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

Re: FDA-2011-D-0376
Dietary Supplements: New Dietary Ingredient Notifications and Related Issues; Revised Draft Guidance for Industry; Extension of Comment Period
[81 *Federal Register* 68434; October 4, 2016]

Dear Madam or Sir:

The American Botanical Council (ABC) is submitting the following comments in response to the U.S. Food and Drug Administration's (FDA) issuance of a revised draft guidance for industry titled, "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues" (2016 draft guidance).[1]

ABC is an independent, tax-exempt, nonprofit research and education organization that promotes the responsible use of herbal medicine based on scientific and clinical research and a rational interpretation of traditional use. Its members include medicinal plant and natural product researchers; educators; health care professionals; members of the herb, tea, dietary supplement, food, and cosmetic industries; the media; consumers; and other parties interested in medicinal plant and related research. Operating under §501(c)(3) of the Internal Revenue Code, ABC does not in any manner engage in lobbying activities. ABC publishes the quarterly peer-reviewed journal *HerbalGram* as well as other publications on scientific and clinical research, quality control, and other topics in the medicinal plant and herbal products domain.

Per FDA's notice in the *Federal Register*,[2] FDA is accepting comments on any portion of the 2016 draft guidance and is in particular looking for comment on the following: (1) what processes alter the identity of an ingredient marketed prior to October 15, 1994, that ultimately create a new dietary ingredient (NDI); (2) what processes "chemically alter" an ingredient under the Federal Food, Drug, and Cosmetic Act (FDCA) §413(a)(1), 21 U.S.C. § 350b(a)(1), and examples of processes that do not "chemically alter" an ingredient; and (3) how to develop an authoritative list of "grandfathered" ingredients — dietary ingredients that were marketed prior to October 15, 1994.

After careful review of the revised 2016 draft guidance and in light of the above FDA request, ABC respectfully submits the following comments for FDA's consideration.

ABC believes in the importance of fully implementing the provisions of

the Dietary Supplement Health and Education Act of 1994 (DSHEA)[3] as dietary supplements play an integral role in the public's well-being. DSHEA was passed by Congress with a clear objective to empower consumers with choices about their individual health care decisions, to ensure consumers have continued access to safe supplements, and to ensure FDA has the authority to take action against products that are unsafe or adulterated.[4] These founding premises of DSHEA — coupled with the express language of the NDI provision,[5] specifically that the NDI will "reasonably be expected to be safe"[6] — should be the guiding principles in developing and implementing the NDI provisions of the law.

ABC recognizes that FDA's issuance of the NDI guidance document was intended to clarify FDA's current thinking on the NDI provisions of the law with the goal of improving the quality of dietary ingredients and dietary supplements in the marketplace and addressing safety concerns that have been raised. However, ABC believes the 2016 draft guidance as currently drafted exceeds the agency's statutory authority and is inconsistent with congressional intent in passing DSHEA. ABC also believes that the 2016 draft guidance is indicative of the significant gap between industry's understanding of what is required under DSHEA — specifically, the NDI provision — and how FDA interprets the statutory requirements.

Throughout ABC's 28-year history, ABC has fully supported and continues to actively take measures to increase the quality of botanical products in the marketplace. One such undertaking is ABC's Ginseng Evaluation Program that ABC launched in 1993. Through this program, ABC developed a robust laboratory analytical method for the testing of Asian ginseng (*Panax ginseng*) and American ginseng (*P. quinquefolius*) raw materials, extracts, and finished products. The program involved the testing of hundreds of ginseng products sold in North America to determine their authenticity. In 2010 ABC initiated and currently manages the ABC-AHP-NCNPR Botanical Adulterants Program (http://cms.herbalgram.org/BAP/index.html), an international consortium dedicated to researching and educating on problems in the global supply chain of botanical raw materials, extracts, and essential oils. Program partners are the nonprofit American Herbal Pharmacopoeia (AHP) and the National Center for Natural Product Research (NCNPR) at the University of Mississippi, the FDA-funded Center of Excellence in the area of botanical ingredient and finished product analysis. The Botanical Adulterants Program is designed to inform botanical and natural product industry members and other relevant stakeholders about potential and confirmed adulteration of certain botanical ingredients. Another example of ABC's efforts to increase the quality of botanical-based products is the development of a technical reference book on solvents that are utilized in the preparation of botanical extracts used in the food, dietary supplement, drug, and cosmetic industries. ABC is in the final stages and anticipates publication of the book in 2017.[7]

