

**Docket No. FDA-2019-N-1388**

**BEFORE**

**THE UNITED STATES FOOD AND DRUG ADMINISTRATION**

**COMMENTS OF THE**

**AMERICAN HERBAL PRODUCTS ASSOCIATION**

**ON**

**RESPONSIBLE INNOVATION IN DIETARY SUPPLEMENTS**

**July 15, 2019**

# Table of Contents

<b>Prefatory remarks .....</b>	<b>1</b>
<b>Issues related to new dietary ingredient notifications.....</b>	<b>2</b>
FDA should issue targeted guidance on key NDIN subjects rather than issuing a third draft of its comprehensive Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry .....	4
FDA should issue targeted guidance on the subject of ingredient identification in an NDIN	5
FDA should issue targeted guidance to clarify an optional process for submitting a “master file” in relation to an NDIN .....	6
FDA should issue targeted guidance to assist NDIN submitters in describing broad conditions of use for the subject NDIs.....	7
FDA should improve enforcement against NDI “knock-offs” .....	8
<b>FDA should revisit its guidance on dietary supplement claims to harmonize with FTC on “traditional use” claims .....</b>	<b>10</b>
<b>FDA should revise its interpretation of 21 U.S.C. § 321(ff)(3)(B).....</b>	<b>12</b>
<b>FDA should complete rulemaking to define the terms “natural” and “healthy” to support responsible innovation .....</b>	<b>14</b>
<b>Concluding statement .....</b>	<b>16</b>

## **Prefatory remarks**

On April 11, 2019, the Food and Drug Administration (FDA or the Agency) issued a Federal Register notice (the April 11 Notice<sup>1</sup>) in which the Agency announced a public meeting scheduled on May 16, 2019 entitled “Responsible Innovation in Dietary Supplements” (the May 16 Public Meeting).

The April 11 Notice stated the purpose of the May 16 Public Meeting as “to give interested parties an opportunity to present ideas for facilitating responsible innovation in the dietary supplement industry while preserving and strengthening FDA’s ability to efficiently and effectively protect the public from unsafe and unlawful products,” and “to provide interested parties an opportunity to discuss various issues related to responsible innovation in dietary supplements.” The Agency went on to identify four such topics:

- 1) The scope of the phrase “dietary substance for use by man to supplement the diet by increasing the total dietary intake,” as used in [the Dietary Supplement Health and Education Act or] DSHEA (section 201(ff)(1)(E) of the [Federal Food, Drug, and Cosmetic Act]);
- 2) Understanding exceptions to the requirement for premarket notification [for new dietary ingredients], and evaluating whether and how growth in the marketplace since 1994 has altered the impact of those provisions;
- 3) Potential commercial or marketing advantages to incentivize responsible innovation; and
- 4) Promoting overall compliance with the premarket notification requirement through enforcement.

The April 11 Notice also announced the Agency’s establishment of a docket for public comments on the May 16 Public Meeting and also invited public input “about whether and how we should adjust our current dietary supplement regulatory approach to better allow for innovation and growth in the dietary supplement marketplace while maintaining and strengthening our ability to efficiently and effectively evaluate product safety and protect the public health.”

---

<sup>1</sup> 84 Fed. Reg. 14,660 (April 11, 2019).

The American Herbal Products Association (AHPA) is the national trade association and voice of the herbal products industry. AHPA is comprised of domestic and foreign companies doing business as growers, collectors, processors, manufacturers, marketers, importers, exporters and distributors of herbs and herbal products. AHPA’s members include many companies that market dietary supplements (as well as herbal products marketed as foods, cosmetics, and occasionally as nonprescription drugs or in other product categories), and therefore have an interest in the subject of the April 11 Notice.

These comments are therefore submitted on behalf of AHPA and its members. These comments provide several suggestions that AHPA believes are consistent with the intention of the April 11 Notice to gather ideas to facilitate responsible innovation in the dietary supplement industry while preserving and strengthening FDA’s ability to efficiently and effectively protect the public from unsafe and unlawful products.

