

Docket No. 2004N-0454

BEFORE
THE UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

ADDITIONAL
COMMENTS OF THE
AMERICAN HERBAL PRODUCTS ASSOCIATION

ON THE FOOD AND DRUG ADMINISTRATION'S REQUEST FOR COMMENT ON

**FDA's PREMARKET NOTIFICATION PROGRAM FOR
NEW DIETARY INGREDIENTS**

February 24, 2005

The American Herbal Products Association (“AHPA”) filed comments to Docket 2004N-0454 on February 1, 2005 to address numerous issues related to the Food and Drug Administration’s (“FDA’s”, or “the Agency’s”) premarket notification program for new dietary ingredients (“NDIs”), and on the content and format requirements for NDI notifications made under the Federal Food, Drug and Cosmetic Act (“FFDCA” or “the Act”). AHPA now offers additional comments on one specific issue related to FDA’s NDI regulations.

It has come to AHPA’s attention that there may be some confusion as to which party is responsible for filing a notification with FDA in advance of marketing an NDI. These additional comments are therefore addressed to that specific issue.

Redundant notifications for the same NDI are not required

One of the ways that the Dietary Supplement Health and Education Act (DSHEA) amended the FFDCA was to establish that a dietary supplement that contains an NDI may be adulterated unless certain requirements are met. Of specific interest to these comments is the following:

“A dietary supplement which contains a new dietary ingredient shall be deemed adulterated under section 342(f) of this title unless it meets one of the following requirements:

- (1) The dietary supplement contains only dietary ingredients which have been present in the food supply as an article used for food in a form in which the food has not been chemically altered.
- (2) There is a history of use or other evidence of safety establishing that the dietary ingredient when used under the conditions recommended or suggested in the labeling of the dietary supplement will reasonably be expected to be safe and, at least 75 days before being introduced or delivered for introduction into interstate commerce, **the manufacturer or distributor of the dietary ingredient or dietary supplement** provides the Secretary with information, including any citation to published articles, which is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe” (emphasis added). 21 U.S.C. 350b(a).

As is evident from the bolded phrase in this amended section of the Act, either the manufacturer or distributor¹ of either the NDI or of the dietary supplement

¹ The term “distributor” is used by the industry in a manner that is similar to common use of that word, which describes a firm that serves as a wholesaler to store, transport, and supply goods manufactured or marketed by numerous other firms to retailers. AHPA does not believe that distributors should be or is likely to be the party

that contains the NDI must submit the required notification. It is equally clear that there is no need for more than one of these persons to submit a notification for the same NDI, so long as the information submitted by one of them serves as the basis for a conclusion that dietary supplements containing the NDI will reasonably be expected to be safe. The plain meaning of the cited statutory language is that some person, but not all persons, involved in the manufacture and distribution or marketing of an NDI or a dietary supplement containing the NDI must provide the required information to FDA at least 75 days prior to marketing any such dietary supplement.

An NDI notification by the manufacturer of the NDI may obviate the need for notifications by all marketers of dietary supplements containing the NDI

The firm that provides a premarket NDI notification to FDA must submit the information that is the basis for its conclusion that a *dietary supplement containing the NDI* will reasonably be expected to be safe under the conditions of use recommended or suggested in labeling. AHPA believes that, in many cases, and especially when the required notification is submitted by the manufacturer of the NDI, a reasonable expectation of safety is simultaneously established for numerous dietary supplements that may contain the NDI.

It is plausible that an NDI will be reasonably expected to be safe only up to a specific level, per serving dose and per day, and under specific conditions of use. At the same time, many NDIs will be reasonably expected to be safe over a range of serving and daily doses and conditions of use.