Even though FDA states that an alternative approach to satisfy the NDI requirements other than what is indicated in the 2016 draft guidance may be used — and, per FDA regulations, a guidance document does not impose new legal or regulatory requirements and is not binding on either the agency or regulated industry — ABC believes that an FDA guidance document sets a precedent and important guardrails to industry, regulators, and the private plaintiffs' bar. Therefore, ABC urges FDA to revise the 2016 draft guidance to be more closely aligned with the initial intent of Congress in passing DSHEA.[8]

ABC first addresses FDA's specific areas of inquiry, then outlines ABC's additional considerations.

1. **In direct response to FDA's specifically noted areas of inquiry in the August 2016 *Federal Register* notice[9] (as paraphrased by ABC in sections "a", "b", and "c", below), ABC offers its comments:**

A. What processes alter the identity of an ingredient that was marketed prior to October 15, 1994, that ultimately create an NDI? FDA is especially interested in recommendations for clearer examples or criteria to differentiate changes in manufacturing methods and starting materials that alter the identity of the ingredient from changes that do not.

ABC contends that this analysis should be done by the manufacturer (or the agency when evaluating a product, e.g., during an inspection or review of an NDI notification [NDIN]) on a case-by-case basis, and based on the chemical composition of the ingredient rather than the choice of a particular manufacturing process. A change in a manufacturing process may not necessarily, in and of itself, be a trigger that would create an NDI. The critical considerations are the chemical composition and safety profile of the ingredient. A few examples — as especially related to botanicals — are provided below to offer instruction on manufacturing processes that may or may not alter the identity of an ingredient to the degree that a new dietary ingredient is created.

i. Changes in a manufacturing process that *do not* result in an NDI:
   1. A change in the blending ratio of raw materials. Due to variation in growing conditions, for example, lot-to-lot variations in contents of a particular constituent or constituent group may be balanced by mixing the lots at various ratios. This type of mixing is widely used to provide ingredients with a defined content of specific constituents (e.g., the standardization of ginkgo [*Ginkgo biloba*] leaf extracts to comprise 24% flavonol glycosides and 6% terpene lactones), and is not a manufacturing process change that impacts the safety of the finished ingredient or product.
   2. The addition of a step exposing an ingredient to dry heat over a short period of time may not alter the identity of an ingredient but may make it safer due to the reduction of the microbial load.
   3. The addition of an approved antioxidant such as ascorbic acid or tocopherol is not likely to alter the chemical composition of the dietary ingredient but may extend its shelf-life.

ii. Changes in a manufacturing process that *do* result in a NDI: Material changes in an extraction process and/or solvent of an ingredient already in the food supply that has a significant impact on the resultant chemical profile of the extract, i.e., other than relatively modest variations in the ratios (fingerprint) of chemical constituents already found in the grandfathered extracts of the same material (see "b." below re chemical alteration).

B. What processes "chemically alter" an ingredient under FDCA 413(a)(1) and examples of processes that do not "chemically alter" an ingredient? FDA is especially interested in receiving scientific information that shows whether a process actually results in chemical alteration.

ABC contends that this analysis should be on a case-by-case basis and employ a scientific analysis to determine if there is an impact on the safety of the ingredient. The 2016 draft guidance still uses a broad interpretation of what constitutes "chemically altered." A few examples to provide some instruction follow:

i. Processes that *do not* "chemically alter" an ingredient:
   1. The impact on the chemical composition based on changes in the extraction solvent should be evaluated by the brand holder of the product on a case-by-case basis. Manufacturers may

have switched from ethanol to methanol to save costs, e.g., from 70% aqueous ethanol to 50-60% aqueous methanol, without a substantial change (although there will always be some difference) in the chemical composition of the ingredient. Such a change is less likely to affect the ingredient than the environmental conditions in which the plant is grown, and will be less of a change than switching from 40% aqueous ethanol to 70% aqueous ethanol, which is a manufacturing change that is acceptable without triggering a new NDI submission according to the draft guidelines.

