Docket No. FDA–2011–D–0376

BEFORE

THE UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

COMMENTS OF

NATIONAL HEALTH FREEDOM ACTION

ON THE FDA DRAFT GUIDANCE

Entitled:

"Draft Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues; Availability"

Comments Submitted November 28, 2011

I. NHFA – Who we are.

National Health Freedom Action (NHFA) is a 501(c) 4 non-profit corporation working to protect maximum health care options for consumers.[1] NHFA works to protect the right of all people to access their favorite health care practitioners and health care products, as well as to protect the right to access many other healing arts products and services that resonate with people's path to wellness.

NHFA responds to calls year-round from individuals and groups throughout the country that wish to promote legal reform in occupational laws and regulations having to do with complementary and alternative health care on the state level, and with federal and international product laws and regulations having to do with access to desired products. NHFA works with citizens to empower them to take action to address these concerns. NHFA educates and trains citizens on health freedom principles and on how to develop and pass proactive health freedom legislation that will ensure the rights of health care practitioners to offer their services and the rights of consumers to have access to products, practitioners, and information.

NHFA staff draft model legislation, testify at legislative hearings and public policy meetings, and provide strategic support and lobbying assistance, and NHFA hosts and participates in the US Health Freedom Assembly, and is a founding member of the World Health Freedom Assembly. NHFA staff often assist state leaders in developing local health freedom organizations and are currently working with groups in over 30 states and seven countries to support health care reform efforts.

Americans Are Aware and Concerned: There is a growing awareness among Americans that personal choice in health care directly impacts how, and whether, a person will gain a full sense of health and wellness. In addition Americans have become deeply concerned about infringements on their ability to make choices caused by regulatory systems that do not adequately protect a person's ability to choose.

NHFA's Basis for Responding to Draft Guidance presented for Comment

NHFA became aware of the FDA Draft Guidance document entitled *"Draft Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues"*[2] [hereinafter Draft Guidance] through the Federal Register,[3] and through multiple

[1] National Health Freedom Action, www.nationalhealthfreedom.org.
[2] FDA, HHS, DRAFT GUIDANCE FOR INDUSTRY; DIETARY SUPPLEMENTS: NEW DIETARY INGREDIENT NOTIFICATIONS AND RELATED ISSUES [hereinafter DRAFT GUIDANCE], Docket No. FDA-2011-D-0376 (July 5, 2011), *available at* http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/ucm257563.htm.

correspondences sent to NHFA from manufacturers, practitioners, consumers, and state health freedom organizations and leaders across the country requesting an explanation of the document. The correspondences that NHFA has received reflect mass opposition amongst readers of the Draft Guidance.

NHFA responded by researching and reviewing the Draft Guidance, drafting a short action alert and posting it on our website, www.nationalhealthfreedom.org, and encouraging individuals to go to the FDA website to submit their comments.

Many citizens have complained to us regarding the complexity of submitting a comment directly to the FDA. It is our hope that a number of citizens have been successful with that process. NHFA's Board of Directors has approved the submission by our legal staff of formal comments as stated herein. Given that our organization seldom provides comments to the FDA unless we believe we have a strong statement to make regarding an issue impacting consumer access to personal choice, we appreciate the extended date for comments.[4]

Given NHFA's work to maximize access to consumer health care options by reviewing, drafting, revising, and generally creating new solution language for public policy documents, legislative initiatives and literary articles, and NHFA's active participation in legal reform, and because NHFA's members have an interest in dietary supplements and new dietary ingredients used by health care seekers of all kinds around the world, NHFA is therefore providing the following comments.

NHFA's Requests and Recommendations to the FDA

NHFA views the Draft Guidance as unfair and unwarranted given both the actual language of current law and rules,[5] and, also, Congress's specific foundational intent set forth regarding the regulation of dietary supplements.[6] NHFA recommends that the FDA do the following:

1. Stop any further work or document development on the Draft Guidance and withdraw the Draft Guidance in its entirety; or
2. Revise the Draft Guidance Document according to the concerns presented in these comments;

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[3] Notice of Availability; Draft Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues, 76 Fed. Reg. 39111-39112 (July 5, 2011), http://frwebgate2.access.gpo.gov/cgi-bin/TEXTgate.cgi?WAISdocID=te5ysZ/0/1/0&WAISaction=retrieve.
[4] Notice of Extension of Comment Period Draft Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues; Availability; 76 Fed. Reg. 55927 (Sept. 9. 2011), http://frwebgate2.access.gpo.gov/cgi-bin/TEXTgate.cgi?WAISdocID=hPzt32/2/1/0&WAISaction=retrieve.
[5] *See*, *infra*, NHFA Comment Part II(A) at p. 5-13.
[6] *See Id.*

3. Regulate using the least restrictive means with the presumption of safety of new dietary ingredients;
4. Honor the Proxmire Amendment's intent that "more" is not dangerous; [7]
5. Honor the industry's extensive work and documents that report which products were marketed prior to 1994[8]; and
6. Focus on enforcement of existing law regarding known cases of non-compliance rather than attempting to expand regulatory demands on good faith manufacturers.[9]

[7] *See*, *infra*, NHFA Comment Part II(A)(a), at p. 6.
[8] See, *infra*, NHFA Comment Part II(C)(b), at p.26.
[9] See, *infra*, NHFA Comment Part II(C)(c), at p. 34.

II. Foundation for Request to Withdraw Draft Guidance

A. The Draft Guidance goes against the historical wishes of the people of the United States and the important foundational principles Congress passed within the Dietary Supplement Health and Education Act of 1994 (hereinafter DSHEA).[10]

a. Dietary Supplements and New Dietary Ingredients are a category of food items without dosage limits for proper recommended use;

b. Dietary Supplements and New Dietary Ingredients have widespread and safe use by consumers and access to them should be protected to promote wellness and self care; and

c. The burden of proof remains on the government to show lack of safety.

DSHEA reflects the will of the people and is considered the most important consumer product access legislation enacted to date, impacting consumer access to the enumerated items of vitamins, minerals, herbs or other botanicals, amino acids, dietary substances for use by man to supplement the diet by increasing the total dietary intake, or concentrates, metabolites, constituents, extracts, or combinations of any ingredient of these items.[11]

These substances are sought after by millions of Americans, a fact specifically acknowledged in the DSHEA findings in which Congress recognized the widespread use of dietary supplements,[12] and now more recent studies showing an ever increasing use of these products by consumers.[13] Under DSHEA Congress went so far in its findings as to specifically state an intent to protect consumer access to these products and acknowledge that access to these products would be necessary to promote wellness.[14]

In addition to access, DSHEA was passed with the presumption that dietary supplements are safe, specifically mandating that the burden of proof of lack of safety remain on the

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[10] Dietary Supplement Health and Education Act of 1994 [hereinafter DSHEA], Pub. L. No. 103-417, 108 Stat. 4325 (codified as amended in scattered sections of 21 U.S.C.), *available* at http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/ucm148003.htm.

[11] *See id.*

[12] Congressional Findings, DSHEA, *supra* note 10, at §2.(9)("…national surveys have revealed that almost 50 percent of the 260,000,000 Americans regularly consume dietary supplements of vitamins, minerals, or herbs as a means of improving their nutrition;…" *Id.*).

[13] Barnes PM, Bloom B, Nahin R. *CDC National Health Statistics Report #12*. Complementary and Alternative Medicine Use Among Adults and Children: United States, 2007. December 2008. Accessed online November 27, 2011 at: http://nccam.nih.gov/news/2008/nhsr12.pdf.

[14] Congressional Findings, DSHEA, *supra* note 10, at §2.15(A) ("…legislative action that protects the right of access of consumers to safe dietary supplements is necessary in order to promote wellness;…").

FDA[15], and finding that "*dietary supplements are safe within a broad range of intake, and safety problems with the supplements are relatively rare*:"[16]

These presumptions and findings are the basis of the powerful and globally noted United States presumption that these substances are nutrient-dense foods and should be and are regulated as such. These presumptions and findings are also the basis of crucial protection of personal choice and liberty to millions of Americans assuming access to these products and the important nutrients they contain.

a. DSHEA In Context of Proxmire and Supplement History: More is NOT dangerous.

Current dietary supplement law rides on the shoulders of history, history that set a clear foundation for the legislation in effect today, DSHEA.[17] NHFA now asks FDA to honor the will of the people as it has been voiced and progressed through history, and to not get caught up in the slippery slope of over-regulating just because it can. NHFA asks the FDA to look to history and the wishes of the people as it prepares guidance documents that will impact the interpretation of existing laws regarding dietary supplements.

The most important historical event prior to DSHEA that exemplifies consumers' continued demand for protection of access to dietary supplements is the 1976 passage of the Proxmire Amendment, restricting FDA from setting maximum dosage limits on vitamins and minerals.[18] In 1962 the FDA proposed regulations to reform the vitamin and dietary foods industry suggesting restrictions on the sale of vitamins and minerals above certain dosages.[19] This proposal was met with great opposition from citizens across the country, as reported by The Evening Star on October 11, 1962:

> Protests against the Food and Drug Administration's proposed regulations to reform the vitamin and dietary foods industry has produced more mail—and more critical mail—than officials can remember ever receiving on any single subject….cards come from vitamin buyers who believe they are benefiting from the products, from small businessmen who sell them, from women who wonder if FDA is trying to bar the use of carrot juice as well as from the manufacturers of safflower oil products, "sea salts" and protein boosters. [20]

[15] *Id.* at § 4. Safety of Dietary Supplements and Burden of Proof on FDA (codified as amended at 21 U.S.C. 342(f).
[16] *Id.* at Congressional Findings §2.14.
[17] *See generally*, DSHEA, *supra* note 10.
[18] Health Research and Health Services Amendments of 1976 [hereinafter Proxmire Amendment], Pub. L. 94-278, 90 Stat. 410, *available at* http://history.nih.gov/research/downloads/PL94-278.pdf.
[19] COMMISSION ON DIETARY SUPPLEMENT LABELS, REPORT OF THE COMMISSION ON DIETARY SUPPLEMENT LABELS, CH. 2: BACKGROUND ON DIETARY SUPPLEMENTS, 11-13 (Nov. 1997), http://www.health.gov/dietsupp/ch2.htm.
[20] Willima Grigg, *Protests Flood FDA Over Dietary Code*, THE EVENING STAR, Oct 11, 1962, at A15.

From 1962 to 1976 a battle ensued in which the American people voiced their concerns about regulations and restrictions on vitamins and minerals based solely on dosage.[21] In 1973 the Honorable Representative Claude Pepper of Florida made statements to Congress entitled Freedom of Choice stating: "*…the public does have the right to purchase vitamins and minerals in dosage forms which are the most convenient when there is no issue of safety at stake. As long as the products are adequately labeled and unadulterated, the FDA's job is done. For this reason I am introducing a bill to limit the authority of the FDA regarding the regulation of food supplements. In order to issue any regulation which would limit the potency, number, combination, amount, or variety of any vitamin and/or mineral product, the FDA would have to prove that the supplement is intrinsically injurious to health…".*[22]In 1976 the voice of the American people was finally and successfully carried by Senator William Proxmire (D-Wisconsin) in the Proxmire Amendment, also known as the Vitamin-Mineral Amendment to the Federal Food, Drug, and Cosmetic Act, passed into law on April 22, 1976.[23] The Proxmire Amendment prohibits the FDA from establishing maximum limits on the potency of vitamins or minerals or regulating them as drugs based solely on their potency. [24]

But even after the Proxmire Amendment passed there were still concerns about whether the FDA would heed consumer's message regarding access to dietary supplements. The Committee on the Framework for Evaluating the Safety of Dietary Supplements describes the time period between 1976 and 1994 as a confusing and volatile one for industry and consumers.[25] Eventually, however, the debates settled when Congress agreed with those expressing the importance of dietary supplements to health and, in order to protect consumer access to these products, passed legislation that clearly defined and put specific parameters on FDA's regulatory power over them.

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[21] COMMISSION ON DIETARY SUPPLEMENT LABELS, *supra* note 19, at *Id.*

[22] *Freedom of Choice: Hearing on proposed FDA amendments to FD&C Act Before the Subcomm. of Public Health and Environment of the H. Comm. Interstate and Foreign Commerce*, 119th Cong. 176 (1973) (statement of Rep. Hon. Claude Pepper).

[23] Commission on Dietary Supplement Labels, *supra* note 19, at 12.

[24] Proxmire Amendment, *supra* note 18.