In submitting an NDI notification, a manufacturer or distributor or marketer is required to provide, among other things:

“A description of the dietary supplement **or dietary supplements** that contain the new dietary ingredient including:

- (i) The level of the new dietary ingredient in the dietary supplement;
- and
- (ii) The conditions of use recommended or suggested in the labeling of the dietary supplement, or if no conditions of use are recommended or

who is responsible for providing premarket notifications to FDA when they distribute (i.e., supply to retailers, store, or transport) NDIs or dietary ingredient supplements that contain NDIs. Rather, it is much more likely in the case of an NDI that the actual manufacturer of the NDI will bear this responsibility. Similarly, it is much more likely in the case of a dietary supplement that contains an NDI that either the actual manufacturer or the “marketer,” that is, the firm that places its brand and its company name on the retail package of the dietary supplement, of that dietary supplement will bear this responsibility. AHPA has therefore used the terms “distributor or marketer” and “distribution or marketing” throughout these comments. In addition, AHPA suggests that FDA define the terms “manufacturer” and “distributor” for purposes of the relevant regulation.

suggested in the labeling of the dietary supplement, the ordinary conditions of use of the supplement” (emphasis added). 21 CFR 190.6 (b)(3).

The obvious implication of the inclusion of the words emphasized above, that is, “or dietary supplements,” is that a single NDI notification may be submitted for more than one dietary supplement that contains the NDI that is the subject of the notification. AHPA believes this could be accomplished by describing the several dietary supplements as, for example, “dietary supplements that contain up to 100 mg per serving of the NDI; that are in the form of a capsule or tablet; and that are recommended to be used by adults over the age of 18 in a manner that limits daily consumption of the NDI to not more than 1,000 mg per day for up to 6 months.”

It is AHPA’s position that the NDI notification requirement will be satisfied for the entire range of dietary supplements that meet the parameters described in the example above, so long as the information that is provided with the notification is, in fact, the basis for the notifier’s determination that the range of defined dietary supplements are reasonably expected to be safe.

AHPA also believes that, when the manufacturer of an NDI submits a notification that describes the dietary supplement use of the NDI, then there is no need or requirement for a distributor or marketer of a dietary supplement that utilizes the NDI within the described parameters to submit an additional NDI notification. The relevant statutory language clearly intended, by its redundant use of the word “or,” that some person must provide the required information to FDA prior to marketing, but that there is no need for redundant submissions by, for example, both the manufacturer of the NDI and the marketer of a dietary supplement containing the NDI in the manner described in the notification submitted by the NDI manufacturer.

Based on the analysis set forth above, the following information from FDA’s website² entitled “New Dietary Ingredients in Dietary Supplements” is erroneous:

Who needs to submit a notification?

You must submit a premarket notification if you are a:

- manufacturer who intends to market a new dietary ingredient;
- manufacturer who intends to market a dietary supplement that contains a new dietary ingredient;
- distributor who intends to market a new dietary ingredient; or
- distributor who intends to market a dietary supplement that contains a new dietary ingredient.

² Accessed on February 17, 2005 at <http://www.cfsan.fda.gov/~dms/ds-ingrd.html>.

It is AHPA's position that it is not correct, for example, that the persons identified in the second, third and fourth bullet points need to file an NDI notification if the manufacturer of the NDI itself, as identified in the first bullet point, has submitted a notification for that NDI, so long as the parameters in that notification with regard to the level of the NDI and its conditions of use are met in those other persons' products. Similarly, it is not correct that the persons identified in the first three bullet points necessarily³ need to file an NDI notification if the distributor or marketer of a dietary supplement that contains an NDI, identified in the fourth bullet point, has submitted a notification for that NDI when contained in the marketed dietary supplement.

AHPA appreciates the opportunity to provide these additional comments to this important request for comments and information.

Sincerely,

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³ In this second example, the manufacture or distributor or marketer of a *different* dietary supplement that contains the NDI at a different level or for use under different conditions may be required to submit a separate notification. There is no requirement, however, for the manufacturer of the NDI to also file a notification for a specific dietary supplement use for the NDI if the manufacturer or distributor or marketer of that dietary supplement use of the NDI has filed a notification.