

**Before the
U.S. Food and Drug Administration
Washington, D.C.**

***In re* Agency Information Collection
Activities; Proposed Collection; Comment
Request; Premarket Notification for a New
Dietary Ingredient, 76 FR 32214
(June 3, 2011)**

Docket No. FDA-2011-N-0410

**COMMENTS OF
ALLIANCE FOR NATURAL HEALTH – USA**

Alliance for Natural Health – USA (ANH), by counsel and in response to the FDA’s request for comments in the above-referenced docket, hereby submits this detailed economic assessment of the impact of the agency’s Guidance on Premarket Notifications for New Dietary Ingredients issued in July 2011. In particular, these comments respond to “Agency Information Collection Activities; Proposed Collection; Comment Request; Premarket Notification for a New Dietary Ingredient,” 76 Fed. Reg. 32214 (June 3, 2011) (“Request for Comments”). In that notice, the agency solicits comment concerning, *inter alia*, the accuracy of FDA’s estimate of the burden of the proposed requirement and ways to minimize that burden. These comments address those agency concerns. They establish that the agency’s estimate of the burden of the proposed requirement is inaccurate: (1) failing to take into account the cost of removing from the market dietary supplements deemed New Dietary Ingredients (NDIs) for the first time in the Guidance; (2) substantially underestimating the number and cost of New Dietary Ingredient submissions that will have to be filed to adhere to the Guidance; and (3) grossly and dangerously undervaluing the economic impact the Guidance will have on the dietary supplement industry

and on the United States economy as a whole. This comment is being simultaneously filed with the Office of Management and Budget.

Background of the Commenter

The Alliance for Natural Health – USA (“ANH”) is a United States division of an international, not-for-profit, non-governmental organization with headquarters in Arlington, Virginia. ANH is the successor to the American Association for Health Freedom, which, in turn, is the successor to the American Preventive Medical Association. ANH was founded in 2002. Its mission objectives include the promotion of natural health and access to dietary supplements. ANH has a defined membership of 1,271 that consist of practitioners, medical doctors, scientists, business entities, consumers, and patients who variously manufacture, sell, distribute, recommend, and use dietary supplements. As an alliance, ANH represents individuals and entities within the dietary supplement industry that are adversely affected by the FDA’s NDI Guidance published June 3, 2011. Its members must comply with FDA interpretations of the NDI statute (21 U.S.C. § 350b, 21 C.F.R. 190.6) as it pertains to existing dietary supplements and future products. Its members are directly responsible for adherence with the NDI Guidance documents, whether through private labeling, distributing, or manufacturing directly. The NDI Guidance requires that all affected parties prepare and file 75-day premarket notifications for new dietary ingredients subject to 21 U.S.C. § 350b(a)(2). Following the FDA’s latest guidance on NDI 75-day submissions, most of ANH’s members will be required to submit NDI notifications for dietary supplements already marketed to consumers. The expansive requirements in the FDA’s guidance will require new NDI submissions, additional testing, and substantial costs of compliance. Thus, ANH’s members suffer concrete and particularized injury resulting directly from the NDI Guidance.

Comments

In its request for comments, the FDA estimates that the burden associated with its Guidance “will be minimal.” In particular, the FDA anticipates that only “55 respondents will

submit one premarket notification each and that it will take a respondent 20 hours to prepare the notification, for a total of 1,100 hours.” 76 Fed. Reg. at 32215. As explained below and in the attached report of Emory Professor of Law and Economics Joanna Shepherd Bailey, the agency has grossly and irresponsibly underestimated the economic impact of its Guidance. Indeed, when accurately assessed, the Guidance can be expected to cause major disruption in the dietary supplement market, forcing a significant number of products off the market, resulting in revenue losses of over a billion dollars and causing the unemployment of over 100,000 Americans.

The Guidance is the most recent instance in which FDA has articulated an interpretation of the requirements in 21 USC 350b. It differs from all prior agency pronouncements, however, in that it provides the first comprehensive explication of the agency’s interpretation of the provision and it fundamentally alters the plain and intended meaning of key terms in 21 USC 350b, including the term “dietary ingredient” and the term “chemically altered.”

Under 21 USC 350b, a dietary supplement is adulterated and unlawful to sell if it contains a new dietary ingredient (NDI) unless FDA is notified of the NDI and fails to object to the entry of the NDI into the market within 75 days from the date FDA receives the notice. 21 USC 350b(a). A “new dietary ingredient” is one first marketed in the United States after October 15, 1994. 21 USC 350b(c). If a dietary supplement contains an NDI, the supplement will be adulterated and unlawful to sell unless one of two conditions is satisfied. The first condition permits sale of an NDI if the dietary ingredient has “been present in the food supply as an article used for food in a form in which the food has not been chemically altered.” 21 USC 350b(a)(1). The second condition permits sale of an NDI if “there is a history of safe use or other evidence of safety establishing that the dietary supplement will reasonably be expected to be safe” and 75 days before introducing or delivering the NDI into interstate commerce, the

manufacturer or distributor of the NDI provides FDA the information on which the manufacturer or distributor bases its conclusion that the dietary supplement containing the NDI “will reasonably be expected to be safe.” 21 USC 350b(a)(2). FDA is required to issue a decision on an NDI petition no later than 180 days after the petition is filed. 21 USC 350b(b).

The Guidance provides an expansive definition for the term NDI. Consequently numerous dietary ingredients in the marketplace, presumed lawful by the industry and consumed safely for years, are now adulterated by operation of law under the agency’s “current thinking,” explained in the Guidance at IV (B)(1); IV (B)(3); and IV (B) (4), and must be removed from the market.