[25] COMMITTEE ON THE FRAMEWORK FOR EVALUATING THE SAFETY OF THE DIETARY SUPPLEMENTS, NATIONAL RESEARCH COUNCIL, DIETARY SUPPLEMENTS: A FRAMEWORK FOR EVALUATING SAFETY, Pg. 36, (The National Academies Press 2005), accessed online November 27, 2011 at: http://www.nap.edu/openbook.php?record_id=10882&page=36 (explaining that "Amino acids, for example, might be considered unapproved food additives, and some botanicals might be more appropriately considered as drugs (FDA, 1993). Vitamins and minerals were also considered a potential target of regulation, as FDA suggested that their strength should be limited to levels that approximated the U.S. RDAs (FDA, 1993). Industry and consumers reacted quickly and strongly to these potential regulatory restrictions. Extensive public debate ensued over the importance of dietary supplements in health, consumers' freedom to access information about supplements, and the controversy over FDA's regulatory approach. As a result, Congress passed legislation limiting FDA regulation of dietary supplements. This legislation, the Dietary Supplement Health and Education Act (DSHEA), was signed into law in 1994.")

b. The Passage of DSHEA and Findings on Access and Safety

In 1993 Congress introduced DSHEA to regulate dietary supplements as food and to put the burden of proof on the FDA to show harm before restricting marketing of these food products.[26] DSHEA soon became the flagship of the natural health movement.

Included in DSHEA was a list of Congressional findings which set forth the intent of Congress in regulating dietary supplements as food. Congressional findings provide evidence of deliberation prior to enacting legislation[27] and, in the case of DSHEA, they put to rest two persistent debates regarding these products: access and safety.

Healthy debate is an essential part of the conversation of freedom and the conclusion of a debate, such as Congressional findings and intentions, goes a long way in describing the foundational principles upon which eventual laws will be based.

In the case of the DSHEA debates, first and foremost, the battle ground was about access. The access debate was about the tension between the right of citizens to have access to all substances and food products of nature to use in their own health journeys without dosage limit or unnecessary regulatory barriers and the role of the government in protecting citizens from harm as it does with premarket evaluation of toxic drugs. To that affect, the citizen and regulator testimony provided during the passage of DSHEA was remarkable in its breadth of discussion about this conflict. In the end and for this reason in the passage of DSHEA, Congress explicitly stated in its findings that "*…the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers*," DSHEA Findings and Purpose, Sec. 2(a) (13).[28]

This short sentence may seem inconsequential seventeen years later, however from what we hear from American consumers, this finding is even stronger today, with citizens strongly protesting when regulatory barriers are recommended that could unnecessarily and "unreasonably" limit access to these food products.

Secondly, and in addition to the debate about access, DSHEA advocacy had a "sub battle ground" which was safety. What was the role of government and what was the role of citizenry regarding safety? The legal question was whether the burden of proof of harm would be on the government to show harm before restricting access to a product, such as it is with food, or whether a burden of proof of safety before marketing a product would be placed on the manufacturer, as it is with manufacturers of inherently dangerous industrially engineered products, i.e., toxic drugs.

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[26] Commission on Dietary Supplement Labels, *supra* note 19, at 11-13.
[27] *See generally*, DSHEA, *supra* note 10, at §2. Congressional Findings.
[28] DSHEA, *supra* note 10, at §2(13).

DSHEA came down firmly on the side of dietary supplements being regulated as food and solidified into law the presumption that dietary supplements are foods, presumed safe for human consumption as follows: *"…Except for purposes of section 201(g) a dietary supplement shall be deemed to be a food within the meaning of this Act…"*[29] and "*dietary supplements are safe within a broad range of intake, and safety problems with the supplements are relatively rare,…"*.[30]

These conclusions make clear the attitude and approach the U.S. would take regarding dietary supplements: access should be maximized, not inhibited, and dietary supplements are considered safe and a category of food. These presumptions are the cornerstones of DSHEA and of the will of the people and, rather than crumbling over time, these cornerstones are considered foundational in every aspect; the people of the United States continue to access and utilize dietary supplements as nutrient-dense foods that positively enhance their wellness and which are presumed safe unless proven otherwise.

c. DSHEA's Presumption and Burden of Proof

DSHEA established outright the legal presumption that dietary supplements are not toxic drugs or food additives but rather are nutritious foods which would be regulated as foods by including/and included a special section in the bill, entitled "Safety of Dietary Supplements and Burden of Proof on FDA".[31] That section spelled out the parameters of FDA's authority over these products and made it clear that the FDA bears the burden of proof in determining that a dietary supplement ingredient presents a "*significant or unreasonable risk of illness or injury*" before it can restrict a product based on safety concerns; any requirement that the manufacturer must prove to the FDA that a product is safe before going to market, as required by statute for food additives or drugs, was plainly rejected.[32]

However NHFA views the burden of proof issue as one of sensitive complexity because we recognize that DSHEA contains a sophisticated settlement of both sides of the issue. The settlement appears in the language that was added that to compartmentalize the difference between a dietary supplement and a "new dietary ingredient" [hereinafter NDI]. NHFA believes that establishing this arbitrary definition of a an NDI to include all "*dietary ingredients that were not marketed in the United States before October 15, 1994, and not including any dietary ingredient which was marketed in the United States before October 15, 1994*"[33], and then adding language that indicates a different procedure of pre-market notification to the FDA before marketing some NDIs and specifying what types of information a manufacturer must disclose regarding its basis for safety,[34] left room for an

[29] *Id.* at §3(a).
[30] *Id.* at §2(14).
[31] *Id.* at § 4.
[32] *Id.*
[33] DSHEA, *supra* note 10, at §8 (codified as amended at 21 U.S.C. §350b).
[34] *Id.*

ongoing battleground regarding the function of government as it applies to the safety of NDIs.

Looking closely at the law and the regulations regarding the burden of proof for new dietary ingredient safety, we draw FDA's attention first to 21 U.S.C. § 350b, which reads: A dietary supplement that contains a new dietary ingredient is adulterated unless: *"(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" and "(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.*

These paragraphs ask the manufacturer to *provide 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.*[35]

But we point out to FDA, that a law requiring a manufacturer to give information to the FDA indicating the basis for its conclusion of safety before it markets its product **does not** shift the burden of proof or absolve the FDA of its duty to prove harm before restricting a NDI. Whether the manufacturer provides a small amount or a large amount of evidence as to what it based its conclusion of safety on, the law is the same; it does not shift the burden of proof of harm to the manufacturer as it does when the substance is inherently dangerous, i.e., a toxic drug. It needs to be remembered that a NDI is still by definition a dietary ingredient including: *A vitamin; A mineral; An herb or other botanical; An amino acid; A dietary substance for use by man to supplement the diet by increasing the total dietary intake; or A concentrate, metabolite, constituent, extract, or combination of any ingredient mentioned above.*[36]

NDIs do not include substances considered food additives that are regulated separately, and do not include articles approved as new drugs, licensed as biologics, or authorized for clinical investigation under an IND for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, unless the article was previously marketed as a dietary supplement or as a food.[37] And the previously expounded upon findings of DSHEA describing the importance of access to dietary supplements still apply to NDIs.

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[35] 21 U.S.C. § 350b.
[36] DSHEA, *supra* note 10, at §3(a).
[37] *Id.*

At the least, the information presented to the FDA about the manufacturer's conclusions would assist the FDA in its exploration of whether it wanted to restrict the product or not. The law requesting the manufacturer to share their information does not lift the burden of due diligence if the FDA wanted to restrict the marketing of a NDI. The FDA must still do its own homework and provide adequate evidence of harm before restricting a NDI.

d. DSHEA and "New Dietary Ingredients": It is still food.

The definition of dietary supplements in DSHEA and the way in which DSHEA brought forth the concept of a "new dietary ingredient" reflect the historical and contested nature of treatment of dietary supplements. For that reason the current Draft Guidance strikes a raw nerve which brings to the fore the historical conflict regarding the role of government in the regulation of dietary supplements.[38]

NHFA believes that the DSHEA definition of dietary supplements reflects an arrived at agreement between the government's pursuit of its stated concern to protect citizens from harm and the consumer's concern for freedom from unnecessary restrictions on access. Most analysts can see that the language chosen was an attempt to balance these interests. The sentence that reflects this attempt is the sentence that states that a dietary supplement is a substance that, among other requirements, is "*marketed as a dietary supplement or as a food unless the Secretary has issued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 342(f) of this title…*;".[39]

Because the balance was drawn allowing anything within the other elements of the definition, marketed before the bill passed, to be considered a dietary supplement, the bill then also had to address those items that were not marketed before the bill passed. What about the future? What about new ingredients? Would they be dietary supplements or would they be treated as drugs requiring premarket evaluation?

This is when the concept of a NDI became key: even if a substance was a vitamin, mineral, herb or other botanical, amino acid, dietary substance for use by man to supplement the diet by increasing the total dietary intake, or concentrate, metabolite, constituent, extract, or combination of any ingredient of these items,[40] the agreed upon language of DHSEA said that these substance that were not formerly marketed were NDIs and would be considered adulterated under the law unless either of two criteria were true:

(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.

[38] *See supra*, NHFA Comment Part II(A), at p. 1-14.
[39] DSHEA, *supra* note 10, at §3.
[40] *Id*.

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.[41]

And to add to how the statute would be implemented, in 1997 the FDA promulgated rules in 21 C.F.R. 190.6 that spelled out what should be included in this notification process as follows:

(b) The notification required by paragraph (a) of this section shall include:

(1) The name and complete address of the manufacturer or distributor of the dietary supplement that contains a new dietary ingredient, or of the new dietary ingredient;

(2) The name of the new dietary ingredient that is the subject of the premarket notification, including the Latin binomial name (including the author) of any herb or other botanical;

(3) A description of the dietary supplement or dietary supplements that contain the new dietary ingredient including:

(i) The level of the new dietary ingredient in the dietary supplement; and

(ii) The conditions of use recommended or suggested in the labeling of the dietary supplement, or if no conditions of use are recommended or suggested in the labeling of the dietary supplement, the ordinary conditions of use of the supplement;

(4) The 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, including any citation to published articles or other evidence that is the basis on which the distributor or manufacturer of the dietary supplement that contains the new dietary ingredient has concluded that the new dietary supplement will reasonably be expected to be safe. Any reference to published information offered in support of the notification shall be accompanied by reprints or photostatic copies of such references. If any part of the material submitted is in a foreign language, it shall be accompanied by an accurate and complete English translation; and

[41] *Id.* at §8 (codified as amended at 21 U.S.C. § 350b).

(5) The signature of the person designated by the manufacturer or distributor of the dietary supplement that contains a new dietary ingredient.[42]

It is our understanding that, under the above statute and rules, only 700 notifications of NDI have been submitted to the FDA since 1994.[43] And that the FDA thinks there should be more, given its estimate of 55,600 supplements on the market.[44]

Further, it is our understanding that the FDA has concerns regarding the presence of "undeclared active ingredients" in products marketed as dietary supplements and thinks that it is necessary for marketers of dietary supplements to submit NDI notification as an important preventive control to "ensure that the consumer is not exposed to potential unnecessary public health risks in the form of new ingredients with unknown safety profiles."[45]

But NHFA would like to remind the FDA that the language of its concerns strikes a chord with consumers. The words "*undeclared active ingredients*" stated in the Draft Guidance are not terms stated in the statute or rule for NDI notification.[46] And the words "*ensure that the consumer is not exposed to potential unnecessary public health risks in the form of new ingredients with unknown safety profiles*" is not a legal threshold in law or rule either, and this language strikes a chord because consumers view dietary ingredients of all kinds to be food with a presumption of safety.

NHFA reminds FDA that in order to be a NDI, the ingredient must first be a *vitamins, minerals, herbs or other botanicals, amino acids, dietary substances for use by man to supplement the diet by increasing the total dietary intake, or concentrates, metabolites, constituents, extracts, or combinations of any ingredient of these items*.[47] And that the FDA has the burden of proof to show harm before restricting a dietary supplement or a NDI. A required notification does not shift the burden of proof of harm to the manufacturer. Notification is merely a duty to provide information. It is not the manufacturer's duty to prove safety. In fact, NHFA believes from the way that the language in the Draft Guidance is written and the expectations that the FDA suggests therein, that the FDA thinks that the burden of proof is on the manufacturer to prove safety. When really, the only duty the manufacturer has under the law is to provide evidence that establishes that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be

[42] New Dietary Ingredient Notification: Requirement for Premarket Notification [hereinafter Premarket Notification], 21 C.F.R. § 190.6 (1997), http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=32be4fc31c4f2e463b7ee88f97ddf1cd&tpl=/ecfrbrowse/Title21/21cfr190_main_02.tpl.
[43] DRAFT GUIDANCE*, supra* note 2, at §3.
[44] *Id.*
[45] *Id.*
[46] *See supra*, text accompanying note 21.
[47] DSHEA, *supra* note 10, at § 3.

expected by them to be safe.[48] If the FDA disagrees then it must prove otherwise before restricting the supplement.

