CHPA CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
founded 1881

December 4, 2017

VIA ELECTRONIC SUBMISSION

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

Re: Development of a List of pre-Dietary Supplement Health and Education Act Dietary Ingredients; Public Meeting; Request for Comments, 82 Fed. Reg. 42098 (Sept. 6, 2017), Docket No. FDA-2017-N-4625

Herein, the Consumer Healthcare Products Association (CHPA), the 136-year-old trade association representing U.S. manufacturers and distributors of over-the-counter (OTC) medicines and dietary supplements (chpa.org), provides feedback on the Food and Drug Administration's (FDA) proposed development of an authorized list of pre-Dietary Supplement Health and Education Act (DSHEA) dietary ingredients. Many of our member companies market dietary supplement products and we appreciate the opportunity to comment as the FDA determines whether to move forward with the development of such a list. CHPA applauds FDA's public stakeholder outreach as they seek to develop and implement a process that will both meaningfully permit safe dietary ingredients that have been marketed for decades to remain on the market, and reduce the associated burdens on industry and the agency associated with the preparation and review of New Dietary Ingredient (NDI) notifications.

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A. EVIDENCE SUPPORTING pre-DSHEA MARKETING OF A DIETARY INGREDIENT

1. Background

Section 413(c) of the Food, Drug and Cosmetic Act (FDCA) exempts from the NDI submission process "any dietary ingredient which was marketed in the United States before October 15, 1994." These ingredients have typically been referred to as "old dietary ingredients" and may be marketed in dietary supplements without submission of a notification to FDA. Despite the submission of a proposed list of old dietary ingredients by several dietary supplement trade associations following the passage of DSHEA, FDA has not recognized an authoritative list of dietary ingredients considered to be marketed prior to October 15, 1994.

Below we provide our recommendations regarding development of the process used to establish marketing of a dietary ingredient (in a dietary supplement) prior to October 15, 1994. These comments include recommendations for the allowable types of evidence to demonstrate marketing; the composition of the Review Panel responsible for reviewing the evidence; the proposed public process for reviewing evidence associated with the marketing of a dietary ingredient prior to October 15, 1994; and the format of an online list of pre-DSHEA ingredients to be maintained by FDA. As stakeholders in this process, we encourage the agency to develop a process allowing for the transparent evaluation of evidence associated with the marketing of a dietary ingredient prior to October 15, 1994.

At the outset of this process, we recognize and embrace the need to ensure the marketing of safe dietary supplements. However, as a prerequisite for the development of a meaningful list of pre-DSHEA ingredients, FDA must recognize the inherent difficulties associated with establishing evidence for the marketing of a dietary ingredient more than 23 years ago and incorporate flexibility into any review process that is implemented. Similarly, FDA should recognize that information concerning the manufacturing process used to produce a dietary ingredient should have no bearing on whether that ingredient was ***marketed*** prior to October 15, 1994.

CHPA member companies are committed to manufacturing and marketing safe dietary supplement products in accordance with all applicable laws and implementing regulations. We do not envision adoption of an authorized list of pre-DSHEA ingredients as an effort to avoid any aspect associated with the marketing of safe products. We do agree with the agency that this process could have benefit

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for both industry and the FDA. However, our members remain supportive of the need to evaluate and understand the safety of a dietary ingredient prior to its marketing in a dietary supplement.

2. Types and Quantity of Evidence Demonstrating pre-DSHEA Marketing

As a first step in this process, FDA must clarify the amount and type of evidence needed to establish proof of *marketing* of a dietary ingredient prior to October 15, 1994. As we have previously outlined in our 2016 comments to the agency on the New Dietary Ingredient Guidance, we believe a single sales brochure or advertisement may definitively demonstrate the "marketing of the ingredient" in the U.S. We again urge FDA to expand their proposed list of individual pieces of evidence that can be relied upon to confirm pre-DSHEA marketing status to include Certificates of Analysis and affidavits attesting to the existence of Certificates of Analysis as acceptable, in recognition of the fact that such documents may contain trade secret information.

We also propose that FDA include the *Herbs of Commerce* as sufficient documentation of pre-1994 marketing, provided that the plant part is specified in the listing. We also ask that FDA acknowledge that each individual piece of evidence would definitively establish the ingredient as a pre-DSHEA ingredient. In addition, when a marketed product is discussed in a pre-DSHEA journal, magazine or newspaper article, book, patent, or OTC Physicians' Desk Reference, such references should be permitted as definitive evidence of pre-DSHEA marketing status provided that sufficient detail is included. For instance, reference books such as "Edible Wild Plants" or 'Back to Eden', discussed at the October 3, 2017 Public Meeting could be a possible source of documentation. Clearly defining the amount and type of evidence required to demonstrate pre-DSHEA marketing will facilitate evaluation by the Joint Panel and expedite the creation of an authoritative list.

