'Allergy alert' warning in which the

² Comments of the Consumer Healthcare Products Association in Response to the Notice of Hearing on the Over-the-Counter Drug Monograph System (Docket No. FDA-2014-N-0202)

http://www.chpa.org/05_08_14_Monograph.aspx

³ As specified in an [April 29, 2009 Final Rule](#) (21 CFR 201.326), the "**Liver warning**" must be listed first under the Warnings heading. However, for products containing both acetaminophen and aspirin the "**Liver warning**" must appear after the "**Reye's syndrome**" and "**Allergy alert**" warnings.

ingredient name following ‘Allergy alert’ was capitalized.⁴ CHPA members are thus proceeding under the assumption that either approach (*i.e.*, Allergy alert: Acetaminophen ... or ... acetaminophen) will be acceptable. As such, we request clarification regarding this approach.

- c) As specified in the Tentative Final Monograph for Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for OTC Human Use (343.50 (c)(1)(ii)), acetaminophen-containing products labeled for the relief of sore throat pain must contain the following warning:

“Sore throat warning: If sore throat is severe, persists for more than 2 days, is accompanied or followed by fever, headache, rash, nausea, or vomiting, consult a doctor promptly.”

CHPA members are proceeding under the assumption that the “Sore throat warning” should be sequenced after the “Liver warning” and “Allergy alert”. CHPA members ask that FDA clarify the acceptability of this approach. In this regard, an example *Drug Facts* label (containing an Allergy alert warning, Liver warning and Sore throat warning) similar to the one included in the Draft Guidance would be helpful.

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

Respectfully submitted,



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⁴ In a [June 4, 2003 Proposed Rule](#) concerning OTC Internal Analgesic, Antipyretic, and Antirheumatic (IAAA) Drug Products, FDA recommended inclusion of a consistent allergy warning for OTC IAAA products containing nonsteroidal anti-inflammatory active ingredients. The following was proposed: “**Allergy alert:** [insert name of active ingredient (first letter of first word for ingredient in *uppercase*)]...” [emphasis added]