There are many ways to interpret a statute or a rule. NHFA sees that the FDA is couching the notification for NDIs in a way that implies they are inherently dangerous, instead of realistically couching the Draft Guidance in the context of the need for more enforcement of existing law. NHFA finds this to be hostile to consumers and the dietary supplement industry.

Given that the FDA has a history of: wanting maximum upper limits on dosages of vitamins and minerals; a history of opposing DSHEA; a history of advocating for more regulation on dietary supplements,[49] including taking a long time to promulgate good manufacturing standards;[50] supporting legislation for Adverse Event Reporting without proper causation language in it;[51] a history of supporting global guidelines at United Nations Codex meetings that call for the setting of maximum upper limits on vitamins and minerals in international commerce;[52] it is understandable and not surprising that the FDA is using the Draft Guidance to take an aggressive stand in attempting to interpret existing law in a way that reflects its long held stance on regulation of dietary supplements.

NHFA would like to remind the FDA that NDIs are still first and foremost dietary ingredients sought after and used safely by millions of consumers.

B. The Draft Guidance is a violation of the Administrative Procedures Act (hereinafter APA)[53] because it goes beyond the purpose of an interpretive document and presents revisions that require adherence to the formal Notice and Comment rulemaking procedures of the APA;

FDA's disclaimer in the beginning of the Draft Guidance Document that" "*it does not create or confer any rights for or on any person and does not operate to bind FDA or the public*"[54] becomes meaningless as the Draft Guidance proceeds to lay out a detailed plan for new expectations and requirements for manufacturers and distributors to be in compliance with 21 C.F.R. 190.6 and, therefore, not be adulterated under 21 U.S.C. § 350b. The Draft Guidance brings to mind the words of the Supreme Court in *Appalachian*

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[48] *See* Premarket Notification, *supra* note 42.
[49] *See supra* NHFA Comment Part II(A), at p. 1-14.
[50]Current Good Manufacturing Practices [hereinafter CGMPs], 21 C.F.R. § 111 (2007).
[51] Dietary Supplement and Nonprescription Drug Consumer Protection Act, P. L. 109–462 (Dec. 22, 2006) (codified as amended at 21 U.S.C. 371 et seq.) or Serious Adverse Event Reporting for Dietary Supplements [hereinafter AERs], 21 U.S.C. § 379aa–1 (2007).
[52] JOINT FAO/WHO FOOD STANDARDS PROGRAMME, CODEX ALIMENTARIUS COMMISSION, EXECUTIVE SUMMARY REPORT, Twenty-eighth Session, ALINORM 05/28/41, July 2005, Accessed online Nov. 27, 2011 at: http://www.bing.com/search?q=2005+codex+alimentarius+commissin+alinorm+report&FORM=IE8SRC
[53] Administrative Procedure Act [hereinafter APA], 5 U.S.C. 5 (2004), at § 553. Rulemaking, http://www.archives.gov/federal-register/laws/administrative-procedure/.
[54] DRAFT GUIDANCE, *supra* note 2, at 9.

Power Co. v. EPA when it commented on the meaninglessness of EPA's draft guidance disclaimer, as follows:

> This language is boilerplate; since 1991 EPA has been placing it at the end of all its guidance documents. *See* Robert A. Anthony, supra, 41 duke L.J. at 1361; Peter L. Strauss, Comment, The Rulemaking Continuum, 41 Duke L.J. 1463, 1485 (1992) (referring to EPA's notice as "a charade, intended to keep the proceduralizing courts at bay"). Insofar as the "policies" mentioned in the disclaimer consist of requiring State permitting authorities to search for deficiencies in existing monitoring regulations and replace them through terms and conditions of a permit, "rights" may not be created but "obligations" certainly are-obligations on the part of the State regulators and those they regulate. At any rate, the entire Guidance, from beginning to end-except the last paragraph-reads like a ukase. It commands, it requires, it orders, it dictates. Through the Guidance, EPA has given the States their "marching orders" and EPA expects the States to fall in line, as all have done, save perhaps Florida and Texas. *See Natural Resources Defense Council, Inc. v. Thomas*, 845 F.2d 1088, 1094 (D.C.Cir.1988); *Community Nutrition Inst. v. Young*, 818 F.2d 943, 947-48 (D.C.Cir.1987).[55]

The Draft Guidance includes a profound example of increased requirements for manufacturers and distributors in that FDA expects manufacturers and distributors to submit NDI notifications for every dietary supplement containing a particular NDI, instead of only submitting a notification for each NDI itself. This is an example of the phenomenon of the need for rulemaking because it is an explicit contradiction of FDA's own stated historical expectation for submissions under its own regulation, 21 C.F.R. 190.6, promulgated "to assist industry in complying with DSHEA" and "to implement the FD&C Act's premarket notification requirements for dietary supplements that contain a NDI."[56] The Draft Guidance, now here presented 14 years later, submitted to clarify "when the manufacturer or distributor of a dietary ingredient or dietary supplement should submit a NDI notification to FDA under section 413(a)(2) of the FD&C"[57], does not simply provide an interpretation of the NDI notification requirement but, rather, it creates a new expectation in the notification process entirely. This is problematic because use of a Guidance document to inform industry that FDA expects and requires something that the regulation it is "interpreting" does not expect or require, (i.e., separate notifications for every dietary supplement product comprised of multiple dietary ingredients, one of which is a NDI), is a violation of the APA because such a revision would require adherence to the formal Notice and Comment rulemaking procedures of the APA.[58]

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[55] *Appalachian Power Co. v. E.P.A.,* 208 F.3d 1015, 1020-23 (D.C. Cir. 2000).
[56] 62 Fed. Reg. 49886 (Sept. 23, 1997).
[57] Food Safety and Modernization Act [hereinafter FSMA], Pub. L. 111-353 (2011)
[58] APA, *supra* note 53.

FDA's own 1997 analysis of the impact of 21 C.F.R. 190.6 in 1997

The results of FDA's 1997 analysis of the impact of NDI premarket notification, make it clear that the FDA's current thinking on when to submit an NDI notification constitutes an amendment to, rather than an interpretation of, 21 C.F.R. 190.6 or DSHEA because the number of submissions that would result under compliance with the Draft Guidance is exponentially larger than the number of submissions contemplated by FDA in 1997.[59]

This difference is evidenced by FDA's own "Analysis of Impacts" documents created prior to codification of the NDI regulation at 21 C.F.R. 190.6.[60] Prior to promulgating its Final Rule, the FDA was required to include an "Analysis of Impacts" examining the economic implications of the rule in terms of its effect on small businesses and its cost-benefit trade-offs in general.

In the cost-benefit analysis, the FDA stated that "[in] the most recent year the industry introduced six new ingredients … " and estimated that "the number of new ingredients [will] be 0 to 12 per year."[61] Based on these numbers, FDA concluded that the economic impact of 21 C.F.R. 190.6 would not be significant.[62] This meant the FDA determined that 21 C.F.R. 190.6 was not a "major rule" for the purposes of Congressional Review.[63] Additionally, within its small business analysis, FDA stated that "[it] concludes that the total number of businesses affected by the proposed rule will be no more than the number of new ingredients (estimated to be 0 to 12 per year).[64] This led the FDA to a make another conclusion, similar to the one made in the cost-benefit analysis, that 21 C.F.R. 190.6 would not have a significant impact on substantial number of small entities.[65] Finally, pursuant to the Paperwork Reduction Act, FDA's Final Rule included an "Estimated Annual Reporting Burden" published in the federal register.[66] In this report, the FDA estimated the number of businesses required to submit a NDI notification to be 6 per year, the annual frequency of response to be "1" per year, and, therefore, the total annual responses to be 6.[67]

Since the FDA's economic analysis predicted that the number of notifications per year would be equal only to the number of new ingredients, and since a manufacturer of an NDI would likely market its NDI individually, as well as, market it as a component in one or

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[59] *Compare* 62 Fed. Reg. 184 *with* DRAFT GUIDANCE, *supra* note 2, at IV(B)(c)(1).
[60] Premarket Notification for a New Dietary Ingredient, [hereinafter Final Rule] 62 Fed, Reg. 184 (Sept. 23, 1997), pp 49886-49892, http://frwebgate1.access.gpo.gov/cgi-bin/TEXTgate.cgi?WAISdocID=zLpY5B/1/1/0&WAISaction=retrieve.
[61] *Id.* at p 49890.
[62] *Id.*
[63] *See Id.*; *See also* SMALL BUSINESS REGULATORY ENFORCEMENT FAIRNESS ACT § 804(2) (defining "major rule")(codified as amended 5 U.S.C. 8), http://www.archives.gov/federal-register/laws/small-business/804.html.
[64] Final Rule, *supra* note 64, at p 49891.
[65] *Id.*
[66] *Id.*
[67] *Id.*

more of its combination dietary supplement products, the FDA's 1997 understanding of the premarket notification rule contemplated that a single NDI notification would suffice for every use of the NDI. The FDA cannot rationally say that the Draft Guidance would only result in 0 to 12 notifications. This is why it's alarming that FDA does not consider its current understanding of 21 C.F.R. 190.6, as reflected in the Draft Guidance's requirement of a notification submissions for every dietary supplement containing an NDI, to be a fundamental change to its 1997 understanding of the rule.

It is true that notice and comment requirements do not apply, by virtue of subsection (b)(3)(A) of § 553 of the APA, to FDA's "interpretative rules [and] general statements of policy."[68] However, a Guidance document issued by an agency is not *per se* an interpretative rule simply because the agency says it is.[69]
As the Supreme Court has noted, "APA rulemaking is required if an interpretation 'adopt[s] a new position inconsistent with … existing regulations."[70] This means that "when an agency has given its regulation a definitive interpretation, and later significantly revises that interpretation, the agency has in effect amended its rule, which requires notice and comment."[71]

Although the distinction between legislative rules and interpretative rules or policy statements is described as "tenuous", "blurred", and "enshrouded in considerable smog"[72] it is well established that an agency may not label a substantive change to a rule an "interpretation" simply to avoid the notice and comment requirements.[73] This is why courts will set aside agency Guidance interpreting its rules holding that an "agency's broad interpretation of [a subsection of one of its Rules] effectively amended that subsection without adhering to required rulemaking procedures."[74]

FDA's Draft Guidance, couched as being a "dietary supplement based" guidance instead of "new ingredient based" guidance as it is applied and thus requiring notification for each and every dietary supplement recipe that utilizes a NDI, even if the NDI has already provided a NDI Notification without FDA objection, is an example of rulemaking without the proper public procedures involving notice and comment. And

[68] APA, *supra* note 57, at §553(B).
[69] Community Nutrition Institute v. Young, 818 F.2d 943, 946 (Ct. App. 1987) (disagreeing with FDA's representation that it's "… action levels represented nothing more than nonbinding statements of agency enforcement policy.").
[70] Air Transport Assn. of America, Inc. v. FAA, at 56 (citing Shalala v. Guernsey Mem'l Hosp., 514 U.S. 87, 100 (1995); See also Paralyzed Veterans, at 586 (finding that agency violates APA if it makes a "fundamental change in its interpretation of a substantive regulation without notice and comment.").
[71] Id. (citing Alaska Prof'l Hunters Ass'n v. FAA, 177 F.3d 1030, 1034 (D.C. Cir. 1999)).
[72] Community Nutrition, at 946 (listing cases).
[73] Transport Assn of America v. FAA, 291 F.3d 49, 55 (Ct. App. 2002) (citing Appalachian Power Co. v. EPA, 208 F.3d 10115, 1024 (D.C. Cir. 2000)).
[74] *Id.* at 679 (citing Appalachian Power, at 1028; *cf.* EPA Brief at 46 (admitting that Appalachian Power "was ultimately decided on procedural grounds")).

finally, NHFA points to the words of Richard J. Pierce, Jr. as words of wisdom as the FDA proceeds to offer guidance regarding NDIs:

> The phenomenon we see in this case is familiar. Congress passes a broadly worded statute. The agency follows with regulations containing broad language, open-ended phrases, ambiguous standards and the like. Then as years pass, the agency issues circulars or guidance or memoranda, explaining, interpreting, defining and often expanding the commands in the regulations. One guidance document may yield another and then another and so on. Several words in a regulation may spawn hundreds of pages of text as the agency offers more and more detail regarding what its regulations demand of regulated entities. Law is made, without notice and comment, without public participation, and without publication in the Federal Register or the Code of Federal Regulations. With the advent of the Internet, the agency does not need these official publications to ensure widespread circulation; it can inform those affected simply by posting its new guidance or memoranda or policy statement on its web site. An agency operating in this way gains a large advantage. "It can issue or amend its real rules, i.e., its interpretative rules and policy statements, quickly and inexpensively without following any statutorily prescribed procedures." Richard J. Pierce, Jr., Seven Ways to Deossify Agency Rulemaking, 47 admin. L.Rev. 59, 85 (1995).[9] The agency may also think there is another advantage-immunizing its lawmaking from judicial review.[75]

C. The Draft Guidance is Profoundly and Unnecessarily Burdensome in that:

a. It is an arguable and overly broad interpretation of a short concise statute defining whether an article is a "new dietary ingredient";

b. It is an overly broad interpretation of under what circumstances a manufacturer of an identified NDI would have to provide pre-market notification to the FDA;

c. The amount of evidentiary testing and reporting recommendations suggested attempts to give the impression that the government thinks the burden of proof of safety is shifted from the government onto the manufacturer

d. It puts a severe and undue financial burden on all dietary supplement manufacturers leading to loss of businesses, and

[75] Appalachian Power Co. v. E.P.A., 208 F.3d 1015, 1020 (D.C. Cir. 2000).

e. It demonstrates the government's role as a hindrance, rather than a helper, in protecting consumer access to dietary supplements and the regulation of those products.

a. An arguable and overly broad interpretation of a short concise statute defining whether an article is a "new dietary ingredient";

Regarding the first question as to whether a substance is a NDI, the FDA interpretation increases the number of products that would be considered NDIs by its broad brush interpretations of current law. In addition, FDA fails to set forth in an organized manner how manufacturers can answer this extremely important question as to whether their product is a NDI.