Based on Section 350b(a)(1), if a dietary ingredient had been in the food supply as an article used for food in a form in which the food had not been chemically altered, the dietary ingredient would not be unlawful to sell in a dietary supplement. Contrary to the plain and intended meaning of 21 USC 350b(a)(1), FDA’s Guidance declares that a dietary ingredient will be an NDI unlawful to sell even if it was a conventional food before October 15, 1994, unless it was marketed in or as a dietary supplement or for use in a dietary supplement before October 15, 1994. See Guidance at IV(A)(3); (9). Although FDA deems a dietary ingredient an NDI if in a conventional food but not in a supplement, it does not require an NDI submission unless the ingredient is in a form chemically altered from the form occurring in the food. However, FDA has expanded what it deems to constitute chemical alteration to embrace effects that have no nexus whatsoever to consumer harm, including any use of the following methods:

- (1) Application of nanotechnology that results in new or altered chemical properties of the ingredient (Guidance at IV(A)(12); IV (B)(4));
- (2) Use of solvents other than water or aqueous ethanol (tincture) to make an extract (Guidance at IV(B)(4));

- (3) High temperature baking or cooking of an ingredient that has not previously been baked or cooked, unless the process causes only minor loss of volatile components . . . (Guidance at IV(B)(4));
- (4) Changing agricultural or fermentation conditions to alter the chemical composition of the ingredient, such as by sprouting garlic or fermenting yeast using a medium containing large amounts of sodium selenite to create large amounts of organic selenium compounds (Guidance at IV(B)(4));
- (5) Fermentation using a fermentation medium different from the one used to make a conventional food in the food supply (e.g., use of a defined commercial growth medium to produce a microorganism previously made by fermenting milk into dairy products like yogurt or cheese) (Guidance at IV(B)(4));
- (6) Use of botanical ingredient that is at a different life stage than previously used (e.g., making an extract from unripe instead of ripe apples or using the mycellum instead of the fruiting body of a fungus) (Guidance at IV(B)(4));

Contrary to the plain and intended meaning of 21 USC 350b, the Guidance compels the filing of multiple NDI notifications for the same ingredient when used in a supplement containing other dietary ingredients that are not NDIs (Guidance at IV(C)(1)) or when the target population for the dietary supplement changes (Guidance at IV(C)(1)).

Contrary to the plain and intended meaning of 21 USC 350b, if an NDI is permitted to be marketed, FDA's allowance applies only to the manufacturer who sought permission and to no others who wish to sell the same NDI (Guidance at IV (D)(1)). Contrary to the plain and intended meaning of 21 USC 350b, FDA deems not a dietary ingredient a synthetic copy of a constituent of a botanical (Guidance at IV(D)(2)).

The agency's redefinition of key terms in 21 USC 350b achieves the agency's underlying, albeit unarticulated, objective of expanding the definition of what constitutes an NDI and constricting the exemption in 21 USC 350b(a)(1). The logical consequence of those moves is to render a large quantity of dietary supplements on the market unlawful. In addition, the Guidance prescribes costly proof requirements nowhere required by the statute, making it certain

that many supplements now redefined as NDIs will remain off the market even after manufacturers and distributors have filed their NDI submissions.

To assess the regulatory impact of the agency's Guidance, ANH hired a leading expert in assessing the cost of regulation, Emory University Professor of Law and Economics Joanna Shepherd Bailey. Dr. Shepherd Bailey's report and her curriculum vitae are appended to this Comment as Exhibit A.

FDA's estimate of the number of NDI submissions that will be required following its Guidance, of the number of man hours required to satisfy the Guidance criteria, and of the overall economic impact of the Guidance are grossly below those predicted in Dr. Shepherd Bailey's report. *See* Exhibit A. The enormous differences between the agency's estimation and Dr. Shepherd Bailey's reveals that the agency has been derelict in its estimation, failing to account for the consequences that logically flow from each of its specific Guidance requirements.

Rather than 55 NDI submissions as FDA predicts, Dr. Shepherd Bailey expects the Guidance will require between 22,240 and 125,000 NDI submissions. *See* Exhibit A. Rather than 20 hours of employee time to prepare each submission, Dr. Shepherd Bailey expects the Guidance to require between 100 and 350 hours of employee time per submission. Moreover, Dr. Shepherd Bailey expects total costs in employee time to prepare the petitions to be between \$845 million and \$6.1 billion. *See* Exhibit A.

In addition, because dietary supplements containing NDIs not qualified for exemption under 21 USC 350b(a)(1) and (2) may not lawfully be sold (they are adulterated by operation of law) and because FDA has greatly expanded the NDI definition, Dr. Shepherd Bailey expects

between 22,240 and 41,700 dietary supplements to be removed from the market at a cost of between \$5.6 billion and \$10.5 billion.

The cost of each of the 22,240 to 125,000 NDI notifications will be considerable, particularly in light of the evidentiary requirements specified in the Guidance. Dr. Shepherd Bailey estimates the animal and human product safety studies strongly recommended by FDA will cost between \$450,000 to \$6.6 million per NDI notification, resulting in a cost of between \$2 billion to over \$165 billion. Based on FDA's history of denials of NDI submissions, Dr. Shepherd Bailey anticipates that FDA denials of the new submissions will cause between 15,568 and 29,190 dietary supplements currently on the market to be unlawful to sell. The overall economic impact of those denials will cause the dietary supplement market to shrink by between 28 and 52.5 percent, yielding an annual loss for the industry of between \$7.84 billion to \$14.7 billion.

The impact of the Guidance on industry employment levels will also be severe. Dr. Shepherd Bailey estimates that the loss of markets for supplements affected by the Guidance will cause between 55,720 and 104,475 workers to lose their jobs. Collateral damage will occur to those businesses dependent on this sector, including distributors, truckers, warehouse owners, and retailers, thus engendering a significant ripple effect that will increase unemployment levels beyond the immediate dietary supplement industry losses.

Consumer choice will be adversely affected because of the loss of so many products. The loss of competition that has created downward pressure on prices will allow prices to rise for supplements to the detriment of consumers.

The disruption caused by the Guidance to the dietary supplement industry will adversely affect the entire U.S. economy. Dr. Shepherd Bailey explains, "[t]he Guidance will cause a total

economic loss of \$21.2 billion to \$39.8 billion annually. It will cause 127,598 to 239,347 jobs to be lost. It will result in a loss of between \$1.84 billion to \$3.54 billion in federal tax revenues and a loss of \$1.64 billion to \$3.07 billion in state and local tax revenues.”