### **Issues related to new dietary ingredient notifications**

The Food, Drug and Cosmetic Act (FD&CA) defines the term “new dietary ingredient” (NDI) to mean “a dietary ingredient that was not marketed in the United States before October 15, 1994 and does not include any dietary ingredient which was marketed in the United States before October 15, 1994.”<sup>2</sup> The FD&CA requires that manufacturers and distributors who wish to market a dietary supplement that contains an NDI submit a notification to FDA about this ingredient to provide information “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” under the conditions of use recommended or suggested in the labeling.<sup>3</sup> There is an exception to this NDI notification (NDIN) requirement if the NDI is “an article used for food in a form in which the food has not been chemically altered.”<sup>4</sup>

FDA issued draft guidance for industry on two occasions, initially in July 2011 (the 2011 Draft NDI Guidance) and subsequently in revised form in August 2016 (the 2016

---

<sup>2</sup> 21 U.S.C. § 350b(d).

<sup>3</sup> 21 U.S.C. § 350b(a)(2).

<sup>4</sup> 21 U.S.C. § 350b(a)(1).

Revised Draft NDI Guidance). The Agency described these documents as issued “to assist industry in deciding when a premarket safety notification for a dietary supplement containing a new dietary ingredient (NDI) is necessary and in preparing premarket safety notifications,”<sup>5</sup> and “to help manufacturers and distributors of dietary ingredients and dietary supplements ... decide whether to submit a premarket safety notification to FDA ... for a product that is or contains an NDI [and] to help [such manufacturers and distributors] to prepare NDI notifications that [FDA] will be able to review more efficiently and respond to more quickly.”<sup>6</sup>

AHPA submitted extensive comments to both the 2011 Draft NDI Guidance<sup>7</sup> and to the 2016 Revised Draft NDI Guidance.<sup>8</sup> AHPA also submitted in April 2013 separate follow-up comments to the 2011 Draft NDI Guidance to propose that the Agency issue draft guidance on the narrow issue of accurate identification of an NDI in an NDIN (the AHPA 2013 Follow-up Comments).<sup>9</sup>

Availability of new ingredients is essential to innovation in the dietary supplement market, and the robust operation of the regulatory framework that governs NDIs is essential to responsible innovation. There are varying views as to how well this regulatory framework has functioned over the past twenty-five years, and there exist significant differences of opinion on what is needed to best enforce the NDI provisions of the FD&CA. But there is general agreement from all quarters that improvement is needed in the systems that have been established to implement these provisions.

---

<sup>5</sup> Guidance for Industry - Dietary Supplements: New Dietary Ingredient Notifications and Related Issues. July 2011. Docket No. FDA–2011–D–0376.

<sup>6</sup> Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry. August 2016. Docket No. FDA–2011–D–0376.

<sup>7</sup> December 2, 2011. Comments of the American Herbal Products Association on Draft Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues. Docket No. FDA–2011–D–0376.

<sup>8</sup> December 12, 2016. Comments of the American Herbal Products Association on Draft Guidance for Industry (August 2016); Dietary Supplements: New Dietary Ingredient Notifications and Related Issues. Docket No. FDA–2011–D–0376.

<sup>9</sup> April 27, 2013. Follow-up Comments of the American Herbal Products Association on Draft Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues Specific to Guidance Needed on Identification of a New Dietary Ingredient. Docket No. FDA–2011–D–0376.

AHPA therefore offers the following suggestions for improving the NDI notification process and presents each of these in the spirit of supporting responsible innovation in dietary supplements with no diminution of FDA’s ability to efficiently and effectively protect the public from unsafe and unlawful products.

***FDA should issue targeted guidance on key NDIN subjects rather than issuing a third draft of its comprehensive Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry***

In the AHPA 2013 Follow-up Comments, AHPA observed that its review of NDIN records to that time indicated that the most common objection communicated by FDA in its responses to NDINs is that the Agency “is unable to establish the identity” of the dietary ingredient that is the subject of the notification. These comments therefore identified ingredient identification in NDINs as an issue on which guidance is needed, and thus AHPA urged FDA to prioritize issuing guidance on this issue. These comments also included a proposed draft of guidance specific to the ingredient-identity issue for the Agency’s consideration.

AHPA has observed in comments submitted by other trade associations representing the dietary supplement trade in response to the 2016 Revised Draft NDI Guidance a similar suggestion for FDA to issue targeted or separate guidance on specific topics relevant to NDI notifications.<sup>10</sup> In addition, AHPA has recently been informed by other such trade associations of their interest in the concept of having FDA consider issuance of NDI guidance in a targeted manner by focusing on specific NDI-related subjects as priorities. AHPA suggests three such priorities below. Further, AHPA suggests that, in identifying other such priorities, FDA focus on non-controversial issues, rather than on legal interpretations, and seek to identify either topics where greater clarity is needed, as evidenced by specific trends from FDA’s review of NDINs submitted to date, or topics that may directly support innovation.