Instead of stating clearly what the definition of a NDI is, the FDA Draft Guidance mixes the definition of a NDI with the legal concept of adulteration and with the second question, whether notification is necessary for a product. This approach is very confusing and misleading to the manufacturer since the adulteration and notification parameters are not applicable if a substance is not a NDI. For example the adulteration statute begins by saying: "*A dietary supplement which contains a new dietary ingredient shall be deemed adulterated under 402(f) unless*….".[76] We surmise from this language that if a dietary supplement does not contain a "new dietary ingredient", then this particular adulteration statute does not apply.

FDA's drafting is confusing. It only refers to the definition of a NDI indirectly, under question and answer format, and relegates the actual definition to a footnote.[77] This is not typical of guidance documents where the law should be clearly laid out as to what the definitions are. In fact, in the entire 86 page document devoted to NDIs, the definition of a "new dietary ingredient" is not fully spelled out. In addition to being mentioned in a question and answer set, the definition is partially referred to in a later flowchart, however, the terms "chemically altered" and "not chemically altered" in the flowchart[78] give the impression that chemical alteration has something to do with defining a substance as an NDI which it does not.[79] Finally, at the end of the document, a partial definition is given with a footnote once again to the statute.[80]

This kind of drafting does not provide guidance to small manufacturers that do not have staff attorneys to interpret a guidance document. The FDA should have clearly shown that, regarding whether a substance is a "new dietary ingredient", the federal law reads:

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[76] 21 U.S.C. 342(f).
[77] DRAFT GUIDANCE, *supra* note 2, at IV(A)(1) n.6.
[78] *Id.* at VIII(A). Appendix A.
[79] DSHEA, *supra*, note 10, at §§3, 8.
[80] DRAFT GUIDANCE, *supra*, note 2, at VII. Definitions.

> *For purposes of this section, the term ''new dietary ingredient'' means 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.*[81]

There are key words in this definition of NDI that become essential for the manufacturer to understand. For example is the term "dietary ingredient" defined in law? Is the term "marketed" defined in law? And the definition does not say "marketed as a dietary ingredient" so, could a substance be marketed as a regular food? Could it be marketed as something else? These terms need to be spelled out in detail after making the public aware of the definition of "new dietary ingredient" so that a person can assess whether his/her product fits within this definition. Instead, the Draft Guidance leaves these important questions, essential to answering the preliminary question of what is an NDI, unanswered.

To begin, the general term "dietary ingredient" is listed in the glossary of the Draft Guidance on page 76 with a legal footnote.[82] For purposes of guiding the public, the federal law definition of a dietary supplement includes what a dietary ingredient is; it reads as follows:

(ff) The term "dietary supplement" -(1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(A) a vitamin;

(B) a mineral;

(C) an herb or other botanical;

(D) an amino acid;

(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or

(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E)[83]

As FDA may note, this definition does not say anything about whether an article is "chemically altered". The issue of chemical alteration comes up later in the legal argument

[81] 21 USC Sec 350b(c).
[82] DRAFT GUIDANCE, *supra*, note 2, n. 52 and accompanying text.
[83] 21 U.S.C. § 321(ff).

as to whether a product is "adulterated" and not fit for sale.[84] So for now let us still discuss whether a substance is an NDI.

The next term, key to whether a product is anew dietary ingredient, is "marketed". FDA does not produce any legal basis for its interpretation of "marketed" or any rationale for indicating that the "new dietary ingredient" had to be marketed as a "dietary ingredient"[85] as opposed to being marketed as food "fit for human consumption."[86] Since the statute is silent on the definition of "marketed" and what the dietary ingredient was marketed as, FDA produces its opinion only; and it's an industry and self-health care limiting one.

FDA's interpretation of "marketed" could lead to more substances being deemed NDIs and, in some instances, requiring further pre-market notification. For example, FDA states that an ingredient marketed as a conventional food before October 15, 1994, will be considered an NDI: "*The marketing of an ingredient as a conventional food, as a drug, or for any other non-food use cannot be used as evidence that an ingredient is not a NDI.* [87] Is the FDA saying that if a manufacturer decides to take a substance that has historically been marketed in the U.S. as a conventional food and use it in its dietary supplement recipe, it then becomes a NDI? This would be absurd.

Another example of the FDA giving its own interpretation of this issue is in its answer to

Question IV(A)(3)**Is an ingredient that was used to make a conventional food marketed before October 15, 1994, a NDI if the ingredient was not a dietary ingredient marketed in the U.S. before October 15, 1994?** The FDA responds:

> Yes. The use of an ingredient in a conventional food before October 15, 1994 does not determine whether the ingredient is a NDI. What matters is whether the ingredient was marketed as a dietary ingredient -- meaning in or as a dietary supplement, or for use in dietary supplements -- in the U.S. before October 15, 1994. Therefore, an ingredient that was used to make a conventional food before October 15, 1994 is a NDI unless the ingredient was also marketed as a dietary ingredient in the U.S. before October 15, 1994. (See questions IV.A.6 and IV.A.9 for FDA's views on the meaning of "marketing" and "dietary ingredient" in the NDI definition.)[88]

This interpretation of what "marketing" means to the FDA has led to some bizarre, and in the opinion of NHFA, unfair, results. For example, the case of liquid Vitamin B6, a

[84] *See* 21 U.S.C. § 350b.
[85] DRAFT GUIDANCE, *supra* note 2, at IV(A)(2).
[86] *See* 21 U.S.C. § 350b.
[87] DRAFT GUIDANCE, *supra* note 2, at IV(A)(9).
[88] DRAFT GUIDANCE, *supra* note 2, at IV(A)(3).

product that millions of Americans utilize as an important dietary supplement.[89] Here, in part, is what the FDA had to say when it decided to prohibit the sale of Vitamin B6 because a company wanted to move it forward under a new drug application:

> *The fact that pyridoxamine is authorized for investigation as a new drug does not automatically exclude it from being a dietary supplement. This is because under the prior market clause in 21 U.S.C. 321(ff)(3)(B)(ii), pyridoxamine would still qualify as a dietary supplement if it had been "marketed as a dietary supplement or as a food" before being authorized for investigation as a new drug on September 1, 1999.*
>
> *It is not necessary to show that an article has been marketed as a food or dietary supplement in isolation to establish prior marketing, however. A component of a product may, under certain circumstances, constitute an "article ... marketed as a dietary supplement or as a food." The relevant inquiry in determining whether a component present in a marketed product qualifies as such an article for purposes of the prior market clause is whether, in marketing the product, a firm was also marketing the component itself as a food or as a dietary supplement by, e.g., making claims about the component or otherwise highlighting its presence in the product. See Pharmanex v. Shalala, 2001 WL 741419, at *4 & n.5 (D. Utah March 30, 2001). For example, in Pharmanex, the firm marketed lovastatin, a component of its red yeast rice product Cholestin, by promoting the lovastatin content of Cholestin. ld. at *3.*
> *The comments submitted to this proceeding in response to the November 18, 2005 Federal Register notice do not establish that pyridoxamine was marketed as a food or a dietary supplement before the !ND went into effect. Two comments stated that pyridoxamine is present in various common foods, such as frozen fish, fresh and dried yeast, milk, eggs, beef, chicken, and pork. One of these comments stated, "[F]or decades U.S. consumers have regularly bought and consumed Brewer's Yeast for its Vitamin B6 content and benefits." However, neither of these comments provides any evidence that any of the foods mentioned were promoted specifically as pyridoxamine sources or otherwise marketed for their pyridoxamine content. Moreover, neither comment contains any documentation that these foods were marketed with reference to any property that they might have as a consequence of their pyridoxamine content. Thus, even if these foods contain high levels of pyridoxamine, that fact alone does not constitute evidence that pyridoxamine was marketed as a food or a dietary supplement within the meaning of DSHEA's prior market clause.*

[89] *See generally*, FDA Response to Biostatum, Inc. (Kathleen M. Sanzo, Esq.) – Petition Partial Approved and Denial [hereinafter Response to B6 Petition], Docket No. FDA-2005-P-0259 (formerly Docket No. 2005P-0305) (Jan. 22, 2009), http://www.regulations.gov/#!documentDetail;D=FDA-2005-P-0259-0004.

> *The mere presence of a substance authorized for investigation as a new drug as a component of a product found in the food supply does not by itself establish that the substance was ·"marketed" within the meaning of21 U.S.C. 321(ff)(3)(B)(ii). Rather, as discussed above, circumstances must establish that in marketing a product containing such a component, a firm was also marketing the component. The plain language of section 321(ff)(3)(B)(ii) preserves dietary supplement status only for those articles approved or authorized for investigation as new drugs that were "before such approval. . . or authorization marketed as a dietary supplement or as a food" (emphasis added). Judging by Congress's choice of language, Congress did not intend to preserve dietary supplement status for articles that were merely present in the food supply before being approved or authorized for investigation as new drugs. The prior market clause requires the article to be marketed "as", not merely "in," a food or dietary supplement. Moreover, Congress used the phrase "present in the food supply" elsewhere in DSHEA, but chose not to use the phrase in the prior market clause. Compare 21U.S.C. 350b(a)(I) with 21 U.S.C. 321(ff)(3). To argue that the mere presence of a substance in the diet preserves dietary supplement status would mean that even a few molecules of a substance never before recognized as therapeutically beneficial would, if present in some food, defeat any incentives for pharmaceutical manufacturers to develop such a substance into a new drug.*
>
> *The record before the agency contains no convincing evidence that pyridoxamine was marketed as a dietary supplement or food before it was authorized for investigation as a new drug.*[90]

Another FDA interpretation that could increase the number of products considered NDI's unnecessarily is that of claiming a need for each individual manufacturers or distributor to provide extensive proof of marketing,[91] while rejecting trade association and industry lists and input on the history of marketed products[92] and even stating that FDA would reject historical Affidavits where FDA is sure that a person is "honestly stating his or her present beliefs".[93]

First, FDA states its expectations of manufacturers in terms of providing evidence of marketing when responding to Question IVA(8), **What documentation would I need to show that my dietary ingredient was marketed prior to October 15, 1994?,** as follows:

> Documentation to show that a dietary ingredient is not a NDI should consist of written business records, promotional materials, or press reports with a contemporaneous date prior to October 15, 1994. Examples include sales records, manufacturing records, commercial invoices, magazine

[90] *Id*, at (C)(2).
[91] DRAFT GUIDANCE, *supra* note 2, at IV(10).
[92] *Id.*
[93] *Id.* at IV(8).

> advertisements, mail order catalogues, or sales brochures. Documentation should include adequate information to establish that marketing took place in the U.S., the identity (e.g., chemical or botanical name) and form (e.g., ground herb, water extract, oil) of the marketed ingredient, and whether the ingredient was marketed as a dietary ingredient or for some other purpose.[94]

After FDA spells out what it believes to be evidence of marketing before 1994, it then discloses that it has received lists from trade associations and industry groups of "old dietary ingredients".[95] Yet, it goes on to admit that the FDA has not taken any action to verify the lists provided to them.[96] Two lists that came from trusted leaders in the industry included:

1. National Nutritional Foods Association; NNFA List of Dietary Supplement Ingredients In Use Before October 15, 1994 (April 26, 1996). Docket No. FDA-2005-P-0259 [Document ID: FDA-2005-P-0259-0012].[97]
2. Council for Responsible Nutrition; CRN List of Dietary Ingredients "Grandfathered" Under DSHEA (September 1998). Docket No. FDA-2005-P-0259 [Document ID: FDA-2005-P-0259-0010].[98]

NHFA now asks, why has FDA not taken immediate action to verify these lists coming from reputable sources in order to support and serve manufacturers in their process of application so that they do not all individually continue to bring that information forward?