The agency’s notice invites comment on ways to minimize the burden the Guidance creates. The primary way to minimize that burden is to withdraw the Guidance. A secondary way would be to remove from the guidance each method (enumerated 1-6 above) that expands the definition of an NDI without proof that the items prohibited have a direct and substantial nexus to adverse effects to dietary supplement consumers. We prefer the first method, withdrawal of the Guidance, because it is presently exerting a coercive effect on the dietary supplement market causing responsible sellers to believe they must remove products from the market to avoid the risk of being charged with adulteration. Thus, the harmful effects of the Guidance are occurring presently and will grow with time and with agency enforcement.

Conclusion

Because the FDA has greatly underestimated the adverse economic impact of its Guidance, it has failed to comply with the requirements of the Regulatory Flexibility Act. FDA has not undertaken a serious, good faith effort to determine the economic impact of each recommended requirement contained in its Guidance. Indeed, the economic burden imposed by the Guidance is extraordinary, particularly in the midst of a national recession, and will cost the dietary supplement industry billions of dollars in revenues and will increase unemployment by over 100,000 Americans.

Sincerely,

/s/ Jonathan W. Emord

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Docket No. FDA-2011-N-0410

Exhibit A
Report of Dr. Joanna Shepherd-Bailey

**ECONOMIC IMPACT OF THE FDA'S DRAFT GUIDANCE FOR THE DIETARY SUPPLEMENT
INDUSTRY REGARDING NEW DIETARY INGREDIENT NOTIFICATIONS**

**Prepared by:
Joanna M. Shepherd-Bailey, Ph.D.
Emory University School of Law**

**Prepared For:
Alliance for Natural Health-USA**

July, 2011

I. INTRODUCTION

In July 2011, the FDA published a Draft Guidance for the Dietary Supplement Industry regarding New Dietary Ingredient Notifications (“the Guidance”). If followed by the agency, the Guidance creates costly obstacles to the marketing of dietary ingredients in dietary supplements and stringent reporting requirements for manufacturers and distributors of dietary supplements that contain new dietary ingredients (“NDIs”).

Since the Dietary Supplement Health and Education Act of 1994 (DSHEA)¹ was enacted in 1994, manufacturers and distributors have been required to submit premarket notifications to the FDA at least 75 days before marketing dietary supplements containing NDIs. An NDI is defined as “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.” DSHEA exempts from the premarket notification requirement any NDI that has “been present in the food supply as an article used for food in a form in which the food has not been chemically altered.”

While purporting to “clarify” certain aspects of DSHEA, the Guidance in fact broadens the conditions under which dietary supplement ingredients are considered NDIs requiring notification to the FDA and prohibits sale of such ingredients unless and until the FDA deems them safe. For example, the Guidance indicates that an old ingredient manufactured in a new way requires an NDI notification. Baking or cooking an ingredient is considered to be chemical alteration, requiring an NDI notification. Similarly, using any solvent other than water or aqueous ethanol to make an extract is considered to be chemical alteration, requiring an NDI notification. Any application of nanotechnology that results in new properties of the ingredient is considered chemical alteration, requiring an NDI notification. Using an ingredient at a different stage of life (for example, ripe instead of unripe fruits), is considered to be a chemically altered ingredient, requiring an NDI notification. The Guidance also considers normal food products that were not marketed as dietary ingredients before 1994 to be NDIs, requiring notification to the FDA. The Guidance

¹ Dietary Supplement Health and Education Act of 1994 (DSHEA) (Pub. L. 103-417).

specifies numerous other factors that would cause currently-marketed dietary ingredients to be considered NDIs, requiring immediate notification to the FDA.

Moreover, the FDA does not consider synthetic *botanicals* to be NDIs at all under the Guidance. As a result, synthetic botanicals will be treated as drugs and can never be sold as supplements if the Guidance goes into effect.

In addition, the Guidance discusses the extensive information necessary to complete an NDI notification. For example, detailed written business records, promotional materials, or press reports are required to prove that a dietary ingredient was marketed prior to October 15, 1994. The Guidance also indicates the significant amount of historical data necessary to establish the safety of an NDI. An NDI notification must include published evidence documenting that the ingredient has been safely consumed at levels equal to or higher than the recommended use of the NDI by a similar population. Moreover, “the agency considers 25 years of widespread use to be the minimum to establish a history of safe use.”² If the history of safe use is insufficient to establish an NDI’s safety, the Guidance recommends numerous chemical studies, animal studies, and human studies to establish an NDI’s safety.

Finally, the FDA indicates that many dietary supplements will require multiple NDI notifications. For example, the Guidance specifies that separate notifications are required for each NDI in a dietary supplement. In addition, separate notifications are required for different supplements containing the same NDI if the other dietary ingredients in the supplement were not included in the original NDI notification, if the target populations are different, or if the conditions of use materially differ. Moreover, NDI notifications are company specific, so that a favorable FDA safety determination for one company’s NDI does not transfer to other companies using the same ingredient. As a result, the Guidance will result in redundant filings and safety tests.

Thus, because the Guidance expands the current definition of an NDI, and therefore expands its de jure market ban, it will require many manufacturers and distributors of currently-marketed products to submit NDI notifications. Moreover, because the Guidance increases the recommended amount of historical information and safety data provided in

² Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues at VI.B.9

each NDI notification, new NDI notifications require a significant amount of time, effort, and monetary costs.

I have been retained by the Alliance for Natural Health-USA to estimate the economic impact of the Guidance on the dietary supplement industry. After reviewing the details of the Guidance, historical industry data, and details of currently-marketed dietary supplements, I conclude that the Guidance will impose significant burdens on dietary supplement manufacturers and distributors. Manufacturers and distributors will spend a significant amount of time and money preparing NDI notifications and performing additional safety tests when necessary. Moreover, many dietary supplements will be rejected by the FDA under the stringent requirements of the Guidance, resulting in a significant loss of sales and the forced termination of many employees. The Guidance's impact will extend beyond the dietary supplement industry as employment, output, and tax revenues throughout the economy are affected. These losses will be especially devastating in the current economic climate. Specifically,

1. Industry estimates indicate that between 22,240 and 41,700 of the currently-marketed dietary supplements will require NDI notifications. The average number of separate NDI notifications required per dietary supplement will be between 1 and 3. Thus, I estimate that the Guidance will result in between 22,240 and 125,100 NDI notifications for currently-marketed dietary supplements.
2. The Guidance requires new NDI notifications to include a considerable amount of chemistry information, processing information, production information, and safety information. The onerous reporting requirements under the Guidance will require between 100 and 350 hours of employee time. In addition, many manufacturers and distributors will consult with scientific, regulatory, and legal experts to help navigate the notification process. At current wage rates, I estimate that the total cost to the industry of simply preparing NDI notifications will be between \$845 million and \$6.1 billion.