2. Switching from hexane to supercritical carbon dioxide would not only be beneficial with regard to the ingredient safety (with respect to residual solvent issues), but will likely not change the chemical profile dramatically.

ii. Processes that *do* "chemically alter" an ingredient:
   1. Manufacturing changes in which the polarity of the solvent changed substantially (e.g., a change from hexane to 70% ethanol, or from pure acetone to 40% aqueous acetone) will generally result in a significant change in chemical profile and thus create a new dietary ingredient.
   2. Substantial changes in the extraction temperature and pressure under which the extraction is performed may lead to a significantly different chemical composition.
   3. The use of purification steps, such as column chromatography or precipitation/crystallization methods, to obtain highly purified ingredients (e.g., 98% pure apigenin obtained from parsley).

Another consideration regarding a "chemically altered" ingredient is the use of solvents. In extracting constituents from plant materials the type of solvent used may or may not "chemically alter" an ingredient. The determination of whether an NDI notification is warranted or not when using a solvent to produce botanical extracts is driven by the chemical profile and safety of the resulting extract. The 2016 draft guidance — as with the 2011 draft guidance — continues to hold a narrow view on the types of solvents that do not trigger an NDI notification requirement (i.e., tincture/aqueous ethanol or water). ABC believes other solvents in addition to water and ethanol were likely used pre-DSHEA (i.e., prior to October 15, 1994); however, due to the 22+ years since the passage of DSHEA the documentation to establish such use may be difficult to obtain or perhaps no longer extant.

As noted above, since 2010 ABC has been producing a comprehensive reference book on solvents used in botanical extracts (whether the extracts are to be used in foods, dietary supplements, food additives, drugs, cosmetics, and/or industrial uses) that is expected to be published in 2017. While currently in draft form, the book draft covers 23 solvents, including water, ethanol, methanol, supercritical carbon dioxide, acetone, hexane, and other solvents.

C. How to develop an authoritative list of "grandfathered" ingredients for dietary ingredients that were marketed prior to October 15, 1994?

ABC requests FDA to remove the topic of developing an authoritative list of "grandfathered" ingredients from the 2016 draft guidance, and requests FDA to address the development of such a list under a separate notice and comment period.

As previously recommended in 2011,[10] ABC proposes the establishment of an expert advisory panel — comprised of industry members and trade associations; academic, nonprofit, and/or independent consultants; and representatives from FDA — to assess the viability of a "grandfathered" ingredients

database, and how to develop and maintain the database. To ensure the database is sound and robust is a massive undertaking and needs to be handled with extreme care. Such matters to be considered by the expert advisory panel include the following:

(1) the viability of developing an accurate and comprehensive list of "grandfathered" ingredients;
(2) if such a list is not viable, develop alternate options to address this matter such as resetting the date to establish a sound list of "grandfathered" ingredients;
(3) if developing a list is viable, identify what types of evidence will satisfy the requirement that an ingredient was "marketed"[11] pre-DSHEA, such as magazine advertisements, affidavits, and personal attestations; and
(4) articulate what type of identifying characteristics (i.e., concentration, product formulation, or specifications, such as plant part) are needed for each "grandfathered" ingredient.

Industry has been broaching this topic with FDA since shortly after the passage of DSHEA by compiling lists of dietary ingredients that had been marketed prior to October 15, 1994. However, FDA has indicated that it does not recognize these lists as authoritative for the purposes of determining NDI or pre-DSHEA ingredient status of items on such lists.[12] Now, 22+ years later the FDA is suggesting that it may request marketers of supplement products to prove the ingredients used in their products are "grandfathered" when DSHEA does not prescribe such burden.

The development of a database that captures an authoritative list of "grandfathered" ingredients is related to NDIs; however, developing such a list would be a massive undertaking and should be independent of the NDI notification process. As such, ABC believes addressing this matter in a separate notice and comment period is preferable.