In suggesting that FDA focus on “non-controversial issues, rather than on legal interpretations,” AHPA recommends that FDA refrain from prioritizing presentations in NDI guidance of its interpretations and opinions on such issues as, for example,

---

<sup>10</sup> For example, the Natural Products Association (NPA) requested in its comments that FDA provide a separate guidance on what is required when submitting an NDI Master File. December 12, 2016. NPA to FDA’s Division of Dockets Management (HFA-305). RE: Docket Number FDA-2011-D-0376; Draft Guidance for Industry: “Dietary Supplements: New Dietary Ingredient Notifications and Related Issues”; 81 Federal Register 53486-53490 (12 August 2016).

the following: when an NDIN is required; whether synthesized constituents of botanicals meet one or another clause of 21 U.S.C. § 321(ff)(1); when a minor change in manufacturing for an old dietary ingredient renders the ingredient an NDI. Stated another way, AHPA recommends that the Agency provide specific guidance to companies that have already decided to submit an NDIN to assist such firms in preparing submissions that meet the Agency’s expectations for compliance.

AHPA believes FDA can support responsible innovation in dietary supplements with no diminution of FDA’s ability to efficiently and effectively protect the public from unsafe and unlawful products by providing good guidance to support those manufacturers and distributors of NDIs and supplements that contain NDIs who have already determined that the innovative ingredient they want to market is, in fact, an NDI that may require submission of an NDIN.

***FDA should issue targeted guidance on the subject of ingredient identification in an NDIN***

In the intervening six years since AHPA’s submission of the AHPA 2013 Follow-up Comments to the 2011 Draft NDI Guidance, FDA has continued to observe lack of information on ingredient identity as a common flaw in NDINs. AHPA therefore incorporates by reference the AHPA 2013 Follow-up Comments and restates here the requests contained therein.

Specifically, AHPA recommends that FDA issue the “DRAFT Guidance for Industry: Information to be included in an NDI notification to identify the new dietary ingredient” included in the AHPA 2013 Follow-up Comments, or significantly similar draft guidance. AHPA prepared this draft primarily by revising Section VI.A. of the 2011 Draft NDI Guidance to more closely focus on information needed to provide an accurate description of an ingredient that is the subject of an NDIN. AHPA recognizes and expects that issuance by FDA of this or any similar revised guidance on information to be included in an NDIN to identify the new dietary ingredient will be subject to additional public comments.

To the degree that responsible innovation for dietary supplements is dependent on the marketing of NDIs, and recognizing that incomplete descriptions of the identity of an NDI in a submitted NDIN is a hindrance to bringing NDIs to market, AHPA

believes FDA can support responsible innovation in dietary supplements with no diminution of (and in fact, in furtherance of) FDA’s ability to efficiently and effectively protect the public from unsafe and unlawful products by providing good guidance on how best to identify an NDI within a submitted NDIN.

***FDA should issue targeted guidance to clarify an optional process for submitting a “master file” in relation to an NDIN***

In the 2016 Revised Draft NDI Guidance, FDA introduced the idea of optional use of a confidential “NDI master file” that would contain information needed to completely describe a dietary ingredient that is the subject of an NDIN. As presented in that Draft:

“You may also submit a confidential ‘NDI master file’ to FDA which contains the manufacturing, specifications and other identity information needed to completely describe the ingredient. You may incorporate by reference the contents of the master file into an NDI notification. You may also authorize other firms to reference the contents of the master file in notifications describing the ingredient they obtain from you. FDA expects that most submitters will identify the contents of NDI master files and ingredient specifications as trade secrets ... and will only discuss them with the firm which submitted them.”

AHPA encourages FDA to establish use of an NDI master file as one option that can help provide an efficient path to compliance for responsible companies and, significantly, also protect the intellectual property of those investing in costly safety studies and interpretive reports. Importantly, FDA should make clear that all safety data submitted in an NDI master file, including unpublished studies, will be considered trade secret information pursuant to 21 C.F.R. § 20.61(a) and therefore remain undisclosed except as directed by the original NDIN submitter.