3. All supplements for which NDI notifications must be filed may not be lawfully marketed for 75 days following the NDI notifications. Thus between 22,240 and 41,700 dietary supplements will have to be removed from the market for an average of 75 days (assuming FDA requires no further action or resubmittal). As a result, the Guidance will cause a disruption in industry sales totaling \$2.3 billion - \$4.3 billion.
4. The FDA strongly recommends that manufacturers and distributors conduct animal or human studies to establish product safety if historical data is insufficient to establish an NDI's safety under the Guidance. The recommended studies will range in cost from \$450,000 to \$6.6 million for each NDI notification. If even twenty percent of the 22,240-125,100 NDI notifications of currently-marketed dietary supplements require clinical studies, the studies alone could cost the industry from \$2 billion to over \$165 billion.
5. Despite spending millions of dollars on clinical studies and preparation of NDI notifications, most NDIs will not be accepted by the FDA. I estimate that between 15,568 and 29,190 of the currently-marketed dietary supplements will be rejected by the FDA under the stringent requirements of the Guidance, eliminating them from the market as legally available for sale.
6. Because many currently-marketed dietary supplements will be rejected by the FDA, the market for dietary supplements will shrink by between 28-52.5 percent, translating into an annual loss of \$7.84 billion-\$14.7 billion for the industry.
7. The Guidance will also cause a significant loss of employment in the dietary supplement industry as the market for supplements shrinks and sales revenues decrease. I estimate that between 55,720 and 104,475 workers in the dietary supplement industry will lose their jobs. In the current economy, many of these workers will remain unemployed for indefinite periods of time.
8. Many manufacturers and distributors in the dietary supplement market, and especially the small-businesses, will be unable to sustain the expenses and losses.

These firms will go out of business altogether, further shrinking the market and industry.

9. Because the Guidance significantly increases the costs of bringing new dietary supplements to market, it will have a stifling effect on innovation.
10. As a result of the Guidance, the 82 percent of U.S. adults that use dietary supplements will encounter fewer supplement choices and higher prices for remaining supplements.
11. A significant disruption to the dietary supplement industry will also affect the greater U.S. economy. The Guidance will cause a total economic loss of \$21.2 billion-\$39.8 billion annually in the economy. It will also cause 127,598-239,247 jobs to be lost throughout the U.S. economy. Moreover, it will result in a loss of \$1.84 billion - \$3.54 billion in federal tax revenues and a loss of \$1.64 billion - \$3.07 billion in state and local tax revenues.

II. AUTHOR

My name is Joanna M. Shepherd-Bailey, Ph.D. My curriculum vitae is attached as exhibit 1. I received a Ph.D. in Economics from Emory University, with concentrations in Econometrics and Law and Economics. Currently a tenured professor at Emory University School of Law, I am an expert in theoretical and empirical analyses of legal changes. I have taught courses in economics, statistics, econometrics, and other analytical subjects to undergraduates, Ph.D. students, and law students. I have published many theoretical and empirical articles that have appeared in leading peer-reviewed economics journals, peer-reviewed law journals, and law reviews. I have also testified about my work before both the U.S. House of Representatives' Judiciary Committee and the National Academy of Sciences.

III. CONSEQUENCES OF FDA'S DRAFT GUIDANCE FOR NDIs IN DIETARY SUPPLEMENTS

The FDA's Draft Guidance for NDIs in dietary supplements will impose significant costs on the dietary supplement industry, dietary supplement consumers, and the economy as a whole. Below I discuss each cost in detail, quantifying as many of the costs as possible.

A. Costs to Dietary Supplement Manufacturers and Distributors

The dietary supplement industry has grown into a significant industry in the United States. At the time DSHEA was enacted in 1994, an estimated 600 U.S. dietary supplement manufacturers marketed about 4,000 dietary supplement products.³ Currently, the FDA estimates that there are 55,600 dietary supplement products on the market, with 1,000 new dietary supplements introduced each year.⁴ Approximately 900 companies manufacture these dietary supplements; there are approximately 773 contract manufacturers⁵ and 127 branded product manufacturers or private label manufacturers.⁶ In addition, approximately 250 distributors or brokers of dietary supplements sell manufactured products to retailers.⁷

Although the industry includes some large multinational corporations, it is dominated by small businesses. Approximately 85 percent of dietary supplement manufacturers produce less than \$20 million in annual sales.⁸ These small businesses will be especially hard hit by the stringent and costly requirements of the Guidance.

Under the Guidance, either the manufacturer or the distributor of an NDI is required to submit an NDI notification. The short comment period provided by the FDA does not permit an exact calculation of the impact of the Guidance on each individual dietary supplement. However, industry estimates indicate that between 40-75 percent of the 55,600

³ CDSL (Commission on Dietary Supplement Labels). 1997. *Report of the Commission on Dietary Supplement Labels*. Washington, DC: U.S. Government Printing Office.

⁴ Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues at III.

⁵ Nutrition Business Journal, Strategic Information for the Nutrition Industry, 16(6) U.S. Market Overview 5 (June/July 2011).

⁶ Dobson DaVanzo & Associates, LLC, The Economic Contribution of the Dietary Supplement Industry, 13 (May, 2009), available at: <http://naturalproductsfoundation.org/clientuploads/NPF%20-%20Economic%20Impact%20Study.pdf>.

⁷ Dobson DaVanzo & Associates, LLC, The Economic Contribution of the Dietary Supplement Industry, 13 (May, 2009), available at: <http://naturalproductsfoundation.org/clientuploads/NPF%20-%20Economic%20Impact%20Study.pdf>.

⁸ Nutrition Business Journal, Strategic Information for the Nutrition Industry, 16(6) U.S. Market Overview 5 (June/July 2011).

currently marketed dietary supplements will contain NDIs as defined by the Guidance, requiring an immediate NDI notification to the FDA.⁹ Thus, between 22,240 and 41,700¹⁰ of the currently-marketed dietary supplements will require NDI notifications and will be unlawful to sell unless and until the FDA approves them for marketing.

