

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**

September 23, 2005

The American Herbal Products Association (“AHPA”) filed comments to Docket 2004N-0454 on February 1, 2005 and on February 24, 2005 to address numerous issues related to the Food and Drug Administration’s (“FDA’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. AHPA now offers additional comments on two specific and related issues that are relevant to FDA’s NDI regulations.

**Only one notification is needed for NDIs that are unprocessed botanicals**

It is reasonable to expect that NDIs will include ingredients that are unprocessed herbs or other botanicals that were not marketed in the United States prior to October 15, 1995 and that are not articles that 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. Such unprocessed herbal NDIs would therefore be subject to the notification requirements set forth in 21 CFR §190.6. Such unprocessed herbal NDIs might include, for example, roots; barks; leaves; flowers; seeds; fungal fruiting bodies or fungal mycelium; and other plant parts, or might consist of a species of algae. The meaning intended here by “unprocessed” is to describe botanical ingredients that have been subjected to only minimal post-harvest processing, limited to cleaning, dehydration, and size reduction.

It is AHPA’s position that the NDI notification requirement set forth in 21 CFR §190.6 for any NDI that is an unprocessed herb or other botanical, as described above, is satisfied by the first complete notification submitted for that NDI, and that there should be no requirement for any other distributor of exactly the same raw botanical NDI that has been subjected to the same or significantly similar minimal post-harvest processing, who will market the NDI with the same recommended or suggested conditions in dietary supplements that will contain the NDI, to submit a separate notification.

AHPA’s position is based on the realization that the NDI regulations require submission of evidence of safety, consisting of either the history of use or other evidence of safety, that establishes 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. Once this requirement is satisfied there is no rational reason to require that it be satisfied by all subsequent marketers of the exact same unprocessed herb or other botanical.

**Each manufacturer of a “semi-purified extract” of an herbal NDI should submit a separate notification**

It is also reasonable to expect that NDIs will include ingredients that are extracts of herbs or other botanicals that were not marketed in the United States prior to October 15, 1995, and that such extracts are not articles that 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. Such herbal extract NDIs would therefore be subject to the notification requirements set forth in 21 CFR §190.6.

In prior communications to this docket, AHPA has identified publications that have been produced by our association and its members, including a document titled *Guidance for Manufacture and Sale of Bulk Botanical Extracts* (“the AHPA Extract Guidance”),<sup>1</sup> that was incorporated by reference in our comments to this docket dated February 1, 2005, and another document titled *Standardization of Botanical Products: White Paper* (“the AHPA Standardization White Paper”),<sup>2</sup> sections 4, 5, and 7 of which were similarly incorporated by reference.

The AHPA Extract Guidance, among other things, differentiates between “traditional-style extracts” and “semi-purified extracts.”<sup>3</sup> Both the AHPA Extract Guidance and the AHPA Standardization White Paper identify “traditional-style extracts,” which are manufactured using common, uncomplicated technologies and typically comprise a broad spectrum of the native plant constituents; and “semi-purified” extracts, in which a relatively narrow spectrum of the native botanical constituents are highly concentrated, often using modern technologies such as selective solvents or preparative chromatography.

As a general rule, semi-purified extracts are unique to a particular manufacturer. Even preparations which are nominally the same can vary considerably between manufacturers. Thus, for example, a “*Magnolia officinalis* bark powdered extract containing 50% honokiol” made by one manufacturer may be significantly different than that made by a second manufacturer, because the unique manufacturing process used by each manufacturer can cause significant differences in the unidentified remainder of the extract (i.e. the 50% which is not honokiol). In one manufacturer’s product the remaining 50% may be filler; for another manufacturer it may be a second quantified magnolia-bark constituent such

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<sup>1</sup> Eisner, S., managing editor. 2001. *The American Herbal Products Association’s Guidance for Manufacture and Sale of Bulk Botanical Extracts*. Silver Spring, MD: AHPA.

<sup>2</sup> AHPA Botanical Extracts Committee. 2003. *The American Herbal Products Association’s Standardization of Botanical Products: White Paper*. Silver Spring, MD: AHPA.

<sup>3</sup> *Ibid*, page 12.

as magnolol; from a third manufacturer it may be a mixture of other magnolia-bark constituents which are not quantified and quite possibly are not even identified.

It is AHPA's position that each manufacturer of a "semi-purified extract" of a new herbal dietary ingredient, as such term is defined in the above cited AHPA documents, must file a separate notification. Because each manufacturer may produce a semi-purified extract by their own proprietary process, and because the end product of separate proprietary processes for extraction of the same new herbal ingredient may result in significantly different end products, it should be assumed that the information that serves as a basis for a conclusion that one such end product will be reasonably expected to be safe may not be relevant to an evaluation of whether another such end product will be reasonably expected to be safe, even though it is derived from the same herb or other botanical, and even if both products are recommended for the same or similar conditions of use. It is on this basis that AHPA has arrived at its position that each manufacturer of such semi-purified extracts should each submit an NDI notification with the requisite safety information.

AHPA is aware, in submitting these comments, that the comment period for this docket has been closed for many months. Nevertheless, we trust that FDA will consider these comments as the process of reviewing the regulations for new dietary ingredients goes forward.

Sincerely,

/s/

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