2. Applicability of NDI provision to ingredients versus products

As with FDA's 2011 draft NDI guidance, the 2016 draft guidance continues to focus on the supplement *product* versus the safety of the dietary *ingredient*.

The explicit language of the NDI provision in DSHEA — including the title of the NDI provision in DSHEA that reads, "New Dietary Ingredients" — speaks to the safety of the dietary ingredient. Therefore, the NDI notification should focus on the dietary ingredient which does not extend to every supplement product that contains the NDI.

The following is an exceptional analysis of the NDI language in DSHEA by the law firm Amin Talati (2011)[13] that reinforces ABC's position that the focus of an NDI notification should be on the ingredient and not on the finished product:

> The plain reading of the statute becomes more clear when we parse 413 (a) (2) into three parts. Specifically:
>
> Part 1
>
> *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* (emphasis added)
>
> The plain reading of this part is that the evidence of safety is to establish that the new dietary ingredient will reasonably be expected to be safe.

Part 2

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,

The plain reading of this part is that the notification can be submitted by either the manufacturer or distributor of the dietary ingredient or dietary supplement. The inclusion of "dietary supplement" here along with "dietary ingredient" indicates that a finished product manufacturer or distributor can submit notification for the new dietary ingredient as well.

Part 3

*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)

FDA interprets "has concluded that a dietary supplement" as to require notification for the dietary supplement. This interpretation is not supported by the plain reading. Although the statu[t]e requires the dietary supplement to be "reasonably be expected to be safe", it does not require the notification for the dietary supplement. The notification is for the dietary ingredient. The adjective "such" according to Webster's dictionary means "of the same class, type, or sort." Also, the statute uses the term "a dietary supplement." "A" is an indefinite article and not a specific object. If Congress wanted supplement specific notifications, it would have used the word "the" which is a definite article.

Therefore, as so eloquently deconstructed by the Amin Talati firm, the NDI provision expressly requires NDI notifications for new dietary ingredients and not the supplement product themselves.

Further support for ABC's position that the 2016 draft guidance exceeds the scope of the explicit text of the NDI provision in Section 8 of DSHEA is evidenced by previous FDA *Federal Register* notices where FDA estimated 0 to 12 NDI notifications would be filed per year and at a cost of $410 per NDI notification (1997), and another notice 14 years later, where the estimated number of NDI notifications per year increased to only 55 and an estimated 20 hours to compile data for each (2011).[14]

Therefore, the plain language of the statute, the applicable regulations,[15] and historic FDA behavior speaks to the dietary ingredient and not the finished dietary supplement product. If FDA is interested in moving towards a full product registration system, then ABC believes FDA should engage in an open conversation with industry, community stakeholders, lawmakers, and the general public instead of what appears to be a misrepresentation of the NDI provision to achieve full product registration.

3. **Combination of NDIs**

The 2016 draft guidance states that the "combination of two NDIs is itself an NDI."[16] ABC takes issue with this position in that there is no statutory authority for this requirement nor is there a safety justification to require such notification. A manufacturer must ensure that a dietary supplement does not present "a significant or unreasonable risk of illness or injury" and that a dietary supplement is manufactured in compliance with current good manufacturing practices.[17]

ABC is not aware of any actual case in which the addition of two or more safe ingredients — i.e., ingredients that are considered duly appropriate NDIs, which have undergone the proper notification process with FDA and for which FDA had no objection — have resulted in a dietary supplement product

that was subsequently determined to be unsafe for human use. While ABC suspects that FDA may be concerned about the combination of NDIs *on a purely theoretical basis*, ABC believes that FDA should provide specific examples of cases where the combination of duly notified NDIs have resulted in a problematic situation from a human safety perspective. Otherwise, lacking such specific example, ABC finds no rational basis for this proposal by FDA and strongly encourages FDA to remove this provision from the final NDI guidance.