Instead of a helpful approach and working with the industry, FDA insists in its answer to Question IV(A)(10) that it requires redundant submissions from every manufacturer of distributor planning to use an ODI. When asked, **"Is there an authoritative list of dietary ingredients that were marketed prior to October 15, 1994 (a so-called "grandfathered list" or "old dietary ingredient list")?", FDA states** as follows, in part: **"**No. Each supplement manufacturer or distributor is responsible for establishing that the dietary ingredients in its dietary supplements comply with the NDI notification requirements.…"[99]

This approach appears hostile to common sense and demonstrates a lack of willingness on the part of FDA to endeavor to create an endorsed list of verifiable supplements that will not be considered NDIs and which manufacturers could easily access.

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[94] *Id.* , *supra* note 2, at IV(A)(8).
[95] *Id.*, supra note 2, at IV(8).
[96] *Id.*, supra note 2, at IV(10).
[97] DRAFT GUIDANCE, *supra* note 2, at n.8, and accompanying text.
[98] *Id. supra* note 2, at n.9 and accompanying text.
[99] *Id.* at IV(10).

Requiring each individual manufacturer to continually provide this type of evidence to the FDA when it has already been submitted and accepted by the FDA on behalf of other companies is a clear example of FDA's bad faith intentions in carrying out its role as servant to the people of the United States.[100]

In summary, whether a product is a "new dietary ingredient" is a foundational question which will determine the next steps for manufacturers to take in working to comply with current laws and regulations. It is a question of both legal analysis and common sense. It is also a question that to which the FDA could provide great assistance by working with its vast information base and relationships to create the beginnings of, at least, a partial list of substances considered verifiably to be marketed before 1994.

If FDA disagrees with a company's decision to market a product because the company determines that the product does not contain a NDI, then NHFA believes that the government bears the burden of proof to show that the substance is a NDI requiring notification submission and that the product is therefore adulterated.

b. The Draft Guidance is an overly broad interpretation of the circumstances under which a manufacturer of an identified NDI would have to provide pre-market notification to the FDA;

In the instance that both manufacturer and FDA agree that a product is a NDI, then the next question becomes whether or not the NDI would be considered adulterated or in need of a pre-market notification to the FDA specifying the reasons why the manufacturer thinks the NDI is reasonably safe.[101] Once again, FDA's interpretative answer to this question is very feasibly requiring many more notifications than are currently taking place. If enforced, this interpretation could change the entire face of the dietary supplement industry.

First, DSHEA established two new areas of law having to do with adulteration of a dietary supplement containing a new dietary ingredient.[102] The Draft Guidance fails to note that the two main laws are adulteration laws and goes right to the NDI and notification questions instead of providing the foundational explanation of the adulteration laws. In addition FDA should have shown in the Draft Guidance where the burden of proof lies regarding proving harm before restricting a dietary supplement in the market, and how adulteration fits in with pre-market notification requirements. NHFA notes that the FDA does not mention its burden of proof in the Draft Guidance. Possibly because it wants to characterize the pre-market *notification* process in 350(b)(2) more as a pre-market application for market approval with the burden to prove safety on the manufacturer before

[100] *Id.* at IV(10).
[101] *See generally*, 21 U.S.C. §§ 342(f), 350b(a)(2). (
[102] DSHEA, *supra* note 10, at §§ 4,8; *See also Id.*

a product goes to market. However, that is not what DSHEA nor the citizens asked FDA to do![103]

The first adulteration law created by DHSEA established a new section, Section 342(f), in the adulteration food code just for dietary supplements and NDIs.[104] This section spells out when a dietary supplement or a NDI would be considered an adulterated food and the fact that the FDA has the burden of proof of harm when it comes to adulteration as follows:

> *A food shall be deemed to be adulterated –[...]*
> *(f) Dietary supplement or ingredient: safety*
> *(1) If it is a dietary supplement or contains a dietary ingredient that -*
> *(A) presents a significant or unreasonable risk of illness or injury under -*
> *(i) conditions of use recommended or suggested in labeling,*
> *or*
> *(ii) if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use;*
> *(B) is a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury;*
> *(C) the Secretary declares to pose an imminent hazard to public health or safety, except that the authority to make such declaration shall not be delegated and the Secretary shall promptly after such a declaration initiate a proceeding in accordance with sections 554 and 556 of title 5 to affirm or withdraw the declaration; or*
> *(D) is or contains a dietary ingredient that renders it adulterated under paragraph (a)(1) under the conditions of use recommended or suggested in the labeling of such dietary supplement. In any proceeding under this subparagraph,* ***the United States shall bear the burden of proof on each element to show that a dietary supplement is adulterated****.[bold added] The court shall decide any issue under this paragraph on a de novo basis.*[105]

The second adulteration related law is at Section 350b, where the definition of a "new dietary ingredient" is located.[106] The first part leading up to the definition starts out right away by stating that a dietary supplement containing a new NDI would be considered adulterated unless it met certain criteria:

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[103] See, supra, Part IA, at p.1-14; Institute of Medicine, Dietary Supplements: A Framework for Evaluating Safety, 24 (2005) (explaining that the 75 day premarket notification submission of information requirement for manufacturers of dietary supplements that contain new dietary ingredients "is not a premarket approval process." , http://www.nap.edu/openbook.php?record_id=10882&page=24.
[104] DSHEA, supra note 10, at §4 (codified as amended at 21 U.S.C. § 342).
[105] *Id.*
[106] *Id.* at §8(codified as amended at 21 U.S.C. § 350(b)).

> *A dietary supplement which contains a new dietary ingredient shall be deemed adulterated under section 402(f) unless it meets one of the following requirements:*
> *(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.*
> *(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.*[107]

And if part (2) of § 350(b), above, applies, then manufacturer or distributor of that supplement, or of the NDI, could look to 21 C.F.R. 190.6, the rule that FDA made to help implement § 350b, for further guidance.[108]

It is the interplay between these two adulteration laws which leads to the conclusion that, even though a dietary supplement containing a NDI might not be considered adulterated under § 342 (i.e., does not present significant or unreasonable risk of illness or injury), it could still be subject to the adulteration standards of a dietary supplement or NDI in § 350(b)(1) (i.e., being present in the food supply) or § 350(b)(2) (requiring pre-market notification). The provisions of these two laws present four possible scenarios for a manufacturer facing entering a NDI into the market and four corresponding regulatory responses by the FDA.

Scenario one: the NDI is not deemed to be an adulterated food under Section 342.

In general, there is the possibility that foods may be marketed to consumers that are not fit for safe human consumption. The food code's main adulteration law, displayed earlier in § 342, gives the FDA a tool and helps to protect consumers from harm from adulterated food products.[109] The adulteration food code addresses dietary supplement or ingredients specifically and provides parameters for manufacturers to abide by.[110] Given the presumption of safety that dietary supplements hold, the dietary supplement adulteration law clearly states that the United States bears the burden of proof on each element to show that a dietary supplement is adulterated.

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[107] *Id.*
[108] Premarket Notification, *supra* note 42.
[109] 21 U.S.C. § 342.
[110] *Id.*

However, the recent Court cases regarding Ephedra are examples of the complexity and the importance of the wording of the food adulteration law regarding burden of proof issues when restricting dietary supplements.[111] In the case of *Nutraceutical v. Crawford*, a case having to do with whether ephedrine-alkaloid dietary supplements (EDS) pose an unreasonable risk of illness or injury at 10 milligrams or less a day, the wording of § 342 (f)(1)(A) was pivotal, being interpreted differently by two courts.[112] The disagreement between the courts hinged on the lower Court's support of a straightforward harm standard and the Appeals Court's acceptability of the use of the risk-benefit analysis for Ephedra used for toxic drugs analysis.[113] This all had to do with the interpretation of "*significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling*" test.[114] Reading over the positions of FDA in those cases, it is clear that it has a wish to interpret DHSEA as if dietary supplements are dangerous substances requiring pre-market toxic substance risk benefit analysis rather than having the presumption of safety in recommended dosages.[115]

Scenario two: the NDI has been present in the food supply.

Even if the manufacturer is certain that the product will not be a dangerous dietary supplement under the general food adulteration law,[116] manufacturers who wish to market a dietary supplement containing what they know to be a "new dietary ingredient" must abide by Section 350(b)(1) and (2).[117] They can do this after assessing first whether a food was *present in the food supply as an article used for food in a form in which the food has not been chemically altered.*[118] Assuming that the substance is a NDI that has not been marketed before 1994, when asked the first part as to whether it has been in the food supply, the FDA describes a narrow approach and goes back to the concept of marketing (which they used to determine whether something was a NDI in the first place) to see if something is present in the food supply; the Draft Guidance says that FDA will consider it *in the food supply* if it has been "legally marketed as a conventional food" either in the U.S. or outside the U.S..[119] But FDA does not comment on what other types of ways a person could establish whether a product is in the food supply.

NHFA argues that marketing is not the only way to show something was, or is, in the food supply and that the vast majority of items in the natural world that are not inherently dangerous for human consumption have at one time or other been "present in the food supply" and the threshold of showing that fact is much lower than the marketing threshold

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[111] DRAFT GUIDANCE, *supra* note 2, at IV(10).
[112] Compare: *Nutraceutical Corporation v. Crawford*, U.S. District Court, Utah (D.C. No. 2:04-CV-00409-TC) April 13, 2005, and; *Nutraceutical Corp. v. Eschenbach*, 459 F.3d 1033 (10th Cir. 09/17/2006)
[113] *Id.*
[114] *Id*.
[115] *Id.*
[116] 21 U.S.C. § 342.
[117] 21 U.S.C. § 350b.
[118] *Id.* at (b)(1).
[119] DRAFT GUIDANCE, *supra* note 2, at IV(B)(2).

and evidence requirement of marketing because it opens up all of the sociological and historical data available to manufacturers.

Scenario 3: the NDI was present in the food supply without chemical alteration

But even if the manufacturer and FDA agree that the NDI has been in the food supply at a particular time in history, there is a further test: whether, when it was present in the food supply, was it "chemically altered".[120]

The test as to whether something has been chemically altered is extremely important to a manufacturer because the answer will dictate whether the product will get bumped into the next section of law requiring a premarket notification after concluding "Yes" to both (1) whether the product is an NDI, and (2) whether the product is present in the food supply.[121]

The FDA sets out a broad field of opinion as to whether something is chemically altered; for example: *any process that makes or breaks chemical bonds; including use of solvents other than water or aqueous ethanol to make an extract; high-temperature baking or cooking of a previously uncooked ingredient; fermentation using a different medium from the one used to make conventional foods in the food supply; or use of a botanical ingredient that is at a different life stage than previously used, such as making an extract from unripe rather than ripe apples.*[122]

The FDA also sets out what it would not consider "chemical altered" under the adulteration 350(b) section.[123] To enlighten the public as to the foundations of FDA's "not chemically altered" conclusion we offer the following information:

Immediately before DSHEA was passed a final amendment was added that stated what Congress believed to be the final clarifying amendment. This amendment addressed "chemical altered" as used in section 350(b)(1). The FDA Draft Guidance refers to this agreement in footnotes[124] but, for purposes of guiding the public, it reads as follows:

> *"Statement of Agreement*
>
> *This statement comprises the entire legislative history for the Dietary Supplement Health and Education Act of 1994, S. 784. It is the intent of the chief sponsors of the bill (Senators Hatch, Harkin and Kennedy, and Congressmen Richardson, Bliley, Moorhead, Gallegly, Dingell, Waxman) that no other reports or statements be considered as legislative history for the bill.*

[120] 21 U.S.C. § 350b(1).
[121] *Id.*
[122] DRAFT GUIDANCE, *supra* note 2, at IV(B)(4).
[123] *Id.* at IV(B)(3).
[124] *Id.* at n.10.

1. The bill does not affect the Food and Drug Administration's existing authority under the Federal Food, Drug and Cosmetic Act to prohibit the import or sale of any product marketed as a drug in a foreign country.

2. In section 201(ff)(3)(B)(ii), added by section 3 of the bill, the term `substantial clinical investigations' does not include compassionate investigational new drug applications or an investigational new drug application submitted by a physician for a single patient.