Moreover, many individual dietary supplements will require several NDI filings for different ingredients within the supplement. Industry estimates indicate that the average number of separate NDI notifications required per dietary supplement will be between 1 and 3, although many dietary supplements will require between 5-8 separate NDI notifications.¹¹ Thus, the Guidance will result in between 22,240 and 125,100¹² NDI notifications for currently-marketed dietary supplements.

This will create significant burdens on dietary supplement manufacturers and distributors. Manufacturers and distributors will spend a significant amount of time and money preparing NDI notifications and performing additional safety tests when necessary. Moreover, many dietary supplements will be rejected by the FDA under the stringent requirements of the Guidance, resulting in a significant loss of sales and the forced termination of many employees.

i. Cost of Preparing NDI Notifications

For the first time, the Guidance spells out the type and scope of chemistry information, processing information, production information, and safety information to include in an NDI notification. The onerous reporting requirements will impose significant burdens on manufacturers and distributors of currently-marketed NDIs.

The FDA has estimated that the average time necessary to generate data to meet the requirements of an NDI notification is 20 hours.¹³ However, this estimate is based on the time burden of NDI notifications filed prior to the Guidance when there were few guidelines detailing the type and scope of information expected in an NDI notification.

⁹ See Affidavit of Gretchen DuBeau (Attachment A).

¹⁰ 40% of 55,600=22,240; 75% of 55,600=41,700

¹¹ See DuBeau Affidavit (Attachment A).

¹² 3*41,700=125,000

¹³ Food and Drug Administration, HHS, Agency Information Collection Activities; Proposed Collection; Comment Request; Premarket Notification for a New Dietary Ingredient, 76(107) Federal Register (June 3, 2011).

With the new, more extensive reporting requirements, the time burden will necessarily increase. Moreover, the FDA estimate of 20 hours is based on the average time burden of both successful and unsuccessful notifications. As many of the prior notifications failed because they lacked sufficient information, the time burden will necessarily be higher for manufacturers and distributors attempting to submit successful NDI notifications.

As a result, industry estimates of the time burden of filing NDI notifications are significantly longer than FDA estimates. The Council for Responsible Nutrition (CRN), a trade association representing the dietary supplement industry and including as members some of the largest manufacturers of dietary supplements, has consulted with manufacturers with experience filing NDI notifications. They estimate that NDI notifications under the Guidance will require 100-350 hours of time.¹⁴ The typical hourly rate for employees with a science background that can provide the necessary information required in an NDI notification is \$30-\$40 per hour.¹⁵ Thus, the cost of allocating 100-350 hours of employee time to preparing NDI notifications is between \$3,000 and \$14,000 per notification.¹⁶

Moreover, these estimates do not include the significant expense of hiring scientific, regulatory, and legal consultants to help navigate the notification process.¹⁷ Manufacturers and distributors of NDIs regularly contract with scientific consultants to prepare and review the evidence necessary for NDI notifications. In addition, legal consultants are hired to aid in the preparation, submission and prosecution of the notification. Scientific consulting per NDI notification averages \$20,000 and legal consulting per notification averages \$15,000.¹⁸

Thus, a conservative estimate of the cost of allocating employee time and hiring outside consultants for the preparation of an NDI notification is \$38,000-\$49,000 per notification. Because the Guidance will require between 22,240 and 125,100 NDI notifications for currently-marketed dietary supplements, the total cost to the industry of

¹⁴ Council for Responsible Nutrition, Letter to the Division of Dockets Management, Food and Drug Administration (July 25, 2011) available at: http://www.crnusa.org/pdfs/CRNComments_FDA_ProposedCollectionInfoPremarketNotificationNDI072511.pdf.

¹⁵ See DuBeau Affidavit (Attachment A).

¹⁶ 100 hours * \$30 per hour=\$3000; 350 hours * \$40 per hour=\$14,000.

¹⁷ Council for Responsible Nutrition, Letter to the Division of Dockets Management, Food and Drug Administration (July 25, 2011) available at: http://www.crnusa.org/pdfs/CRNComments_FDA_ProposedCollectionInfoPremarketNotificationNDI072511.pdf.

¹⁸ See DuBeau Affidavit (Attachment A).

simply preparing NDI notifications will be between \$845 million and \$6.1 billion.¹⁹ However, as I discuss in the next section, the preparation costs represent only a small portion of the overall cost of NDI notifications. A much more significant cost is the cost of safety testing.

ii. Costs of Safety Testing

The Guidance also details the extensive evidence required to establish the safety of an NDI. For some NDIs, the FDA indicates that providing evidence of a history of safe use is sufficient to establish safety. However, the history of safe use is only sufficient if it (1) establishes that the ingredient was safely consumed at levels equal to or higher than the anticipated intake level of the NDI in the dietary supplement, (2) proves that the NDI will be used in a largely identical way to its historical usage (i.e. similar dosage, route of administration, duration of use, etc.), (3) verifies that the population expected to consume the NDI is the same as, or a subset of, the population that safely consumed the substance in the past, and (4) documents that there is a minimum of 25 years of widespread use establishing the safety of the NDI.²⁰ Moreover, to prove an NDI's history of safe use, the NDI notification must include published data such as peer-reviewed scientific articles.

Oftentimes, one or more of these requirements will not be met, and the historical data will not be sufficient to establish an NDI's safety under the Guidance. For example, the intended usage or target population may vary slightly from the historical use. Alternatively, there may not be 25 years of usage that is documented in published sources. In these situations, the FDA strongly recommends that manufacturers and distributors conduct animal or human studies to establish product safety.²¹

The FDA recommends specific studies depending on how the usage and target population differ from the historical use. At minimum, the FDA strongly recommends:

¹⁹ $22,240 * \$5,000 = \$111,200,000$; $125,100 * \$15,000 = \$1,876,500,000$

²⁰ Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues at VI.B.3-11.