4. **Synthetic copy of an herbal or botanical constituent**

The FDA has categorically set forth in the 2016 draft guidance that "a synthetic copy of an herb or other botanical" does not qualify as a dietary ingredient under 21 USC 321(ff)(1)(C).[18] ABC takes issue with this position. ABC's preference has long been for any dietary ingredient that is either directly extracted from plant or fungal raw material or otherwise produced to mimic a naturally occurring plant or fungal constituent to be as natural as is appropriately reasonable. However, ABC recognizes that in certain situations various forms of industrial processes to extract, modify, and/or otherwise produce such constituents may be warranted.

DSHEA does not explicitly prohibit a synthetic or semi-synthetic compound as a dietary ingredient nor has FDA set forth data to support a safety concern for the use of a synthetic or semi-synthetic copy of an herbal or botanical constituent. ABC continues to emphasize that the safety of an ingredient is the primary consideration and if a synthetic or semi-synthetic compound is chemically identical to the natural compound and has the same level of safety as the natural compound, then ABC supports the availability of the synthetic or semi-synthetic version as a legitimate dietary ingredient.

5. FDA's authority to reverse a no-objection ruling

ABC takes issue with FDA's unilateral ability to reverse its position post-issuance of an "acknowledgement letter without objection" (no-objection) in response to a NDI notification when safety is not the basis for the reversal. ABC believes that regulatory certainty may lend itself to innovation and for companies to invest in and comply with the NDI provision; however, industry must have some degree of assurance that receipt of an "acknowledgement letter without objection" in response to a NDI notification has value.

If FDA intends to continue with this course of action, ABC recommends FDA include in the final NDI guidance document a protocol that clearly defines a route of recourse for industry when FDA reverses its position post-issuance of an "acknowledgement letter without objection" in response to a NDI notification and the reversal is not based on a safety consideration.

6. Level of science to satisfy "reasonable expectation of safety"

For botanical ingredients that have a long and extensive use as dietary supplements over a large range of extracts — e.g., chamomile (*Matricaria recutita*), where traditional use includes hot water extracts, alcoholic tinctures, and essential oil, plus extracts that were made with solvents of intermediate polarity, such as a well-characterized aqueous methanol extract — should be accepted as dietary ingredients without having to submit additional safety data. For herbal ingredients wherein relatively minor changes have been made in the composition compared to the composition of the herb and its traditional preparations in the established use, additional safety data may be required in an NDI notification — but the manufacturer or marketer submitting such data should be able to rely mainly on the available safety

record based on the established use, as noted in the 2016 draft guidance (page 60, example 10). When major changes to the composition are made, or an entirely new botanical ingredient is intended to be marketed, the submission of data from safety tests is appropriate.

The standard under the NDI notification provision in Section 8 of DSHEA is that the NDI has a "reasonable expectation of safety"; however, as the 2016 draft guidance is currently written, FDA has created a heavier lift for the NDI and is imposing a standard closer to that for a food additive which is a reasonable certainty of no harm.[19]

As FDA stated in 1997[20] in response to a comment during the rulemaking phase of the NDI regulations, the level of science needed to satisfy the NDI standard is less than that of a food additive and the concept of generally recognized as safe (GRAS) is not relevant.