AHPA believes establishment of a clear mechanism for an NDI master file will support responsible innovation in dietary supplements with no diminution of FDA’s ability to efficiently and effectively protect the public from unsafe and unlawful products. Developers of NDIs may view this process as protective of their intellectual property and of the financial investment needed to produce an NDI and

develop the safety record needed to bring new and innovative dietary ingredients to market.

AHPA therefore encourages FDA to issue separate and targeted guidance on this topic. In so doing, the Agency should provide clear directions for a manufacturer or distributor of an NDI to utilize a master file as an efficient option in submitting a required notification.

***FDA should issue targeted guidance to assist NDIN submitters in describing broad conditions of use for the subject NDIs***

AHPA recommends that FDA prepare and issue guidance to assist manufacturers or distributors of dietary ingredients in preparing NDINs that contain general descriptions of the many dietary supplements that may contain an NDI to comply with 21 C.F.R. § 190.6(b)(3). Such guidance should provide specific recommendations for the manufacturers or distributors of an NDI to provide in their NDIN broad descriptions of all of the dietary supplements that will include or may include the NDI, so long as the information submitted provides the basis for the submitter's conclusion that the dietary supplements containing the NDI will be reasonably expected to be safe. Such targeted guidance may include instructions or other information on use of a master file in support of broad use of an NDI (or reference the Agency's separate targeted guidance on use of master files if that is issued prior) but must also clarify that the same goal of meeting the NDIN obligation for a range of supplements that contain the NDI can be accomplished without a master file if that is a submitting firm's preference.

For example, an NDI notification could reasonably describe dietary supplements that may contain the NDI to be marketed "in the form of a tablet, capsule, softgel, gelcap, powder, or liquid," as long as the information that is the basis of the NDI manufacturer's or distributor's conclusion that the dietary supplements containing the NDI will reasonably be expected to be safe applies to each of these forms.

Similarly, an NDI notification could reasonably describe dietary supplements that may contain the NDI to be "formulated to contain the NDI as the sole dietary ingredient, or to contain one or more additional dietary ingredients," as long as the information submitted provides the basis of the NDI manufacturer's or distributor's

conclusion that dietary supplements containing the NDI will reasonably be expected to be safe applies to all such described dietary supplement products.

AHPA's recommendation here relies on the central tenet that, except in rare and unlikely circumstances, combining safe food ingredients (or dietary ingredients) will with near certainty produce safe foods (or dietary supplements). AHPA acknowledges that elements of the 2016 Revised Draft NDI Guidance appeared to take contrary positions, although comment #E1 of AHPA's comments to that Draft addressed these contrary points. AHPA therefore incorporates by reference comment #E1 of its comments to the 2016 Revised Draft NDI Guidance.

FDA's issuing clear guidance that facilitates providing general descriptions of the many dietary supplements that may contain the NDI that is the subject of the NDIN, as requested here, will support responsible innovation in dietary supplements with no diminution of FDA's ability to efficiently and effectively protect the public from unsafe and unlawful products. Responsible innovation will be enhanced when the ingredient manufacturers that develop NDIs find these ingredients to be attractive to a large number of potential finished supplement brand partners, as would be the case if the submitted NDIN identifies a range of possible products in the description of the dietary supplements that will contain the NDI and demonstrates the basis on which the manufacturer has concluded that all such described dietary supplements will reasonably be expected to be safe.

AHPA therefore recommends FDA issue separate and targeted guidance to assist manufacturers and distributors of NDIs to submit their required notifications in a manner that broadly describes the dietary supplements that will or may contain the identified NDI to include all product forms and formulations for which the submitted information supports a reasonable expectation of safety.