3. Section 403B, added by section 5, does not apply to a summary of a publication other than an official abstract of a peer-reviewed scientific publication.

4. Section 403(r)(6)(A), added by section 6, does not permit premarket approval or require premarket review by the FDA of any statement permitted under that provision.

5. In section 413(a)(1), added by section 8, the term `chemically altered' does not include the following physical modifications: minor loss of volatile components, dehydration, lyophlization, milling, tincture or solution in water, slurry, powder, or solid in suspension.

Mr. HATCH. Mr. President, any statement I could make would pale in comparison to the elation I feel over passage of S. 784 tonight.

Our compromise bill is a tremendous victory. It is a victory for the American people. It is a victory for consumers who want to lead healthy lifestyles.

And it is a victory for the legislative process, for it shows that the Congress can act decisively to affirm the desires of the American public.

I want to thank each and every one of the individuals who have made this legislation a possibility."[125]

As to what would be considered chemically altered in today's world of dietary ingredients, NHFA encourages FDA to listen carefully to the industry experts in their evaluation of this question. Rather than resorting to narrow interpretations that do not include common sense, such as, whether a ripe or a unripe apple is used in a product,[126] FDA is challenged to present a good faith effort to avoid creating unnecessary barriers to market, in alignment with the foundational intentions of DSHEA. And NHFA encourages manufacturers to have their reasons thought out to conclude that their product was present in the food supply in a form that was not chemically altered.

[125] Statement of Agreement, 140 Cong. Rec. S14801 (daily ed. Oct. 7, 1994).
[126] DRAFT GUIDANCE, *supra* note 2, at IV(B)(4).

Regarding burden of proof, if the manufacturer concludes he/she is within 350(b)(1) (in food supply and unaltered) and goes ahead and markets without doing the 350(b)(2) notification, then the question arises: What if FDA disagrees? It is the contention of NHFA that the FDA would have to prove otherwise given the many elements and historical data of DSHEA addressing dietary supplements as foods with the burden to show harm on the FDA before marketing.

Scenario four: the NDI requires pre-market notification of the manufacturer's or distributor's basis for believing it is safe

Even though the FDA has the burden of proof regarding the safety of dietary supplements and NDIs, manufacturers are careful to meet the first test of adulteration regarding potential for causing illness and injury and the second set of tests regarding whether it has been in the food supply unaltered or requiring pre-market notification.[127] That is because manufacturers are working to provide successful, safe, and nutritious products to consumers, and because they are fully informed of the law and that if the FDA was able to prove the product is *"adulterated under paragraph (a)(1) under the conditions of use recommended or suggested in the labeling of such dietary supplement",* it could feasibly be restricted or taken off the market.[128] Manufacturers also function under the compliance requirements of the extensive Good Manufacturing Practices[129] and the new Adverse Event Reporting laws.[130]

DSHEA requirements were meant to involve a simple notification process, *not* a convoluted ingredient approval process.[131] In other words, the implication in DSHEA was *not* that the FDA would require supplement manufacturers to submit extensive applications for ingredient approval, but simply that manufacturers would notify the FDA that they are using of a new ingredient that is presumed to be safe until proven dangerous, *not the other way around as the FDA is proposing*.[132]

The public is reasonably negatively responding to the Draft Guidance because instead of clarifying a simple method of notification as it was supposed to do, FDA's Draft Guidance distorts the NDI notification process by "turning it into a type of regulatory approval process, similar to what drug companies are required to complete in order to get new drugs approved."[133]

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[127] See generally, 21 U.S.C. §§ 342, 350b.
[128] *Id.*
[129] See generally, CGMPs *supra* note 50.
[130] See generally, AER Requirements, *supra* note 51.
[131] *See* Premarket Notification, *supra* note 42.
[132] *Id.*
[133] Ethan A. Huff **,** *Take action NOW to stop FDA from turning your vitamins and supplements into unapproved 'food additives'* ,
http://doctorapsley.com/FDAAlerts.aspx

And finally, even if a manufacturer's product contains an NDI, and even if it fails the "in the food supply" and the "chemical alteration" tests of 21 U.S.C. § 350b, thus requiring pre-market notification to FDA, the FDA's interpretation of who then would need to provide a pre-market notification is astoundingly broad because it not only (1) requires the manufacturer of the NDI to provide notification, but it also (2) requires the manufacturer or distributor of the dietary supplement that the NDI will go into to provide a notification as well.[134]

These multiple notifications are the result of a shift in the law, jumping from the "ingredient" focus of DSHEA to the "dietary supplement" focus of the Draft Guidance. This shift loops thousands of dietary supplements into the pool of mandatory pre-market notifications because, even if the NDI has successfully met the "reasonable safety" notification requirement for a NDI, if companies use that ingredient in a number of dietary supplement combination recipes, they would have to submit a notification each time the ingredient was used.

Not only is this a violation of the APA as described above,[135] but this is where the entire legal treatment of NDIs displays the true politics of the compromises made in the passage of DSHEA. If a substance is pre-DSHEA it is considered a dietary supplement presumed to be safe with no pre-market notification needed including need for notifications of any of the many ways to utilize ingredients and dietary supplement recipes. Yet, if you take that same dietary supplement and add a green apple in the recipe instead of a ripe apple, the supplement supposedly becomes subject to a cascading set of laws and regulations that appear to have some of the same overtones as drug regulations despite clearly not being justified by safety concerns.

The Draft Guidance lists circumstances of when a manufacturer or distributor would need to submit a pre-market notification.[136] That list brings all of the drug-like considerations into play, as if new dietary ingredients.[137]

For example:

Drug Terminology – Dosage Matters: The FDA rational for needing a notification if the amount of a NDI in a daily intake recommendation is higher, smacks of drug-like treatment. The Proxmire Amendment of 1976 prohibited the FDA from establishing maximum limits on the potency of vitamins or minerals or regulating them as drugs based solely on their potency.[138] And DSHEA was passed with this maxim in mind that potency should not be, in and of itself, a presumption of danger, and so the FDA has the burden to show harm under *conditions of use recommended or suggested in labeling.* So how is it

[134] Draft Guidance, supra note 2, at IV(C)(2).
[135] *See*, *supra*, Part I(B), at p. 14-18.
[136] Draft Guidance, supra note 2, at IV(C)(1).
[137] *Id.*
[138] Proxmire Amendment, *supra* note 18.

that the FDA has the right to target increased dosage as a way to hook more ingredients into the notification laws?

Drug Terminology – Looking for Ingredient interactions: The FDA rational for each dietary supplement using the same safe dietary ingredient in the same amount, but needing to know whether there were varying ingredients in the recipe is a drug-like concept. A manufacturer of pre-DSHEA dietary supplements without new dietary ingredients can mix and match their ingredients. That is because they are considered foods and presumed to be safe at the dosage level recommended. The concept of mixing foods in recipes is age old and should not be treated like drug interactions. New dietary ingredients that have provided notification of reasonable safety should be treated similarly as a food, able to be used in any dietary supplement recipe.

Drug Terminology – Target Populations: The FDA's burden to show harm under conditions of use recommended or suggested in labeling is just that: it is the FDA's burden to show harm, and not the manufacturer's burden to do the work of the FDA for them. These are foods, dietary ingredients, they are not inherently toxic drugs. There are many categories of populations in the world that are impacted by food as well as drugs differently. But food is food, and people make choices. And populations choose their foods. And if there is a new ingredient that requires notification and the manufacturer has disclosed information that they are aware of on a particular population, then if a manufacturer wants to market to a different population, they should be able to do that without a further notification because all people will want access to the dietary supplement. By requiring further notification for additional populations just encourages manufacturers to not say anything about population and go with the FDA fall-back: "*For purposes of review, the highest described serving size and number of servings with a duration of daily lifetime use by all age groups and other populations will be assumed, unless the notification specifies otherwise.*[139] NHFA's view is that all foods are for everyone and we need different ones at different time because nutrient-dense foods bring different benefits to the body and function in unique ways to restore and maintain health.

c. The amount of evidentiary testing and reporting recommendations suggested by the FDA is an attempt to overwhelm and instill fear in manufacturers and gives the impression that FDA thinks it can shift the burden of proof of safety from the government to the manufacturer.

NHFA's mission, to protect consumer access to options in health care, here now aligns with comments being presented by many industry leaders of trusted products when providing key feedback regarding the evidentiary expectations of FDA.[140] FDA should

[139] Draft Guidance, supra note 2, at V(A)(4).
[140] NHFA, Mission, http://www.nationalhealthfreedom.org/nhfa/aboutNHFA/nhfa_mission_statement.html.

listen carefully to comments from industry leaders in regard to their concerns about FDA's suggested evidentiary testing and reporting recommendations.[141]

NHFA urges FDA to stop action on the Draft Guidance and redraft with the following facts in mind: these products are dietary ingredients defined by law to be regulated as foods and they should not be over-regulated and treated as drugs requiring in-depth safety pre-market approval.[142] NHFA requests that any redraft done by FDA honor the notification system of 21 C.F.R. 190.6 which alerts FDA of pre-market entry and allows FDA to follow-up if it has further concerns.[143]

In addition NHFA requests that FDA take into consideration small companies providing unique products on which consumers depend. These companies are counting on introducing natural safe ingredients into the market under the *notification* system of 21 C.F.R. 190.6 as opposed to under the Draft Guidance's new drug-like "approval" process. All in all, NHFA is aware that small and large dietary supplement companies are providing, without harm to consumers, excellent products in compliance with laws and regulations.

The FDA should not try to scare and overwhelm product companies into providing FDA with information. The attempt to instill fear is evidenced throughout the numerous questions and answers on evidentiary and reporting requirements in which the FDA insists manufacturers provide FDA with information that is in excess of that necessary to substantiate a determination of reasonable safety.[144] The attempt to shift the burden of proof is demonstrated in requests for evidence, such as: (1) information regarding substances that are not the subject of the NDI notification, (2) referring to European Union standards of 25 years history of use, a Union that considers dietary supplements to be presumed dangerous requiring pre-market approval; and (3) requiring human and clinical studies whenever history of use differs, even in minimal ways, from the proposed use of the NDI, or else the manufacturer risks a determination that its notification will be deemed incomplete. These requests seek evidence of the type which the FDA would have to produce if objecting to a notification's basis for reasonable safety. Below, NHFA demonstrates how FDA's coverage of and request for evidentiary and reporting information in the Draft Guidance are arbitrary, overwhelming, and verge on improper burden-shifting.

(1) information regarding substances that are not the subject of the NDI notification:

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[141] *See* generally, Docket Folder contents for Docket No. FDA-2011-0376, available at http://www.regulations.gov/#!searchResults;rpp=10;po=0;s=fda-2011-d-0376.
[142] *See*, *supra*, NHFA Comment Part IIA(a), at p. 5-14.
[143] Premarket Notification, *supra* note *42*.
[144] DRAFT GUIDANCE, *supra* note 2, at VI (presenting 72 questions and answers, which includes 19 questions addressing what information should be included in a notification, as well as, 43 questions and answers about the history of use or other evidence of safety).

The Draft Guidance asks manufacturers and distributors to submit information not required under 21 C.F.R. 190.6 when FDA asks for information regarding: (i) different chemical forms of the NDI, (ii) all other ingredients to be marketed with the NDI including those governed under separate FDA rules and regulations, and (iii) antibiotic resistance and other genetic information.

Draft Guidance Question and Answer VI(A)(7) provides: "*What additional chemistry information should I submit if my ingredient is a salt?* [Answer:]…*Specific discussion of whether different salt forms have different toxic properties also should be included*…." [145]

Manufacturers should not be asked to provide FDA with information on molecules that are not the subject of the notification because the notification in 21C.F.R. 190.6 does not require a manufacturer to provide information about ingredients other than the one the manufacturer intends to market.[146] There is no basis for the manufacturer to study all other salts of a substance, let alone provide FDA with a discussion of the toxicology of them, unless the manufacturer believes it a volatile salt or knows of another reason relevant to its basis of safety. Further, and for the same reasons, if the salt form of the NDI doesn't have any toxic properties, then the manufacturer should not need to provide toxicology information on the other salt forms.

Those manufacturers who source ingredients from an ingredient supplier are likely to receive product specifications from the supplier specific to their salt. Requiring them to seek out additional information about substances they do not wish to market, is overwhelming and outside the requirements of 21 C.F.R. 190.6.

