CHPA

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Michael S. Furness, Ph.D.
Director of the Division of
Nonprescription Regulation Development, ONP, CDER
Food and Drug Administration
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Re: Federal Register / Vol. 74, No. 81 / April 29, 2009 [pages 19385-19409] (Final rule) Organ-Specific Warnings; Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use; Final Monograph [21 CFR Part 201 / Docket No. FDA-1977-N-0013] -- **Clarification of Provisions in the Final Rule**

Dear Dr. Furness:

CHPA has formed an Internal Analgesics task group that is comprised of eleven member companies -- B.F. Ascher and Company, Bayer Consumer Care, Chattem, GlaxoSmithKline, Lil' Drug Store Products, McNeil Consumer Healthcare, Novartis Consumer Healthcare, Perrigo Company, The Procter & Gamble Company, Wyeth Consumer Health, and Schering-Plough HealthCare Products. To be able to execute the changes needed in full compliance with the final rule published in the April 29, 2009 Federal Register (FR), this CHPA task group seeks the agency's clarification of three provisions of the final rule.

1) Acetaminophen in multiple-ingredient products:
Under § 201.326(a)(1)(iii)(A), (iv)(A)(1), and (v)(A) the following liver warning is required: *"This product contains acetaminophen. Severe liver damage may occur if [bullet] ... takes more than [insert maximum daily dosage units] in 24 hours, which is the maximum daily amount."* [underlining added] Under FDA's tentative final monograph for OTC internal analgesics, the maximum daily amount of acetaminophen is 4 grams. For OTC single ingredient products containing acetaminophen, arriving at the maximum number of daily dosage units is easy and accurate: 8- 500 mg tablets, 12- 325 mg tablets, etc. For OTC combination products which contain the maximum single dose of acetaminophen, arriving at the maximum number of daily dosage units is similarly easy and accurate: 4- 1000 mg packets, 8- 500 mg tablets, etc. However, for OTC combination products which contain less that the maximum single dose of acetaminophen, the maximum number of daily dosage units to be taken under labeled directions for that particular product in a 24 hour period can yield considerably less than the maximum daily amount of acetaminophen. Because the phrase "which is the maximum daily amount" refers back to acetaminophen in the liver warning, this means that, taken at its most literal, the phrase "which is the maximum daily amount" is not accurate and could potentially lead to consumer confusion, that is, that a lower than a 4 gram dose of acetaminophen could cause severe liver damage (see Example below).

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Example:
There are multi-ingredient products containing acetaminophen 325 mg, guaifenesin 200 mg, and phenylephrine HCl 10 mg per tablet. The Directions section of such products states that 6 tablets are the maximum daily dose on the basis of the maximum recommended daily amount of phenylephrine HCl. The maximum daily dose of acetaminophen in these products is 1,950 mg, i.e. less than 50% of the maximum recommended daily amount of acetaminophen (4 grams per day). However, the liver warning would say "*This product contains acetaminophen. Severe liver damage may occur if [bullet] you take more than 6 tablets in 24 hours, which is the maximum daily amount.*"

This scenario is true for any multi-ingredient product formulated with the minimum amount of acetaminophen, but the maximum amount of another ingredient. CHPA requests that the agency consider whether such a warning statement is appropriate and accurate for combination products containing less that the maximum daily dose of acetaminophen. Phrasing of this warning statement will need to vary depending on the level of acetaminophen.

2) Blister packaging:
Under section III.C. - Immediate Container of the final rule in the third column on page 19389, it is stated: *If the immediate container of an OTC IAAA drug product is a blister pack, the labeling space may need to be expanded to accommodate these warnings along with other required labeling. We believe the need for these warnings justifies any expansion of the labeling space that may be necessary. Ideally, the blister pack should be designed so that the warnings can be read after removal of individual doses from the blister pack.* While not likely FDA's intent, this could reasonably be interpreted to require full warning language on each individual blister cell of the blister pack/card. CHPA requests the agency clarify that the full warning language is not required on each individual dose.

3) Other unit dose packaging:
Similar to Point 2 above, immediate containers such as stick packs and sachets present space limitations for labeling. These individual doses are unlikely to be taken from the outer carton until time of use. CHPA therefore requests the agency clarify that the full warning language is not required on each individual dose.

Many thanks in advance for your attention. Please do not hesitate to contact me, should you require any clarification.

Sincerely,

Barbara A Kochanowski

Barbara Kochanowski, Ph.D.
Vice President, Regulatory Affairs

cc: Charles Ganley, M.D., Director, Office of Nonprescription Products
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