***FDA should improve enforcement against NDI "knock-offs"***

The supplement industry has encountered instances in which a company develops a proprietary or otherwise complex NDI and submits the required NDIN only to soon find itself competing with another company claiming to offer the exact same ingredient but who has not submitted an NDIN for its version of the ingredient. In these circumstances, detailed information on the specific identity of or manufacturing processes used to produce the NDI have likely been redacted from

the public version of the NDIN on the basis that this information qualifies as confidential commercial information or a trade secret. The absence of publicly available information on the precise identity of and manufacturing methods used to produce such an NDI raises legitimate questions about whether another company who has not filed its own NDIN can lawfully rely on an NDIN previously submitted by another company for a proprietary or otherwise complex NDI. In other words, without access to this redacted information, a company seeking to rely on another company's previously submitted NDIN may lack the ability to demonstrate that its ingredient is in fact the same ingredient as covered by the NDIN or that the evidence of safety submitted in the NDIN applies to the ingredient offered by the company claiming reliance on the first submitted NDIN.<sup>11</sup>

It does not appear that, to date, FDA has taken consistent action to ensure that companies claiming reliance on third-party NDINs to market complex NDIs can demonstrate that their ingredients are identical to (and, as appropriate, produced using manufacturing methods identical to those used to produce) NDIs subject to such third-party NDINs. This apparent inaction has likely decreased incentives for companies to submit NDINs in order to bring NDIs to market. Consistently instituting such efforts and, as warranted, enforcing the NDIN requirements against firms who cannot demonstrate the appropriateness of their reliance on third-party NDINs would likely increase incentives for companies to submit NDINs. Under these circumstances, firms would have greater confidence that competitors would not inappropriately profit from their investments in making such NDIN submissions.

AHPA therefore requests that FDA develop a mechanism to enforce the NDIN requirements against dietary ingredient manufacturers or distributors marketing such “knock-off NDIs” without submitting a notification and when, due to public unavailability of information on the precise identity and manufacturing methods used to produce a proprietary or otherwise complex NDI subject to a third-party NDIN, such firms cannot demonstrate that an existing NDIN actually applies to their versions of the subject ingredient. However, in enforcing the NDIN requirements as

---

<sup>11</sup> In describing the NDIs relevant to this specific comment as “proprietary or otherwise complex” AHPA is intentionally differentiating such ingredients from ingredients that are identified as NDIs through the NDIN process but that may be simple ingredients, such as a dehydrated plant part or a simple water or ethanolic extract of a botanical ingredient. For such a simple ingredient, if in fact an NDI, it may well be that one NDIN that provides the required safety information will serve as the basis for a conclusion that the ingredient is reasonably expected to be safe when used under the conditions identified in the original NDIN, irrespective of the identity of the manufacturer or distributor of the ingredient.

proposed here, FDA should first ensure that the ingredient that is the subject of the notification is, in fact, actually an NDI to which the NDIN requirements apply.<sup>12</sup>

Responsible dietary ingredient companies submit NDINs to meet their requirements under the FD&CA and make significant financial investments to do so. Active enforcement by FDA would provide a commercial advantage to responsible and compliant marketers of NDIs and so would support responsible innovation in dietary supplements.

### **FDA should revisit its guidance on dietary supplement claims to harmonize with FTC on “traditional use” claims**

FDA in 2009 issued final guidance for industry intended to describe the amount, type, and quality of evidence FDA recommends a manufacturer have to substantiate a claim made for a dietary supplement under section 403(r)(6) of the FD&CA (the 2009 Claims Guidance).<sup>13</sup> This document “describes criteria to be considered in evaluating the nature of the claim and the amount, type, and quality of evidence in support of the claim,” and in it FDA provides several examples of “claims that might be made for a dietary supplement.”

FDA acknowledges in the 2009 Claims Guidance that the Federal Trade Commission (FTC) has primary jurisdiction over advertisements for dietary supplements; notes that FTC typically applies a substantiation standard of “competent and reliable evidence” to dietary supplement claims; and states it “intends to apply a standard for the substantiation of dietary supplement claims that is consistent with the FTC approach.” In discussing this FTC substantiation standard, FDA cites guidance issued by FTC in

---

<sup>12</sup> In reviewing NDIN records, AHPA finds numerous submissions for ingredients that are not actually NDIs, including many which are, in fact, rather common dietary ingredients that existed in the market prior to October 15, 1994; examples include food grade phosphoric acid and matcha tea (from *Camellia sinensis* (L.) Kuntze). In initiating the enforcement requested in this comment, the Agency will therefore need to evaluate whether an ingredient subject to an NDIN is actually an NDI in order to avoid inadvertently incentivizing any party to submit an NDIN for the purpose of seeking to inappropriately cast other firms formulating products with that ingredient as in violation of the NDIN requirements or asserting some claimed proprietary interest in the ingredient.