A second example of FDA requesting information beyond the scope of 21 C.F.R. 190.6 is FDA's response to Question VI(C) (3), "***What should I include in my dietary supplement Safety Narrative?"***[147] The FDA responds that, for supplements containing dietary ingredients other than the NDI, the notification's Safety Narrative section should identify an overwhelmingly long list of items such as:

> *the NOAEL and Acceptable Daily Intake (ADI) for each ingredient (see questions VI.C.4 and VI.C.5), describe the toxicity data or adverse events that were the basis for determining the NOAEL, state the basis for the margin of safety for each ingredient…*[And,] "*…[f]or each dietary ingredient other than the NDI, … evaluat[ion of] known safety concerns and descry[ption of] how the notifier concluded that the combination of ingredients can reasonably be expected to be*

[145] DRAFT GUIDANCE, *supra* note 2, at VI(A)(7).
[146] Premarket Notification, *supra* note 43.
[147] DRAFT GUIDANCE, *supra* note 2, at VI(C)(3).

> *safe*…[And that a manufacturer should]"…*describe the function of each food additive, color additive and GRAS substance (i.e., each non-dietary ingredient), including the technical effect and the quantity needed to achieve that technical effect t… [and]… [i]f any ingredient in the dietary supplement is present at a level close to the ADI, the presence of that ingredient from other sources in the diet should also be addressed*.[148]

FDA requirements of submitting and discussing evaluative information, chemical analysis, toxicology data and safety concerns for ingredients that are not NDI's and which are governed by their own set of safety regulations for proper use, just because they're present in the recipe that includes an NDI is overwhelming. FDA also overwhelms industry by including requirements for submitting information regarding pre-1994 ingredients or approved food additives and GRAS substances,[149] and of discussing the presence of ingredients from other sources in the diet "*if any ingredient in the dietary supplement is present at a level close to the ADI"*,[150] are far beyond the scope of 21 C.F.R. 190.6's request for information that constitutes the manufacturer's basis of reasonable safety for its NDI.

Another example of overwhelming and improper information gathering is:

- Question VI. B. 42: "***What information should I submit to demonstrate the safety of a microbial NDI (live or killed)?***" The FDA response provides that: "*You should document resistance to any clinically relevant antibiotics, and if applicable, the genetic nature of the resistance. If the microbial NDI is resistant to any clinically relevant antibiotics, it is also recommended that you perform an assessment of the ability of the antibiotic resistance genes to mobilize and transfer to human pathogens under the conditions of use of the dietary supplement.*"[151].

Manufacturers are able to document resistance of a microbial NDI to any clinically relevant antibiotic by doing basic sensitivity testing. And most microbials are sensitive to some antibiotics and resistant to others. One would think that providing the FDA with information regarding whether a microbial is sensitive to the relevant antibiotics in addition to whether a microbial has complete resistance, is **not** sensitive to any antibiotics but rather resistant to all relevant antibiotics, would be important. Conversely, requesting genetic information regarding all microbial resistance to antibiotics when there is full knowledge that the microbial is able to be managed and is sensitive to relevant antibiotics is unnecessary and overwhelming.

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[148] *Id.*
[149] *Id.*
[150] *Id.*
[151] *Id.* at VI(B)(42).

If FDA wishes to understand why a particular microbial is resistant to a particular antibiotic and explore the genetic nature of the resistance and the "assessment of the ability of the antibiotic resistance genes to mobilize and transfer to human pathogens"[152] under the condition use of the dietary supplement, given FDA's vast experience with the drug industry, then FDA can proceed to gain that information by other means. This information is an improper request from industry under 21 CFR 190.6it is not relevant for showing reasonable safety of a microbial.

(2) arbitrary adoption of European Union standard of 25 years history of use as FDA's definition;

FDA's adoption of the European Union standard is arbitrary, overwhelming, and verges on burden shifting because (i) the EU's food supplement laws have a burden of proof that is dis-analogous to that in the U.S.,[153] (ii) the adoption introduces new terms that FDA does not define and (iii) the adoption impacts negatively the clarity of 43 answers in the Draft Guidance.

The Draft Guidance says FDA will look to the EU standard when evaluating the reliability of history of use data.[154] The EU standard provides: "*that the safety of the food in question is confirmed with compositional data and from experience of use and continued use for at least 25 years in the customary diet of a large part of the population of a country*".[155] FDA tells manufacturers that the European Union's 25 year threshold is FDA's "minimum" for establishing a history of safe use.[156]

(i) the EU's dietary supplement laws have a burden of proof that is dis-analogous to that in the U.S.

The EU definition comes from a group of countries that considers dietary supplements to be inherently dangerous requiring pre-market approval.[157] Given that the U.S. regulatory system includes a presumption of safety for dietary supplements while the EU system presumes the exact opposite, NHFA finds FDA's adoption of the EU definition to be contrary to the intent of DSHEA and contrary to the premarket notification requirement at 21 C.F.R. 190.6.

(ii) the adoption of the EU definition introduces new terms that FDA does not define

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[152] *Id.*
[153] DIRECTIVE 2002/46/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL, 10 June 2002, Article 4, Section 1. (Setting forth the positive list concept that only vitamins and minerals listed in Annex I, in the forms listed in Annex II, may be used for the manufacture of food supplements, subject to paragraph 6.) (Amended 2006, 2009, 2011)
[154] DRAFT GUIDANCE, *supra* note 2, at n. 27 and accompanying text.
[155] *Id.*
[156] *Id.* at VI(B)(9).
[157] DIRECTIVE, *supra* note 154.

When FDA tells industry that it is adopting the EU standard as its threshold for assessing reliability of history of use evidence, does FDA mean to adopt the entire EU definition, or was FDA just adopting the 25 year language?[158] And, if adopting the entire EU definition, then how does FDA define "continued use"? How does FDA define "gaps"? Is a manufacturer now supposed to look up the EU definitions for these terms? Or wait for another FDA Guidance document to provide those definitions?

If FDA adopted the entire EU definition, then did FDA intend that the burden of 25 years of "continued use", couldn't be met where the "large part of the population" using the substance temporarily ceased doing so due to, for example, a drought or pest infestation impacting access to the substance? Could such a break in continued use cause otherwise continuous evidence of use to become unreliable, i.e. a gap? And, again given the FDA's adoption of the definition quoted above and its failure to define the terms used therein, does the FDA mean to imply that if a manufacturer can't precisely establish the elements comprising the "customary diet", let alone inclusion of its NDI in the "customary diet" of a "large part" of the population, does the FDA mean to imply that the manufacturer can't reasonably rely on that population's history of use data?

(iii) the adoption impacts negatively the clarity of 43 answers in the Draft Guidance.

FDA's choice to adopt the EU definition is troubling because it impacts 43 questions and answer sets in the Draft Guidance referring to evidence demonstrating history of use or other evidence of safety.

For example, FDA says that "*[s]ubmitting clinical and/or animal studies in addition to history of use data would be appropriate when the history of use evidence contains gaps…*"[159]

Based solely on the frequency with which the term "history of use" appears in the Draft Guidance, clarity regarding the scope of the FDA's adoption of the EU standard should have been provided. Clarity when adopting a term becomes especially important to industry and to NHFA when the standard comes from a regulatory system that is foreign to ours, literally and in terms of the presumption of safety given to dietary supplements.

> (3) requiring human and clinical studies whenever history of use differs, even in minimal ways, from the proposed use of the NDI, or else the manufacturer risks a determination that its notification will be deemed incomplete

Question VI. B. 11. attempts to indicate that human studies are just a possible requirement for a complete notification when it says that "*In many cases, no additional animal or*

[158] DRAFT GUIDANCE, *supra* note 2, at n. 27 and accompanying text.
[159] *Id.* at VI(B)(2).

human safety data are needed because the NDI is reasonably expected to be safe based on a large margin of safety between the level shown to cause no observed adverse effects in humans and the intake level that would result from the proposed use of the NDI in the dietary supplement, or based on longstanding and widespread use of the ingredient as a constituent of conventional food at or below the intake level that would result from the proposed use of the NDI in the dietary supplement."[160] And in the answer to Question VI B 3, FDA states "*additional supportive data may be needed. Examples of differences in a NDI's proposed use that might necessitate further supportive data"*.[161] And yet, in the answer to Question VI B 12, FDA goes in a different direction and states that:

> *The following are examples of situations where FDA would typically recommend that history of use data be supplemented with additional animal or human safety studies:*
>
> - *Higher proposed serving level or total daily intake level*
> - *Longer proposed duration of consumption than historically reported (e.g., notification states that NDI will be marketed with labeling that recommends or implies continuous daily use for improved digestive function, but the history of safe use involves only infrequent, short-term use for indigestion)*
> - *Different proposed route of administration (e.g., data about historical use of a substance as a poultice or by injection ordinarily would not be sufficient to support the safety of a NDI for use in a dietary supplement, which by definition is intended for ingestion)*
> - *A change from historical use that might increase potential toxic effects (e.g., the NDI will be sold as capsules of a ground leaf, but the form historically used was a tea made from the plant's roots)*
> - *A change in the target population (e.g., history of safe use has been established in adults, but NDI will be used in a dietary supplement marketed for use by young children)*[162]

NHFA would like to point out the overarching issue and fundamental principle that it disagrees with regarding FDA's approach in reasoning for recommendation of animal or human safety studies in order to show FDA that FDA is following a drug model as opposed to a food model of research: When you market a food substance, you don't generally recommend to consumers what amount they should eat and how many days in a row should they eat the food, or how much of it they should eat before they get nauseous, or who else always eats this food. Conversely, when a consumer considers taking a toxic drug substance, he/she is sure to ask those questions (i.e., how much of this should I ingest, how many days in a row should I eat this drug, how much of this drug is the maximum

[160] *Id.* at VI(B)(11).
[161] *Id.* at VI(B)(3).
[162] *Id.* at VI(B)(12).

amount that I should take that won't make me sick, and who should ingest this drug and for what reason?).

NHFA contends that FDA's list of when to recommend costly animal or human studies is treating dietary ingredients like drugs. People utilize the same dietary ingredient for a broad array of reasons and in a broad range of potencies. That is because it is a food form. It is not like the use of a drug where off-label use is a major concern.

FDA is well aware that the legal definition of a drug is based on the intent of use, how you plan to use a substance. And FDA is aware that a substance is a drug under the law if it is used to prevent, cure, or treat disease. FDA is additionally aware that DSHEA made a groundbreaking amendment to the definition of a drug when it changed that definition by saying that foods used to impact the structure function of the body will not legally be considered a drug and that dietary supplements would be regulated as foods.

The list FDA generated, above, providing when additional human and animal studies are necessary appears to be from the position that NDIs are presumed unsafe, as if substances similar to drugs or food additives. But NHFA points FDA back to the fact that in order to be a NDI in the first place, a substance first has to not be a drug or a food additive, but rather a dietary ingredient i.e. vitamin, mineral, herb, etc.[163]

Conditions of use for food have to do with assessing reasonable safety assuming that the ingredient is a dietary ingredient presumed safe. But conditions for use for toxic drugs require a risk benefit analysis because consumers need to weigh the risks of taking a toxic substance with the expected benefits. The list submitted by FDA requiring animal or human studies begins to look like a list for drug analysis. Requiring animal and human studies to establish reasonable basis for safety should be a highly unusual circumstance since there are so many other less costly and practical ways to establish conditions of use of dietary ingredients and to form a basis for them to be reasonably considered safe. NHFA is aware of the current GMP[164] and AER requirements[165] and believes that the current extensive laws and regulations regarding dietary supplements and NDIs are completely adequate to address any issues of safety for consumers. The evidentiary testing and reporting recommendations spelled out in the Draft Guidance are, once again, "drug-like" in nature and attempt to solicit as much information from manufacturers and distributors as possible, while also instilling fear in manufacturers and distributors that cannot or will not comply with these recommendations. The FDA's treatment of NDIs according to this Draft Guidance, will unnecessarily decrease consumer options yet, at the same time, not provide any additional benefit of safety to the public.

[163] DSHEA, supra, note 10, at § 3.
[164] CGMPs, *supra* note 50.
[165] AERs, *supra* note 55.

NHFA asks FDA to provide enforcement of products it believes and can prove are truly dangerous, those presenting a risk of harm to consumers, instead of expanding unnecessary regulatory evidentiary recommendations for manufacturers in compliance with the GMP and AER requirements.

d. It puts a severe and undue financial burden on all dietary supplement manufacturers leading to loss of businesses and loss of self-care options for consumers.

FDA's actions, postings, and financial conclusions have been unreasonable regarding its requests for comments on the agency's estimate of the likely financial impact of compliance with the premarket notification requirement on industry.

