Docket No. FDA–2022-D-0281

BEFORE

THE UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

COMMENTS OF THE

AMERICAN HERBAL PRODUCTS ASSOCIATION

ON

DRAFT GUIDANCE FOR INDUSTRY: POLICY REGARDING CERTAIN NEW DIETARY INGREDIENTS AND DIETARY SUPPLEMENTS SUBJECT TO THE REQUIREMENT FOR PRE-MARKET NOTIFICATION

July 19, 2022

Prefatory remarks

The American Herbal Products Association (AHPA) is the national trade association and voice of the herbal products industry. AHPA members include domestic and foreign companies doing business as growers, importers, processors, manufacturers, and marketers of herbs and herbal products. AHPA serves its members by promoting the responsible commerce of products that contain herbs, including conventional human foods, dietary supplements, health and beauty products, animal products, and other products.

The Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Dietary Supplement Health and Education Act (DSHEA), establishes certain definitions and requirements for new dietary ingredients (NDIs) for implementation by the U.S. Food and Drug Administration (FDA or the agency). Among these requirements, section 413(a) of the Act (21 U.S.C. § 350b(a)) deems a dietary supplement containing an NDI "adulterated" under section 402(f) (21 U.S.C. § 342(f)) of the act unless either:

> "(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." [or]
>
> "(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."

This latter paragraph describes the requirement for a premarket safety notification for a new dietary ingredient (NDIN), and issues related to both paragraphs remain subjects of longstanding discussions between FDA and stakeholders.

On May 20, 2022, the agency issued a Federal Register notice announcing the availability of a draft guidance, "Policy Regarding Certain New Dietary Ingredients and

Dietary Supplements Subject to the Requirement for Pre-market Notification"[1] (the May 20 draft guidance). Upon finalization, this draft guidance would offer a 180-day period of enforcement discretion for the NDIN submission requirement in certain circumstances. Specifically, a firm that did not submit a required NDIN could do so without penalty during this period, provided the firm can demonstrate that the subject product "was marketed in the United States as of May 20, 2022."

Comments on the May 20 draft guidance

AHPA supports FDA's proposal to offer a period of enforcement discretion for late submission of NDINs. AHPA further appreciates the flexibility that the agency has shown in proposing to accept postmarket safety data in NDINs submitted via this route. AHPA has some optimism that issuance of a final version of the May 20 draft guidance may result in the submission of at least some NDINs that the agency may not have otherwise received. AHPA nonetheless has some specific recommendations for revising the May 20 draft guidance, as articulated in this section of these comments.

The May 20 draft guidance states that FDA "estimate[s] that more than 4,600 notifications should have been submitted and were not." In attempting to justify this number, the agency refers to the transcript of a public meeting[2] in which Steven Tave, then the director of the FDA Office of Dietary Supplement Programs, posits this number as an "assumption," a supposition ("let's suppose"), and a simple assertion ("we'll say"). Estimates are generally made with reference to some source of evidence from the environment, but the 4,600 value is explicitly not based on any assessment justifying its inclusion in an FDA guidance document.

AHPA has no alternative basis to assess the scope of late NDINs, but, at root, an "estimation" is not necessary to support the purposes of the May 20 draft guidance, and the agency should not include an unsupported assumption as an "estimate" of unsubmitted but required NDINs in any final guidance. AHPA therefore requests that any such quantitative estimate be removed from this guidance.

[1] 87 Fed. Reg. 30,843 (May 20, 2022).

[2] Transcript, FDA Public Meeting on Responsible Innovation in Dietary Supplements (May 16, 2019).

The May 20 draft guidance also states that the agency will confirm receipt of an NDIN within 75 days of the agency's receipt but further states that the agency does not "anticipate being able to complete [its] scientific evaluation and provide a response within 75 days…". As NDINs submitted under the proposed enforcement discretion policy would inherently cover products already on the market, public health considerations would demand timely review of and responses to these submissions. AHPA therefore requests that FDA deploy the appropriate resources to ensure that it substantively responds to all NDINs, including those submitted pursuant to any finalized version of the May 20 draft guidance, within 75 days.