<sup>13</sup> FDA. Office of Dietary Supplement Programs. January 2009. Guidance for Industry: Substantiation for Dietary Supplement Claims Made Under Section 403(r) (6) of the Federal Food, Drug, and Cosmetic Act – Final. Docket No. FDA-2004-D-0303.

its 2001 publication, *Dietary Supplements: An Advertising Guide for Industry* (the *FTC Advertising Guide*)<sup>14</sup> wherein FTC defines competent and reliable evidence as:

“...tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.”

Of additional interest, though not mentioned in FDA’s 2009 Claims Guidance, is that the *FTC Advertising Guide* explicitly addresses the issue of traditional use claims made for dietary supplements. Specifically, FTC suggests that, even when marketers lack otherwise-required scientific evidence demonstrating a particular benefit for which a product has been historically or traditionally used (e.g., supporting digestion), marketers may lawfully describe historical or traditional uses of products “in such a way that consumers understand that the sole basis for the claim is a history of use of the product for a particular purpose.” The *FTC Advertising Guide* provides meaningful guidance to firms that wish to market dietary supplements with traditional use claims by, for example: indicating that such firms may need to qualify these claims to ensure that consumers understand when marketers base these claims only on historical or traditional use; explaining when traditional use evidence alone would be inadequate (e.g., noting that an advertiser “should not suggest, either directly or indirectly, that a supplement product will provide a disease benefit unless there is competent and reliable scientific evidence to substantiate that benefit”); and identifying specific requirements for substantiating traditional use claims (e.g., “The advertiser should also make sure that it can document the extent and manner of historical use and be careful not to overstate such use [and] make sure that the product it is marketing is consistent with the product as traditionally administered.”).

AHPA requests here that FDA revise its 2009 Claims Guidance to harmonize with FTC’s guidance on making traditional use claims for dietary supplements, as expressed in the *FTC Advertising Guide*. More specifically, AHPA requests that the Agency identify criteria that would support a truthful and nonmisleading claim for a supplement based on traditional use through reliance on clear evidence of traditional

---

<sup>14</sup> FTC. Bureau of Consumer Protection. April 2001. *Dietary Supplements: An Advertising Guide for Industry*.

use, as documented by contemporary and historical authoritative references, and recognition that such evidence is, in fact, competent and reliable.

In undertaking such an effort AHPA further recommends FDA review and evaluate how FTC addresses the issue of traditional use claims in the FTC Advertising Guide and consider that agency's policies for such claims (e.g., FTC's recommendation that marketers basing claims solely on evidence of traditional use present them in a manner that ensures consumers understand this point). AHPA also suggests that the Agency review regulations and guidance now in place in several other countries that support truthful use of traditional use claims for products that would qualify as dietary supplements if marketed in the U.S., including Canada, Australia, and the European Union.

In summary, AHPA requests that FDA revise its 2009 Claims Guidance's discussion of traditional use claims to clarify how traditional use claims can be made based on documented historical use, provided that consumers' understanding of the basis of such claims is clear. AHPA firmly believes that such a revision in FDA's position would support responsible innovation in dietary supplements as more supplement marketers would use the revised guidance requested here to bring accurately labeled and traditionally used products to the market. Establishment of clear guidance on use of substantiated traditional use claims for dietary supplements would also preserve and strengthen FDA's ability to efficiently and effectively enforce the substantiation requirements for such claims by setting a clear standard for their appropriate use. Doing so would also harmonize FDA's policies with FTC's.

### **FDA should revise its interpretation of 21 U.S.C. § 321(ff)(3)(B)**

The dietary supplement "drug exclusion clause", 21 U.S.C. § 321(ff)(3)(B) states that a dietary supplement does not include:

- “(i) an article that is approved as a new drug under section 505, certified as an antibiotic under section 507, or licensed as a biologic under section 351 of the Public Health Service Act (42 U.S.C. 262), or
- “(ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public,

“which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary’s discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter.”