²¹ Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues at VI.B.12

- (1) A two-study genotox battery (bacterial mutagenesis and *in vitro* cytogenetics) that includes a test for gene mutations in bacteria, either an *in vitro* mouse lymphoma thymidine kinase+/- gene mutation assay (preferred) or another suitable *in vitro* test with cytogenetic evaluation of chromosomal damage using mammalian cells;
- (2) a 14-day range-finding oral study to establish a maximum tolerated dose (MTD) in an appropriate animal model;
- (3) a 90-day sub-chronic oral study (same species as the range-finding study) to establish an MTD and a NOAEL for use in calculating the margin of safety;
- (4) a single-dose or repeat-dose tolerability study in humans and/or an ADME study in animals and/or humans; and
- (5) a teratology study (rodent or non-rodent); except that the teratology study is not needed if the product is labeled as not for use by women of childbearing age, pregnant or lactating women, and children 13 and younger.²²

However, in the many instances where there is no reliable history of safe use according to the stringent Guidance standards, the FDA strongly recommends even more tests:

- (1) A three-study genetic toxicity (genotox) battery (bacterial mutagenesis, *in vitro* cytogenetics, and *in vivo* mammalian test) that includes a test for gene mutations in bacteria, either an *in vitro* mouse lymphoma thymidine kinase+/- gene mutation assay (preferred) or another suitable *in vitro* test with cytogenetic evaluation of chromosomal damage using mammalian cells, and an *in vivo* test for chromosomal damage using mammalian hematopoietic cells;
- (2) 14-day range-finding oral studies to establish a maximum tolerated dose (MTD) in at least two appropriate species, at least one of which is non-rodent;
- (3) two 90-day sub-chronic oral studies (one for each species for which there is a range-finding study) to establish an MTD and a NOAEL for use in calculating the margin of safety (see footnote "‡" in Table 2: Safety Testing Recommendations Matrix);
- (4) a repeat-dose tolerability study in humans and/or an ADME study in animals and/or humans (30-90 day duration);
- (5) if proposed use is either intermittent or daily chronic, a one-year chronic toxicity study or a two-year carcinogenesis study in at least two animal species;
- (6) a multi-generation rodent reproductive study (minimum of two generations); and
- (7) a teratology study (rodent or non-rodent); except that the latter two studies are not needed if the product is labeled as not for use by women of childbearing age, pregnant or lactating women, and children 13 and younger.

Note: Based on the nature of the NDI and the results of other testing, special studies (e.g., carcinogenicity, ADME) may be needed to provide a reasonable expectation of safety. Other nonclinical studies to assess immunotoxicity and neurotoxicity should be conducted on a case-by-case basis, as appropriate.²³

²² Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues at VI.B.19.

²³ Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues at VI.B.20.

These studies will impose significant monetary costs on manufacturers and distributors submitting NDI notifications. Table 1 documents the expected cost of each of the recommended safety tests discussed in the Guidance.²⁴

Table 1: Cost Estimate for NDI Toxicology Studies

Study	Estimated Cost (\$)
Genotox Studies (3 study genotox battery)	
<i>Salmonella typhimurium</i> / <i>Escherichi coli</i> Plate Incorporation Mutation Assay in the Presence and Absence of Induced Rat Liver S-9 (Ames Test)	\$20,000
Lymphoma Mutagenesis in the L5178Y TK+/- Mouse with Colony Size Evaluation in the Presence and Absences of Induced Rat Liver S-9 with a Confirmatory Study	\$25,000
<i>In vitro</i> Chromosomal Aberration	\$22,500
Total Cost of Genotox Studies:	\$67,500
Repeat Dose Studies	
14-Day dose range-finding oral study for max. tolerated dose (MTD) in rats	\$100,000
90-Day sub-chronic oral toxicity study (NOAEL) in rats	\$250,000
52-Week chronic toxicity (NOAEL) in rats	\$550,000
14-Day dose range-finding oral study (MTD) in dogs	\$150,000
90-Day sub-chronic oral toxicity study (NOAEL) in dogs	\$300,000
52-Week chronic toxicity (NOAEL) in dogs	\$650,000
2 -Year carcinogenicity study in mice	\$1,250,000
2-Year carcinogenicity study in rats	\$1,350,000
Total Cost of Repeat Dose Studies:	\$4,600,000
Reproduction Studies	
Pilot Teratology Study in Rats	\$40,000

²⁴ See DuBeau Affidavit (Attachment A). Estimates are based on experience with pharmaceutical trials.

Teratology Study in Rats	\$125,000
Pilot Teratology Study in Rabbits	\$50,000
Teratology Study in Rabbits	\$150,000
Two-Generation Study in Rats	\$650,000
Total Cost of Reproduction Studies:	\$1,015,000
Other Studies	
Repeat-Dose Tolerability study in Humans (30 patients)	\$888,000
ADME Study in Rats	\$65,000
Total Cost of Other Studies:	\$953,000
TOTAL COST OF ALL STUDIES:	\$6,635,500

Although most NDI notifications will not require all of the studies in Table 1 because there will be some history of safe use, even the minimum number of tests recommended by the FDA will impose significant costs. The minimum tests recommended in the Guidance—a two-study genotox battery, a 14-day range-finding oral study, a 90-day sub-chronic oral study, and an ADME study in animals—will cost over \$450,000.

Clinical studies ranging in cost from \$450,000 to \$6.6 million for each NDI notification will present a significant burden for the dietary supplement industry. If even twenty percent of the 22,240-125,100 NDI notifications of currently-marketed dietary supplements require clinical studies, the studies alone could cost the industry from \$2 billion to over \$165 billion.²⁵

As a result, the Guidance will impose an impossible financial burden on many manufacturers and distributors of dietary supplements. Moreover, the majority of the companies deal with more than one dietary supplement and most dietary supplements will require between one and three NDI notifications under the Guidance. Thus, many manufacturers and distributors of dietary supplements will be forced to complete numerous costly clinical studies. Although large dietary supplement manufacturers may be able to

²⁵ (20% of 22,240)*\$450,000=\$2.016 billion; (20% of 125,100)*\$6,600,000=\$165.132 billion.

afford millions of dollars of clinical studies, many manufacturers will not be so fortunate. Approximately 85 percent of dietary supplement manufacturers produce less than \$20 million in annual sales.²⁶ For these manufacturers, clinical studies costing millions will be unaffordable.

iii. Cost of Marketing Interruption while NDI Notification is Pending

In addition to the costs of preparing notifications, hiring outside consultants, and conducting expensive clinical trials, manufacturers and distributors must refrain from marketing the dietary supplement containing an NDI for 75-days after filing the NDI notification. This means that currently-marketed dietary supplements will have to be pulled from the shelves until NDI notifications are prepared, filed, and the 75-day period has expired.