The May 20 draft guidance encourages firms to submit late NDIN submissions via the CFSAN Online Submission Module (COSM). While the agency acknowledges that companies may alternately submit NDINs in physical media and paper forms, the draft guidance does not provide the current address at which CFSAN accepts such submissions. Rather, it directs the reader to FDA's website for this information. AHPA encourages FDA to include an accurate address for NDIN submission in any final guidance, particularly since the address listed in 21 C.F.R. § 190.6(a) is no longer fully accurate.

Additional NDI guidance and enforcement are needed

On January 31, 2022, FDA released a list of foods program guidance under priority development during 2022 and issued an updated list of these priorities on June 30, 2022. These communications record the agency's intention to issue further guidance addressing "NDI notification procedures and timeframes" before the end of this year. AHPA looks forward to the issuance of such guidance and notes that guidance addressing outstanding questions about the NDIN process may increase the number and quality of required NDIN filings that the agency receives. In the event that FDA issues such guidance prior to the finalization of the May 20 draft guidance, the number and quality of late NDINs submitted during the period of enforcement discretion may likewise increase. AHPA therefore encourages FDA to prioritize the issuance of such additional guidance documents before finalizing the May 20 draft guidance and formally starting the clock on the enforcement discretion period.

In selecting topics for further NDIN guidance, AHPA encourages the agency to focus on the development of draft guidance targeted specifically to issues and elements of the NDIN process that concern companies likely to consider filing NDINs.

In this regard, AHPA requests that FDA prioritize issuance of standalone guidance on NDI identity issues. Based on a review of past agency NDIN responses, AHPA finds that FDA's assertion that an NDIN includes inadequate information on identity is among the most commonly cited reasons for FDA's identification of "significant concerns" regarding an NDIN.

When FDA raises concerns in its responses to NDINs about characterization of ingredient identity, the agency also commonly raises concerns about inadequate information on ingredient and product specifications as well as documentation of compliance with the applicable current good manufacturing practice regulations at 21 C.F.R. Part 111. For this reason, AHPA also requests that FDA prioritize the issuance of standalone guidance documents addressing these topics.

As other stakeholders have commented, FDA has not enforced the NDIN submission requirements to a degree sufficient to deter noncompliance and incentivize compliance. This concern appears most pronounced in situations where one manufacturer or distributor of an NDI makes the substantial investment to prepare and file a high-quality NDIN submission, but competitors marketing similar (but likely not identically produced[3]) NDIs do not. In such circumstances, FDA should prioritize compliance assessments[4] and, where appropriate, enforcement actions against firms that flout the law and inappropriately seek to rely on competitors' NDINs. FDA should include such a commitment in any final version of the May 20 draft guidance. Doing so would further the goals of the guidance, increase incentives for compliance, protect compliant firms' investments in preparing and submitting high-quality NDINs, and deter firms from seeking to inappropriately profit from marketing so-called "knock off" ingredients that likely have not undergone required FDA safety reviews.

[3] Given FDA's redactions of confidential commercial and trade secret information from publicly released versions of NDINs, competitors seeking to piggyback on a submitter's NDIN and market products covered by it generally cannot ensure identical production solely from reliance on and review of redacted NDINs released by the agency.

[4] For the avoidance of doubt, AHPA does not advocate that FDA seek to enforce against every non-submitting marketer of an ingredient for which another party files an NDIN. This reflects how, in numerous instances, firms have submitted NDINs for ingredients that do not actually qualify as NDIs and how FDA typically does not address the NDI status of ingredients when reviewing NDINs.

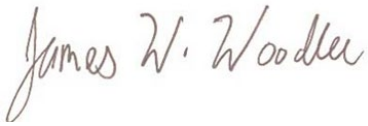
Conclusion

AHPA greatly appreciates the opportunity to present comments on the May 20 draft guidance. AHPA staff and counsel will make themselves available at any mutually convenient time to further address any of the topics addressed herein. If FDA requires clarification or additional discussion on any of the issues raised in these comments, please feel free to contact us.

Respectfully submitted,

Michael McGuffin
President, American Herbal Products Association
mmcguffin@ahpa.org

Robert Marriott
Director of Regulatory Affairs, American Herbal Products Association
rmarriott@ahpa.org



James W. Woodlee
Kleinfeld, Kaplan and Becker, LLP
General Counsel, American Herbal Products Association
wwoodlee@kkblaw.com