In the 2016 Revised Draft NDI Guidance, FDA suggests that the date before which a substance needed to have been marketed in a food or dietary supplement is the date that an investigational new drug application (IND) for the article went into effect. This interpretation of the statute stifles dietary supplement innovation and cannot appropriately reflect Congressional intent. For example, under FDA’s interpretation, a dietary supplement manufacturer could develop and market a product in compliance with the FD&CA while the existence of an IND is maintained by FDA and the IND sponsor as confidential. Upon the publication of information about substantial clinical investigations conducted under the previously confidential IND, FDA could assert that the manufacturer may no longer market the product as a dietary supplement because the company introduced the product after the effective date of the previously confidential IND. This interpretation disincentivizes dietary supplement innovation because it leaves dietary supplement firms vulnerable to total or substantial losses of their investments in innovative ingredients when, unbeknownst to them, drug developers submit confidential INDs for the same articles at some point prior

Proper statutory construction and fairness demand that, for the drug exclusion rule to be triggered, all three elements noted above (effective IND, substantial clinical investigations, and publication of their existence) must occur and that the date by which a food or dietary supplement must be marketed to avoid this exclusion is the date on which the drug developer has satisfied all three conditions (and not merely the date on which the confidential IND took effect). FDA’s interpretation does not give full effect to the three elements in 21 U.S.C. § 321(ff)(3)(B)(ii).

Instead, FDA’s interpretation puts dietary supplement innovators at complete risk of having their investment in ingredient development rendered valueless to them, including as a result of abuse of this provision by drug developers. For example, a firm could obtain an IND authorization and hold its drug development program in abeyance until a dietary supplement ingredient and a market for the ingredient are developed by other parties. Then clinical studies could be undertaken and published, thus rendering the dietary supplement ingredient unlawful because it was not marketed in food or dietary supplements prior to the confidential date of the IND’s authorization. As a

result, the drug developer may then capitalize on the dietary supplement market developed for the ingredient when introducing a drug product containing it, even if necessarily marketed with different intended uses and claims than the previously marketed dietary supplement product.

While this provision was intended to preserve appropriate incentives for new drug developers, FDA’s interpretation has inappropriately transformed these incentives into protections for the drug industry to the detriment of dietary supplement innovation in a manner that Congress could not have contemplated. AHPA therefore urges FDA to revise its prior interpretation as described above.

### **FDA should complete rulemaking to define the terms “natural” and “healthy” to support responsible innovation**

On November 12, 2015 FDA issued a Federal Register notice in which it reported opening of a docket to receive information and comments on use of the term “natural” in the context of food labeling.<sup>15</sup>

AHPA submitted comments in May 2016 to the above-referenced docket<sup>16</sup> (the AHPA 2016 “Natural” Comments) that, in summary, expressed support for FDA’s conducting rulemaking to define the term “natural” when used on the labeling of human food products, and to also consider defining additional terms, such as “100% natural” or “made with natural [named ingredient(s)]” if such additional terms would contribute to consumers’ understanding of particular desirable or sought-after qualities of a food. AHPA’s comments also suggested that the Agency may need to adopt regulations to establish conditions that must be met for a food to be labeled as “natural,” “100% natural,” “made with natural [named ingredient(s)],” and any other such “natural”-related terms as may come to be defined.

AHPA hereby incorporates by reference into the present comments the AHPA 2016 “Natural” Comments on the subject of use of the term “natural” in the context of food (including dietary supplement) labeling.

---

<sup>15</sup> 80 Fed. Reg. 69,905 (Nov. 12, 2015); Docket No. FDA–2014–N–1207.

<sup>16</sup> May 10, 2016. Comments of the American Herbal Products Association on Use of the Term “Natural” in the Labeling of Human Food Products. Docket No. FDA–2014–N–1207.

Also, on September 28, 2016, FDA published a Federal Register notice in which the Agency invited comments on the term “healthy” as a nutrient content claim in the context of food labeling, and FDA reported that a variety of stakeholders had requested that the Agency update nutrition labeling regulations for nutrient content and health claims, including the implied nutrient content claim “healthy.”<sup>17</sup>

AHPA also submitted comments, in April 2017, to the above-referenced notice<sup>18</sup> (the AHPA 2017 “Healthy” Comments). In these comments AHPA expressed support for FDA’s stated intention to exercise enforcement discretion, until such time as the Agency amends 21 C.F.R. § 101.65(d)(2), with respect to some of the existing criteria for the implied nutrient content claim “healthy” if the alternative nutrient criteria described in a “Healthy” Guidance issued by FDA at the same time the Agency issued its Federal Register notice on this topic.<sup>19</sup> AHPA’s comments also encouraged the Agency to promptly amend 21 C.F.R. § 101.65(d)(2).