> [Starting on p. 49888]
>
> Significantly, §190.6(b)(4) simply tracks the language of section 413(a)(2) of the act. It is appropriate that the regulation do so because, contrary to what the comment asserts, the ***manufacturer or distributor is not required to do a complete literature search. It is required only to provide ''the basis on which [it] has concluded*** that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe'' (section 413(a)(2) of the act). ***That is all that the regulation requires***. … (emphasis added)
>
> The fact that Congress did not create a minimal safety data requirement in section 413(a)(2) of the act does not render the DSHEA void for vagueness. The manufacturer's or distributor's obligation under section 413(a)(2) of the act is clear. It must make a showing as to why it considers that consumption of a new dietary ingredient will be safe.
>
> FDA also does not agree that the GRAS concept has relevance here. The concept of GRAS was adopted by Congress in 1958, as a limitation on the scope of the ''food additive'' definition (section 201(s) of the act). Congress excluded from the definition of ''food additive'' substances that are generally recognized, among experts qualified by scientific training and experience to evaluate their safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food) to be safe under the conditions of their intended use. However, ***dietary ingredients, which are used in dietary supplements, are not food additives***. Congress excluded them from the definition of a ''food additive'' in the DSHEA (section 201(s)(6) of the act, which was added by section 3(b) of the DSHEA). Thus, ***the concept of GRAS is not relevant to how dietary ingredients are regulated.*** (emphasis added)
>
> Furthermore, there is a fundamental difference between who is to make at least the initial judgment as to the safety of an ingredient under section 413(a)(2) of the act and whose judgment is relevant to a determination that an ingredient is GRAS. Whether an ingredient is GRAS is based on the judgment of ''experts qualified by scientific training and experience to evaluate'' the ingredient's safety. In contrast, the requirement in section 413(a)(2) of the act that a notification be made for a new dietary ingredient provides that the manufacturer or distributor is to determine whether a dietary supplement containing such dietary ingredient will reasonably be expected to be safe. While this determination is subject to review by FDA, section 413(a) of the act does not specify that the manufacturer or distributor must rely on any specified third party in making its judgment....
>
> Section 413(a)(2) of the act requires only that the notification 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 when used under the conditions recommended or suggested in the labeling.'' Thus, the statute does not specify or limit what evidence a manufacturer or

> distributor may rely on in determining whether the use of the ingredient will reasonably be expected to be safe. Nonetheless, FDA expects that, in making a determination that a new dietary ingredient is reasonably expected to be safe and does not present a significant or unreasonable risk of illness or injury, a manufacturer or distributor will consider the evidence of safety that is available in the scientific literature and from examination of reports of adverse effects associated with the use of a new dietary ingredient.
>
> ***FDA does not find that the statute requires that the agency determine the relative merit of different types of evidence of safety***, and therefore, the agency is not modifying § 190.6 to specify specific safety requirements for new dietary ingredients or to establish standards that the evidence of safety must meet. … (emphasis added)

ABC therefore requests that FDA revise the 2016 draft guidance to reflect more accurately the level of evidence required under the dietary supplement regulatory framework.

7. **Economic impact**

ABC requests FDA undergo a new economic impact analysis of the 2016 draft guidance. If the 2016 draft guidance becomes final as it is currently written, the potential cost to the both agency and to members of the industry — and ultimately, the consumer — is currently unknown.

ABC also requests that as part of the economic impact analysis, the FDA consider the financial impact on smaller business entities. Small business entities — frequently the source of innovative ingredients and products that can benefit consumer health — often, although not always, outsource a large portion of their operations. Therefore, the financial impact analysis on the smaller entities needs to include any competitive disadvantages due to the increased administrative burden these small businesses may face, e.g., an inadequate number of available consultants and laboratories to compile and submit data on behalf of the smaller businesses.

Additionally, ABC encourages FDA to consider its internal resources — human and financial — to be able to effectively handle the volume of NDI notifications that FDA will receive if the 2016 draft guidance as currently written becomes final.

The NDI guidance should be drafted in a manner that will facilitate the submission of high quality NDI notifications and provide FDA to effectively manage incoming notifications.

8. **Compliance period**

Insofar as it has taken the FDA more than 22 years since the passage of DSHEA for FDA to complete its rulemaking and guidances with respect to implementation of DSHEA's Section 8 on NDIs, if the agency moves forward with a Final NDI Guidance, ABC recommends the Final NDI Guidance incorporate a reasonable and appropriate compliance period where FDA does not intend to take enforcement actions against sellers of ingredients that are deemed to be NDIs and/or manufacturers and sellers of finished dietary supplement products that are deemed to contain NDIs, but instead, allow these parties a reasonable and appropriate period of time to either file a NDI notification for such NDIs and/or make appropriate adjustments in their dietary supplement product ingredients as to be compliant with the Final NDI Guidance. Such a "reasonable and appropriate compliance period" would not apply, of course, to any ingredient deemed to be unsafe for its intended use by FDA.