3. Consideration of Probiotic Ingredients

CHPA is supportive of oral comments made by the International Probiotics Association (IPA) at the October 3, 2017 public meeting recognizing that probiotics have been safely consumed for many years and that the health benefits of these products are well-known. As with other dietary supplement products, probiotics are held to the same standards for manufacturing and safety. Modern science now allows probiotics to be characterized at the strain level, something that was not available back in 1994. Although FDA does not currently require manufacturers to label probiotic products at the strain level,

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CHPA does have a voluntary guideline covering dietary supplement probiotic products and recommends that members provide strain level information. We recommend that the process for evaluating probiotics focus on inclusion of those species marketed prior to October 15, 1994 and that all strains of those species should be included.[1] As with all other types of dietary ingredients, we understand the need for probiotic manufacturers to ensure that products meet the established standards of identity and safety.

As we will discuss below for other types of dietary ingredients, we recommend that FDA focus solely on the demonstrated marketing of a probiotic ingredient to determine inclusion on a pre-DSHEA list. Changes in the manufacturing process for a probiotic (*e.g.*, use of a different fermentation media) should have no bearing on the pre-DSHEA status of an ingredient again with the understanding that the manufacturer has data establishing the safety of the ingredient for use.

4. Manufacturing changes/Chemical alteration

The definition of a dietary ingredient in Section 413(d) of the FDCA is based solely on whether the ingredient was marketed prior to October 15, 1994. Not included in that definition is information about the ingredient's physicochemical structure, purity, biological properties, serving level, and/or source. In establishing an authoritative list of pre-DSHEA ingredients, FDA must recognize that the manufacturing processes used to produce a grandfathered ingredient should have no bearing on whether an ingredient was marketed (*i.e.*, "grandfathered") nor should changes to the manufacturing process alter the pre-DSHEA status of an ingredient. Advances in manufacturing processes and any associated change to such processes, are only relevant to the extent that they change the safety profile of the grandfathered ingredient.

The safety of dietary ingredients and the dietary supplements containing them marketed prior to October 15, 1994 is critically important. In a 2014 Guidance,[2] FDA articulated a policy to address postmarketing safety issues resulting from changes to manufacturing processes for food ingredients and food contact substances. The Guidance includes a procedure for evaluating whether changes in manufacturing methods would alter the safety profile of an ingredient. This type of approach could be

[1] See International Probiotics Association comments to 2016 FDA Guidance for a complete list of species
[2] "Assessing the Effects of Significant Manufacturing Process Changes, Including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that Are Color Additives" (June 2014)

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applied to pre-DSHEA ingredients. Rather than requiring industry to provide manufacturing information that is likely unavailable, FDA should rely on the safety provisions in Section 402(f) of the FFDCA to ensure the safety of dietary supplement products. As stated earlier, information regarding the manufacturing of a dietary ingredient is not a requirement to demonstrate pre-DSHEA marketing. This is determined solely on the basis of evidence that the ingredient was marketed prior to October 15, 1994.

B. PROCESS FOR DEVELOPMENT OF A LIST OF pre-DSHEA DIETARY INGREDIENTS

As noted during the October 3, 2017 public meeting, CHPA is supportive of FDA efforts to develop an authoritative list of pre-DSHEA list. We feel that this successful implementation of this process could create meaningful benefit to industry by providing clarity surrounding the status of dietary ingredients and whether an NDI notification is required. The agency could also benefit through allowance of greater efforts towards other more pressing issues such as enforcement.

Shortly after passage of DSHEA, several of the dietary supplement trade associations (American Herbal Products Association, Council for Responsible Nutrition, National Nutritional Foods Association and the Utah Natural Products Alliance) compiled a list of dietary ingredients that were considered likely marketed when DSHEA was passed. A comprehensive list was finalized and submitted to FDA in September, 1997. FDA later rejected the existence of an authoritative list of "old dietary ingredients" stating in 2011 that "Each supplement manufacturer or distributor is responsible for establishing that the dietary ingredients in its dietary supplements comply with the NDI notification requirements".

Although FDA has rejected this as a list of "old dietary ingredients" we do recommend that FDA use this list as a basis for establishing enforcement discretion at the beginning of this process for the purpose of determining an ingredients status. FDA noted at the October 3, 2017 public meeting that the list that they envision "would be authoritative, but it won't be comprehensive". Thus, an ingredient could still be a pre-DSHEA ingredient despite the fact that it isn't included on the list developed by this process. For this reason, we ask that the agency exercise enforcement discretion on an updated version of this list.

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1. Overview

An outline of key considerations for the pre-DSHEA ingredient review process is provided below. Detail on each of the individual steps is included in greater detail below this bulleted list.

- FDA should convene a Review Panel consisting of 7 individuals (3 scientists designated by industry, 3 designated by FDA and 1 by agreement with the other 6 panelists)
- The evidence necessary to establish that a dietary ingredient was marketed in the United States prior to October 15, 1994 will be established in advance of the first panel meeting.
- A list of dietary ingredients should be assembled for review by the panel based on submissions by ingredient suppliers/manufacturers/others (first-come, first-served).
- The panel would review the evidence pertaining to the marketing of a dietary ingredient in a dietary supplement prior to October 15, 1994 and issue one of two decisions:

  that the ingredient has been confirmed as a pre-DSHEA dietary ingredient subject to section 413 (c) ["An ODI"], or

  that there is either: (a) inadequate evidence to establish that the ingredient was marketed in the United States prior to October 15, 1994; or (b) that there are sufficient safety issues under section 402 (f) to prevent the further marketing of the product.