NHFA is aware that FDA published a notice on June 3, 2011 regarding the financial impact of FDA's information collection activities on manufacturers in complying with FDA reporting requirements in 21 C.F.R. 190.6 (hereinafter Economic Estimate).[166] In the Economic Estimate, the FDA stated that it believed "*there will be minimal burden on the industry to generate data to meet the requirements of the premarket notification program because the Agency is requesting only that information that the manufacturer or distributor should already have developed to satisfy itself that a dietary supplement containing a new dietary ingredient is in full compliance with the FD&C Act.*"[167] FDA even went so far as to say that its estimate of additional financial output per business would be about 20 hours per submission.[168] Comments to this notice began to come in from the industry until the deadline of Aug 19, 2011. Industry comments declared that FDA had drastically underestimated what resources, time wise and financially, a manufacturer would have to spend in order to comply with 21 C.F.R. 190.6 but their comments were made with the Draft Guidance in mind since the Draft Guidance had been made available before the comment period for Economic Estimate had closed.

This was a confusing situation because, not until a month after issuing the Economic Estimate, did the FDA publish a notice on July 5, 2011, announcing availability of the Draft Guidance, entitled "Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues."[169] It was in the Draft Guidance that the FDA's expectations about what information manufacturers or distributors should rely on to satisfy themselves that a dietary supplement containing its NDI is reasonably expected to be safe were presented to industry.[170] This July document also revealed that "*FDA has concerns about the fact that only 700 NDI notifications have been received by them in the*

[166] Comment Request: Agency Information Collection Activities Regarding Premarket Notification for a New Dietary Ingredient, 76 Fed. Reg. 32214 (June 3, 2011).
[167] *Id.*
[168] *Id.*
[169] Notice of Availability, supra note 3.
[170] Draft Guidance, supra note 2, at I.

past 16 years even though there are an estimated 55,600 dietary supplements on the market and that the presence of undeclared active ingredients in products marketed as dietary supplements highlights the necessity for marketers of dietary supplements to submit NDI notifications under CFR 190.6…" and invited submission of comments until October 3, 2011.[171]

Since the Economic Estimate was posted in June before the July Draft Guidance posting, and the Economic Estimate closing date for comment was August 19, 2011, and the subject area of both postings had to do with notification of NDIs, the public naturally gave FDA comments with both documents in mind. However, FDA let the public know that it was not interested in hearing about the financial impact expected to result from its interpretations and recommendations in the Draft Guidance because FDA was only interested in hearing about one thing at a time; the response to its, now irrelevant, June notice was to be discussed separately from the financial impact of the Draft Guidance.[172] FDA clarified that it would put a new posting up in the future regarding financial impact estimates under the Draft Guidance Document as follows:

> *The collection of information analysis in the June 3, 2011, notice was limited to the sole collection of information contained in § 190.6; that is, the regulation itself and not the provisions of the new draft guidance. The notification requirements set forth in § 190.6 remain unchanged. The notice of availability for the new draft guidance (76 FR 39111, July 5, 2011) states that FDA will estimate the paperwork burden of the draft guidance document and submit it for OMB review under the PRA in a future issue of the* ***Federal Register****. Comments on the new draft guidance and any information collection provisions therein are outside the scope of the comment request in the June 3, 2011, notice, and will not be discussed in this document*.[173][Underline added].

NHFA's question is, if FDA knew it was going to post the Draft Guidance, then why did it ask for comments on the financial estimate of complying with the information collection activities of 21 C.F.R. 190.6 before the Draft Guidance Document was posted? And, why did FDA not address the comments that were naturally and with good faith reasoning coming in after the Draft Guidance Document was posted?

Consumers and industry professionals ultimately wasted precious time and economic resources between July and August to provide a comment to FDA that discussed both of FDA's NDI-related notices. It was reasonable for them to comment on FDA's Economic Estimate within their understanding of the burdens they'd face attempting to comply with 21 C.F.R. 190.6 if the Draft Guidance was endorsed.

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[171] Notice of Availability, supra note 3.
[172] 76 Fed. Reg. 51988 (Aug, 19, 2011).
[173] *Id.* (emphasis added).

What is surprising is FDA's response to industry and consumers in August 2011 that evidences disregard for the time and cost by commenters to present their positions: a complete refusal to address comments responding to both documents although submitted to FDA during a time of comment-period overlap coupled with FDA's acknowledgment that it would have to redo its June work to create an economic estimate reflective of the July document's expectations. It's additionally surprising that FDA admits it needs to create a new Economic Estimate in light of the Draft Guidance yet FDA representatives continue to represent that a 20 hour burden is all the FDA is imposing.[174] So on one hand, FDA doesn't think there is a significant burden based on what manufacturers are doing right now to comply with 21 C.F.R. 190.6, but, on the other hand, FDA is saying it doesn't think manufacturers are complying with 21 C.F.R. 190.6 and that they need to start sending FDA more evidence and more notifications as spelled out in the July Draft Guidance Document. Of course the financial impact would be much greater if the manufacturers took the FDA's suggestions.

The lack of FDA appreciation of the financial implications for industry associated with the content and timing of FDA's words demonstrates FDA actions were not well thought out when it came to the welfare of dietary supplement manufacturers and consumers when issuing these two documents. NHFA finds the timing of FDA's release of its two notices to be unjustifiable and a waste of industry and taxpayer dollars.

One further note: FDA's introductory remarks to the Draft Guidance presented the facts that caused FDA concerns regarding the need to submit dietary supplement notifications: *"highlight*[*ed*] *the necessity for marketers of dietary supplements to submit NDI notifications under CFR 190.6.*"[175] FDA's facts cited 55,600 dietary supplements on the market but provided no indication of the number of products that contain NDIs, or that may have contained undeclared active ingredients within products that are marketed as dietary supplements. So it is not understandable why FDA is able to use this concern as substantiation for imposing on industry and consumers the economic burdens and limits on self-health care products presented in the Draft Guidance. FDA's stated concern has no real basis in fact nor a connection to the safety or prevalence in the market of NDIs that are not reasonably safe. NHFA would like to point out that FDA's primary justifications for requesting more notifications are not grounded in fact.

NHFA is aware, and requests that FDA take note, of studies on industry perceptions of the enforcement differences between rules and Guidance documents which suggest that

[174] Interview by NutraIngredients - USA with Daniel Fabricant, Director of the division of Dietary Supplements, FDA (Oct. 2011), http://www.nutraingredients-usa.com/Regulation/Herbalife-Six-steps-to-improve-functionality-of-NDI-guidance.
[175] Draft Guidance, supra note 2, at I.

industry treats Guidance no differently than rules.[176] Explaining that industry is "loath to diverge from the agency's current thinking embodied in the guidance", researchers reveal how Guidance documents can take on the weight of a rule.[177] Knowing that industry often follows Guidance as if they were legally binding rules, FDA should in good faith avoid using the Draft Guidance to broaden the requirements of the NDI notification regulation at 21 C.F.R. 190.6. FDA's actions and recommendations as presented are immediately harmful.[178]

Industry is already struggling in the current economic climate and the costs necessitated for compliance with Draft Guidance Document will only make the hope for an end to their struggle seem all the more distant. And, even more importantly to NHFA, consumers are being provided safe nutritious products backed up by manufacturers complying with Good Manufacturing Practices and Adverse Event Reporting requirements. In addition consumers are facing their own economic hardships and will struggle all the more to make ends meet when their favorite preventative medicines or healing supplements increase in price or are removed from the market entirely.

NHFA completely supports the comments submitted by the Alliance for Natural Health USA, authored by attorney Jonathon Emord, regarding FDA's June Economic Estimate.[179] NHFA completely agrees that the FDA's expectations listed in the Draft Guidance in terms of complying with C.F.R. 190.6 would be so burdensome to the dietary supplement industry that it would destroy thousands of businesses and drastically reduce consumer options in dietary supplement products.[180]

e. It demonstrates the government's role as a hindrance, rather than a helper, in protecting consumer access to dietary supplements and the regulation of those products.

FDA's opinions and actions demonstrate disregard for consumers of dietary supplements and for the intent of DSHEA. FDA has the power to support the people of the USA in their healthy lifestyle choices and informed decisions. FDA has an opportunity to be a helper, to promote nutrient dense options for consumers and self-empowered health-seekers.

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[176] Seiguer, Erica and Smith, John, Perception and Process at the Food and Drug Administration: Obligations and Trade-offs in Rules and Guidances, 60 FOOD AND DRUG LAW JOURNAL 1, 29 (2005).
[177] Id. at 30.
[178] Interview by NutraIngredients - USA with Jonathan Emord (Aug. 2011), available at http://www.nutraingredients-usa.com/Regulation/Emord-on-NDI-guidance-Politics-has-prevailed-over-science-and-common-sense.
[179] Emord, Jonathan, Comments of Alliance for Natural Health - USA, FDA Docket No. FDA-2011-N-0410-007 (Oct. 6, 2011), http://www.regulations.gov/#!documentDetail;D=FDA-2011-N-0410-0007.
[180] *Id.*

The above formal comments have pointed out how the FDA is functioning as a hindrance to the people in a number of areas. Now NHFA would like to offer recommendations as to how FDA might become a HELPER to the American people as opposed to a hindrance. NHFA sincerely hopes that FDA implements the following sincerely submitted recommendations.

1. Respect the findings of DSHEA and do not put up regulatory barriers to access.
2. Respect Proxmire history of "more is not in and of itself dangerous".
3. Honor the needs of consumers and health seekers and do what you can to promote maximum access.
4. Uphold the legal principles of burden of proof shouldering your responsibility rather than making legal arguments based on toxic substance analysis.
5. Create a friendly regulatory environment that embodies the principles that dietary supplements and dietary ingredients are primarily prepared in a way that will be fit for human consumption. FDA could enforce 21 CFR 190.6 for manufacturers where a product is known to create a public harm, instead of unnecessarily threatening and burdening all manufacturers and distributors that are abiding in good faith by the GMPs and Adverse Event Reporting.
6. Honor FDA's original interpretation of DSHEA in that it requires notification for new dietary ingredients which does not mean notification of every dietary supplement recipe that includes the same NDI. Return to the "new dietary ingredient" focus for notification requirements instead of the entire "dietary supplement" recipe focus.
7. Take a strong look at FDA history and attempt to turn around the hostile attitude towards dietary supplements and support consumer maximum options and the immediate need of the population to have access to nutrient dense substances.
8. Use the rulemaking process for major changes in DSHEA and current regulations rather than the use of Guidance.
9. Work with industry to create a "marketed before Oct 15, 1994" list. FDA could endorse the list of products recommended by the industry that were already marketed before 1994 and work hand in hand with industry to provide this helpful information to consumers, manufacturers and distributors. In general, use more common sense when recommending evidence to show whether something was marketed.
10. Help manufacturers and distributors to avoid duplication of efforts where safety is not an imminent concern.
11. Acknowledge that the burden of proof to show harm is FDA's in the adulteration laws which the notification process is founded upon before restricting a product going to market.

12. Request information and evidence from manufacturers that embody common food related regulations instead of requesting burdensome amounts of information that will not significantly increase consumer safety. Avoid solicitation of voluntary NDI notifications or causing undue fear mongering.
13. Refrain from using the EU thresholds for safe use, as the EU does not regulate dietary supplements with the same presumptions as the USA; rather look to New Zealand's draft regulations.
14. Refrain from requesting animal or human studies when there are other more reasonable and cost effective means of showing a basis of reasonable safety.
15. Be attentive to the financial burden FDA recommendations put on industry, especially small business, and especially when the amount of increased evidence of safety is minimal in comparison to the loss of substances from the market due to the burden. Avoid barriers to entry into the dietary supplement manufacturing business.
16. Listen to the people. Be cognizant of consumer impact – what will happen in their everyday lives without their supplements of choice.

NHFA hereby asks FDA to partner with consumers and industry leader to be a helper in protecting access to dietary supplements. By seriously considering how its Draft Guidance unnecessarily hinders industry innovation, economic stability, and could ultimately discourage self-care by conscientious consumers whose support of the dietary supplement industry reduces their contribution to the rising costs of health care for all of citizens, FDA can modify its approach and help Americans protect their important wellness options.

III. Summary

NHFA respectfully urges, and strongly encourages the Food and Drug Administration and the U.S. Department of Health and Human Services Food and Drug Administration Center for Food Safety and Applied Nutrition, to cease any further work on the Draft Guidance Document entitled Draft Guidance for Industry; Dietary Supplements: New Dietary Ingredient Notifications and Related Issues; Availability", [Docket No. FDA–2011–D–0376], and officially withdraw the Draft Guidance in its entirety with notice to the public. In the alternative, if the document continues to be developed, NHFA requests that FDA seriously consider NHFA's comments and recommendations, and those of NHFA's colleagues in the field of dietary supplements, health care, and health freedom, and revise the documents accordingly. Should the FDA wish to directly communicate with NHFA regarding suggested language of such a document NHFA is open to remaining in communication regarding this process. NHFA expresses its deep gratitude for the opportunity to provide comments.

Respectfully Submitted:

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