Even with the proposed reasonable and appropriate compliance period, ABC encourages the FDA to continue to prioritize enforcement actions against adulterated ingredients and products that present a significant or unreasonable risk of illness or injury, and other violations of current Good Manufacturing Practices (cGMP).

In summary,

The NDI notification requirement is a process where the manufacturer or distributor of the NDI or the manufacturer or distributor of the supplement that contains the NDI provides safety data to the FDA. This is a premarket notification process, not an approval process. The FDA has finite resources and ABC requests FDA finalize the guidance in a manner that is manageable and that sets up both the industry and agency for success, in the consumers' best interests.

ABC appreciates that as times evolve and the dietary supplement market matures, that the regulatory environment must also evolve to ensure only safe ingredients and products enter the marketplace. ABC supports FDA's mission to help ensure the availability of safe dietary ingredients and the products in which they are used. As shown above, ABC believes that the agency has exceeded its statutory authority and the intent of Congress with respect to its provisions in the 2016 draft guidance. ABC encourages FDA to continue to prioritize enforcement against adulteration and cGMP violations as these areas have a greater likelihood of positive impact on product quality and public health.

ABC respectfully recommends that FDA revise the 2016 draft guidance to align with the intent of Congress and the explicit text of Section 8 of DSHEA.

ABC notes that its lack of comment on other matters in the 2016 draft guidance does not indicate tacit endorsement or disagreement with such matters.

We thank you in advance for your consideration of our comments.

Respectfully submitted,

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References

[1] FDA Draft Guidance, "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry," August 2016 (replaces draft guidance issued July 2011).
[2] 81 *Federal Register* 53486-53489 (August 12, 2016); 81 *Federal Register* 68434-68435, Extension of Comment Period (October 4, 2016).
[3] Dietary Supplement Health and Education Act of 1994 (DSHEA), Pub. L. 103–417, 108 Stat. 4325.
[4] DSHEA, see §2, Findings.
[5] U.S. Food, Drug, and Cosmetic Act (FDCA) §413 (21 USC 350b).
[6] FDCA §413 (21 USC §350b(a)(2)).
[7] Pierotti JA, Blumenthal M. *Solvents Used in the Manufacture of Botanical Extracts Used in Foods, Dietary Supplements, Food Flavors and Additives, Drugs, and Cosmetics.* Austin, TX: American Botanical Council, 2017 (in press).
[8] DSHEA, see §2, Findings.
[9] 81 *Federal Register* 53486-53489 (August 12, 2016), Food and Drug Administration, "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues; Revised Draft Guidance for Industry; Availability."
[10] ABC's comments dated December 2, 2011, to FDA in response to "Draft Guidance to Industry: Dietary Supplements: New Dietary Ingredient Notification and Related Issues" [76 *Federal Register* 39111; July 5, 2011].
[11] FDCA §413 (21 USC §350b(d)).
[12] FDA has recognized under 21 CFR 101.4(h) the *Herbs of Commerce*, a publication by the American Herbal Products Association that addresses nomenclatural problems by compiling common names "standardized" to the Latin binomial botanical name.
[13] Amin Talati Attorneys at Law (now Amin Talati Upadhye) comments dated December 2, 2011, to FDA in response to "Draft Guidance to Industry: Dietary Supplements: New Dietary Ingredient Notification and Related Issues" [76 *Federal Register* 39111; July 5, 2011].
[14] 62 *Federal Register* 49886 (Sept. 23, 1997); 76 *Federal Register* 32214 (Jun. 03, 2011); 76 *Federal Register* 51986 (19.Aug. 19, 2011)
[15] 21 CFR Part 190.6, Requirement for premarket notification.
[16] 2016 FDA Draft NDI Guidance, p. 30-35.
[17] Food, Drug, and Cosmetic Act (FDCA) §402(f-g) (21 USC 342 (f-g)).
[18] FDA Draft Guidance, "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry" August 2016, (p.38-39).
[19] 21 CFR Part 170-189, Food Additives (specifically 170.3(i)).
[20] FDA, Final Rule, Premarket Notification for a New Dietary Ingredient, 62 *Federal Register* 49886, 49888-49889 (Sept. 23, 1997).