Although DSHEA mandates a 75-day waiting period for NDI notifications, the FDA may request additional information or identify changes that must be made to a notification. Any such request or submission of supplemental data generally resets the 75-day period. Thus, for at least 75-days, and up to half of a year for resubmissions, the dietary supplements in question may not be lawfully sold. Such a disruption in sales could dramatically impact some manufacturers and distributors.

If 22,240-41,700 of the currently-marketed dietary supplements are pulled off the shelves pending the notification period, the dietary supplement industry will face a dramatic reduction in sales. Assuming that sales are relatively constant across supplements, the Guidance will cause a disruption in industry sales totaling \$2.3 billion - \$4.3 billion.²⁷ Although this disruption may be easy for large manufacturers to withstand, over 85 percent of manufacturers of dietary supplements earn less than \$20 million in annual sales revenue. Losing half a year of sales on significant product lines could devastate these smaller companies. However, as I discuss in the next section, these losses will be even more ruinous if the FDA rejects the NDI notification.

²⁶ Nutrition Business Journal, Strategic Information for the Nutrition Industry, 16(6) U.S. Market Overview 5 (June/July 2011).

²⁷ 40% of \$5.753 billion (the expected revenues for 75 days if annual revenues are \$28 billion)=\$2.3 billion;75% of \$5.735 billion=\$4.3 billion.

iv. Costs of FDA Objection

Despite spending millions of dollars on clinical studies and preparation of NDI notifications, many NDIs will not be accepted by the FDA. Even before the Guidance imposed stricter requirements for NDI notifications, the vast majority of NDIs were not accepted by the FDA. Table 2 shows the NDI submission outcomes from the time DSHEA was imposed in 1994 through March, 2007.²⁸

Table 2: NDI submission outcomes, 1994-2007

Total Number of NDI Notifications	359
Rejected/Objected	246
Filed	107
Withdrawn	4
Other(Inconclusive)	2

Of the 246 NDI notifications during this period, 246 were objected to or rejected by the FDA. This translates into an NDI acceptance rate of approximately 30 percent. The acceptance rate has become even more dismal in the last few years; as of 2010, the NDI acceptance rate was approximately 22 percent.²⁹

If the FDA acceptance rate remains the same, the majority of new NDI notifications will be rejected. Of the 22,240 to 41,700 currently-marketed dietary supplements that will require immediate NDI notifications under the Guidance, it is only expected that roughly 30 percent of them will be accepted by the FDA. Thus, between 15,568 and 29,190³⁰ of the currently-marketed dietary supplements will not be accepted by the FDA. The companies with rejected NDIs will have to immediately cease distribution of the rejected dietary supplements or face enforcement action by the FDA. As a result, many manufacturers and

²⁸ Ashish R. Talati, *New Dietary Ingredient Notifications: A Comprehensive Review and Strategies for Avoiding FDA Objections*, 62 Food Drug L.J. 387, 390 (2007).

²⁹ As reported by Loren Israelsen, founder of the United Natural Products Alliance/UNPA; Jennifer Kwok, Editorial: They're Here, *Nutritional Outlook* (May 12, 2011), available at: <http://www.nutritionaloutlook.com/article/editorial-theyre-here>

³⁰ 70% of 22,240=15,568; 70% of 41,700=29,190.

distributors of dietary supplements will face a significant loss of sales and the forced termination of many employees.

a. Loss of Sales and Profits

Annual sales revenues of dietary supplements exceeded \$28 billion in 2010.³¹ However, if 15,568-29,190 of the 55,600 currently-marketed dietary supplements are forced out of the market after rejection by the FDA, the market for dietary supplements will shrink by between 28-52.5 percent.³² Assuming that sales are spread relatively evenly across products, a 28-52.5 percent decrease in the number of dietary supplements on the market will translate into a 28-52.5 percent loss of sales revenue by the industry, or a loss of \$7.84 billion-\$14.7 billion annually.³³

b. Forced Termination of Employees

In addition to lost sales, the Guidance will also cause a significant loss of employment in the dietary supplement industry. More than 199,000 people are directly employed in the dietary supplement industry.³⁴ However, if the market for dietary supplements shrinks by 28-52.5 percent, losing \$7.84 billion-\$14.7 billion in annual sales, then many employers in the industry will have no choice but to terminate numerous workers. Not only will many of the current employees in the dietary supplement industry become unnecessary as companies cease production of approximately 15,568-29,190 products, the companies will also be unable to afford many of the employees' wages after suffering significant reductions in sales revenues.

Although the exact number of workers that companies would be forced to terminate is difficult to predict, there is no doubt that the loss of jobs would be devastating. If dietary supplement companies experience a 28-52.5 percent decrease in annual sales revenues, they would likely be forced to terminate between 28-52.5 percent of their workers. This translates

³¹ Nutrition Business Journal, Strategic Information for the Nutrition Industry, 16(6) U.S. Market Overview 3 (June/July 2011).

³² 15,568/55,600=28%; 29,190/55,600=52.5%.

³³ 28% of \$28 billion=\$7.84 billion; 52.5% of \$28 billion=\$14.7 billion.

³⁴ Dobson DaVanzo & Associates, LLC, The Economic Contribution of the Dietary Supplement Industry, 21 (May, 2009), available at: <http://naturalproductsfoundation.org/clientuploads/NPF%20-%20Economic%20Impact%20Study.pdf>.

into the forced termination of between 55,720-104,475 workers.³⁵ In the current economy, many of these workers will remain unemployed for indefinite periods of time.

c. Going Out of Business

Moreover, numerous manufacturers and distributors in the dietary supplement industry will likely go out of business altogether. Many small businesses in the industry will be unable to afford the million dollar price tag of preparing NDI notifications and conducting clinical trials. Others will be unable to sustain the predicted 28-52.5 percent decreases in annual revenues. Indeed, it would not be surprising if most of the approximately 85 percent of dietary supplement manufacturers that produce less than \$20 million in annual sales went out of business.³⁶ This would translate into hundreds of businesses closing their doors.