AHPA hereby incorporates by reference into the present comments the AHPA 2017 “Healthy” Comments on the subject of use of the term “healthy” in the context of food (including dietary supplement) labeling.

Almost certainly many dietary supplement ingredients, including for example herbs and simple herbal extracts, would meet definitions for “natural” and for “healthy” that are based on the plain meanings of those terms. Defining these terms and establishing clear regulatory criteria that must be met to use these terms in dietary supplement labeling would support responsible innovation for products that are, in fact, natural and healthy, and may motivate supplement companies to produce and market dietary ingredients and supplements that meet such definitions.

As one example, marketers of herbal teas sold and labeled as dietary supplements would likely be motivated to engage in responsible innovation by meeting a regulatory requirement to make an implied nutrient content claim, such as, “unsweetened tea is part of a healthy diet.” Such a statement on a product label would be consistent with a

---

<sup>17</sup> 81 Fed. Reg. 66,562 (Sept. 28, 2016); Docket No. FDA–2016–D–2335.

<sup>18</sup> May 10, 2016. Comments of the American Herbal Products Association on Use of the Term “Natural” in the Labeling of Human Food Products. Docket No. FDA–2016–D–2335.

<sup>19</sup> FDA CFSAN. September 2016. Use of the Term “Healthy” in the Labeling of Human Food Products: Guidance for Industry.

recommendation in the February 2015 *Scientific Report of the Dietary Guidelines Advisory Committee*, which suggests that “added sugars should be reduced in the diet and not replaced with low-calorie sweeteners, but rather with healthy options, such as water in place of sugar-sweetened beverages.” AHPA believes that another legitimate option to sugar-sweetened beverages would be unsweetened teas, including black and green teas and herbal teas, and believes again that companies that market teas would be motivated to provide healthier options if regulations allowed a “healthy” claim for such products.

AHPA therefore reasserts the points made in both the AHPA 2016 “Natural” Comments and the AHPA 2017 “Healthy” Comments in the current context of responsible innovation in dietary supplements, and AHPA requests anew that FDA complete rulemaking to (1) define the term “natural” and associated terms (e.g., “100% natural” or “made with natural [named ingredient(s)]”) when used on the labeling of human food products; and (2) amend 21 C.F.R. § 101.65(d)(2) to clarify the regulation for use of the term “healthy” as an implied nutrient content claim in the context of food labeling.

With regard to the above request for the Agency to complete rulemaking to define the term “natural” in the context of food labeling, AHPA notes that Australia’s Therapeutic Goods Administration (TGA) quite recently issued revised guidance on the use of “natural” and related claims when advertising therapeutic goods products to the public.<sup>20</sup> Note that many of the oral dosage products included in Australia’s definition of “therapeutic goods” also meet the U.S. definition of a dietary supplement under the FD&CA (as long as drug claims allowed in Australia are not associated with these products when marketed in the U.S.), such that this guidance may be directly relevant to FDA’s consideration of rulemaking in this matter.

## **Concluding statement**

AHPA’s comments here recommend several specific actions that FDA could take to support responsible innovation in dietary supplements while preserving and strengthening FDA’s ability to efficiently and effectively protect the public from unsafe

---

<sup>20</sup> Australian Government. Department of Health. Therapeutic Goods Administration. 11 June 2019. Therapeutic goods advertising: Ensuring 'natural' claims are not misleading. Accessed on July 15, 2019 at <https://www.tga.gov.au/therapeutic-goods-advertising-ensuring-natural-claims-are-not-misleading>.

and unlawful products. In AHPA's understanding, several of these recommendations are within the Agency's current authority such that no action would be required by the U.S. Congress to implement them.

AHPA appreciates the opportunity to present comments on this matter and welcomes any questions that may arise from AHPA's comments.

Respectfully submitted,



Michael McGuffin  
President, American Herbal Products Association  
8630 Fenton Street, Suite 918, Silver Spring, MD 20910  
(301) 588-1171 x201 / mmcguffin@ahpa.org

*James W. Woodlee*

Will Woodlee  
General Counsel, American Herbal Products Association  
Kleinfeld, Kaplan, & Becker, LLP  
1850 M Street, NW – Suite 800, Washington, DC 20036  
(202) 223-5120 / wwoodlee@kkblaw.com