- FDA would publish notice of the review panel consideration of each dietary ingredient in the Federal Register, with a 45 day comment period allotted. Public comment would be invited with respect to all dietary ingredient considerations by the panel.
- Until a final determination concerning the marketing status of a dietary ingredient is made (*i.e.*, whether or not the ingredient would be included on the pre-DSHEA list), FDA should permit the marketing of that dietary ingredient.
- We ask that FDA issue a Notice of Enforcement Discretion to be applied to those dietary ingredients *likely to have been marketed* pre-DSHEA (based on a modified version of the list previously submitted to the agency by several trade associations) until a final determination regarding the ingredient's status is made.
- If a marketer of a dietary ingredient objects to a negative finding by the Review Panel, that determination can be appealed to a Federal District Court utilizing a de novo review standard (pursuant to FDCA §402(f)).
- Industry should also be provided time to address a finding of insufficient evidence for marketing

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2. Review Panel Composition and Role

The convening of a panel to review material in support of pre-DSHEA marketing of a dietary ingredient is a critical step in this process. We recommend that the panel be composed of a total of seven individuals with no conflicts of interest. At a minimum, it would be helpful for these individuals to have some experience pertinent to dietary supplement and/or dietary ingredient manufacturing or marketing. However, provided a rigorous process is implemented in regard to the types of allowed evidence and its assessment, we do not foresee the need to restrict panel participation to only those individuals within a certain discipline or possessing a particular experience level. Given that the panel is only reviewing documents to determine whether a dietary ingredient was marketed prior to October 15, 1994 we expect the process to be relatively straightforward.

We recommend that the composition of the panel include three representatives from FDA (chosen according to internal FDA procedures), three representatives from industry without conflicts of interest (such as a financial interest in the outcome of deliberations) and one individual chosen based on unanimous agreement among the other six panelists (FDA and industry). Procedures addressing potential conflicts of interest outlined in a recent FDA draft guidance could be used as a guide.[3]

While we support the ability of any interested party to submit the name of a qualified person to serve on the panel, to streamline the process, we envision industry trade associations jointly submitting to FDA the names of qualified individuals for potential participation on the review panel. Information supporting the nominees' qualifications for participation would be included (*e.g.*, curriculum vitae) as well as a signed statement noting that the nominee appears to have no conflict of interest precluding membership on the panel. FDA would be responsible for choosing the three industry representatives from among the names of those submitted.

The final panel member would be chosen following a joint consultation among the 3 FDA and 3 industry panel members. This member would be chosen based on unanimous support. To maintain consistency in the process, CHPA believes that a single panel should be responsible for reviewing all dietary ingredients submitted for evaluation of pre-DSHEA marketing.

[3] FDA Draft Guidance, Best Practices for Convening a GRAS Panel: Guidance for Industry, November 2017

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3. Process for Nominating Ingredients

The process used to determine which proposed pre-DSHEA dietary ingredients are reviewed to determine their status must be non-biased. CHPA believes that the most efficient way to initiate this process would be through individual companies nominating their dietary ingredients for evaluation on a first-come first-served basis. While this could initially be accomplished through publication of a notice in the Federal Register, we recommend that FDA develop a website to facilitate requests for review as part of creating the authorized list of pre-DSHEA dietary ingredients. We are also aware that the Natural Products Association (formerly the National Nutritional Foods Association) has a list of over 1,800 ingredients for which evidence of marketing prior to October 15, 1994 is available. We propose that this list could also be part of any initial review by the panel.

4. Format of the Final pre-DSHEA List

FDA should maintain a publicly available online database of those dietary ingredients determined by the Review Panel to be "pre-DSHEA ingredients". We recommend that this list be descriptive to the extent that it is relevant to the listing of the dietary ingredient as being marketed prior to October 15, 1994. We recommend that the list include the name of the dietary ingredient and its' status. As noted above, we also believe FDA should develop an online process allowing for nomination of dietary ingredients for review.

CHPA also agrees with the comments made by the Council for Responsible Nutrition at the October 3, 2017 public meeting regarding the expansion of the list to include ingredients in the food supply rather than simply looking for evidence of marketing in (or as) a dietary supplement prior to October 15, 1994. As an example, this could include ingredients contained in the Everything Added to Food in the United States list,[4] food ingredients that are the subject of a Generally Recognized As Safe (GRAS) notice,[5] or substances on the Food Additive Status list.[6]

[4] https://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm115326.htm
[5] https://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices
[6] https://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm091048.htm

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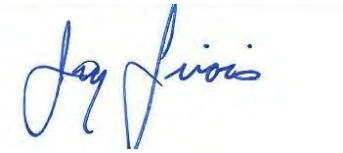
CHPA and our member companies marketing dietary supplement products appreciate the opportunity to comment on this process. Should you have any questions, please do not hesitate to contact me.

Regards,



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