If a significant number of manufacturers and distributors in the dietary supplement industry cease to operate, the loss of revenues and employees in the industry would be substantially larger than previously predicted. Instead of experiencing 28-52.5 percent decreases in sales and employees, these companies would lose 100 percent of their sales and workforce. This could easily translate into industry losses of billions of dollars and tens of thousands or even hundreds of thousands of unemployed workers. These losses would be especially devastating in the current economic situation.

d. Loss of Innovation

In addition, the Guidance will have a stifling effect on innovation in the dietary supplement industry. The Guidance significantly increases the costs of bringing new dietary supplements to market because of the considerable costs of preparing NDI notifications and conducting clinical studies, on top of the typical Research and Development expenses. When the new costs are combined with the high probability of FDA rejection, many manufacturers' cost-benefit analyses will not justify new product development. As a result, not only will the Guidance cause many currently-marketed dietary supplements to leave the market, it will also strongly deter the introduction of new products. The loss of innovation

³⁵ 28% of 199,000=55,720; 52.5% of 199,000=104,475.

³⁶ Nutrition Business Journal, Strategic Information for the Nutrition Industry, 16(6) U.S. Market Overview 5 (June/July 2011).

will mean that important new discoveries will not be made and new products with significant health benefits will not be developed. This will ultimately harm both consumers of dietary supplements and the U.S. economy as healthcare costs increase.

B. Costs to Dietary Supplement Consumers

In addition to harming the companies in the dietary supplement industry, the Guidance will also adversely affect consumers. Eighty-two percent of adults in the U.S. use dietary supplements, and approximately 40% are regular or heavy users of dietary supplements.³⁷ Unfortunately, under the Guidance, these 200 million consumers will encounter fewer dietary supplement options, and higher prices for dietary supplements. These changes will adversely impact consumer health.

i. Fewer Dietary Supplement Choices

The Guidance will significantly constrict the market for dietary supplements as many NDIs are rejected by the FDA and many manufacturers cease production because of the costly notification process and loss of revenues. In addition, the Guidance will deter many manufacturers and distributors from introducing new dietary supplement products to the market. The effect will be a significant reduction of the number of dietary supplements available to consumers. As a result, millions of consumers will no longer be able to purchase products upon which they rely.

ii. Higher Prices for Dietary Supplements

In addition, consumers will pay higher prices for the dietary supplements that do remain on the market for two reasons. First, manufacturers and distributors will pass along the expense of NDI notifications and clinical studies to consumers in the form of higher prices. Second, as the number of available dietary supplements shrinks and many producers cease production, there will be a substantial lessening of competition in the market. A basic law of economics is that reductions in competition in an open market cause prices to increase. With a reduction in the number of manufacturers and products, the remaining manufacturers are able to command higher prices for their products because consumers will

³⁷ Nutrition Business Journal, Supplement Business Report 2009, 3-49 (2009).

pay more to obtain the scarcer products. The result could be a substantial increase in the prices consumers pay for dietary supplements.

iii. Adverse Effects on Health

The increase in prices and reduction in dietary supplement options could adversely impact the health of many consumers. Many dietary supplements provide significant health benefits for consumers. In fact, a 2007 study found that the appropriate use of dietary supplements improves health and saves the U.S. approximately \$5 billion in annual healthcare costs.³⁸

However, with fewer dietary supplements available after the Guidance goes into effect and higher prices for the remaining dietary supplements, millions of consumers will reduce their intake of dietary supplements. Many of these consumers will suffer declines in their health, and, as a result, U.S. healthcare costs will increase.

C. Costs to U.S. Economy

Not only will the Guidance impact the dietary supplement industry, it will also affect the greater U.S. economy. The dietary supplement industry is interconnected in essential ways with many other industries. For example, the dietary supplement industry contributes to output, employment, and spending in the retail and wholesale trade industries, real estate, finance and insurance industries, non-dietary supplement manufacturing, and professional, scientific, and technical services industries, among others. As a result, the Guidance's significant disruption to the dietary supplement industry will have a "ripple effect" on many other industries.

i. Harm to U.S. Economic Output

A mathematical input-output model has recently been used to examine how the economic output, labor income, and employment in the dietary supplement industry affects

³⁸ Joan E. DaVanzo & Jean Freeman, *Effect of Selected Dietary Supplements on Health Care Reduction – Study Update (2007)*.

the economic output and employment in other industries.³⁹ The model is based on the assumption that when money enters a community through investment, revenues, or income, some of it is re-spent in the community, thereby creating additional economic impact.⁴⁰ The model estimated that for every dollar of consumer sales in the dietary supplement industry, an additional \$1.71 was re-spent in other industries.⁴¹ Thus, every dollar of sales generated by the dietary supplement industry produced a total economic contribution of \$2.71 to the U.S. economy.

Correspondingly, a loss in sales revenue in the dietary supplement industry under the Guidance will result in significant harm to the U.S. economy. Every one dollar loss in the dietary supplement industry will translate into a \$1.71 loss in other industries, for a total economic loss of \$2.71. Thus, an annual loss of \$7.84 billion-\$14.7 billion in the dietary supplement industry translates into a loss of \$13.4 billion-\$25.1 billion in other industries, for a total economic loss of \$21.2 billion-\$39.8 billion annually.⁴²

ii. Harm to Employment throughout the Economy

The input-output model was also used to estimate the impact of the dietary supplement industry on job creation in the rest of the economy. The model assumes that for every job in a specific industry, additional jobs are created throughout the community as a result of the spending by the company and its employees. The model estimated that for every job created in the dietary supplement industry, an additional 1.29 jobs are created in other industries.⁴³ Thus, every job in the dietary supplement industry is responsible for 2.29 jobs across the U.S.

Likewise, a loss of jobs in the dietary supplement industry will cause job loss in other industries as well. Every job lost in the dietary supplement industry will lead to 1.29 jobs

³⁹ Dobson DaVanzo & Associates, LLC, *The Economic Contribution of the Dietary Supplement Industry*, 9 (May, 2009), available at: <http://naturalproductsfoundation.org/clientuploads/NPF%20-%20Economic%20Impact%20Study.pdf>.

⁴⁰ *Id.* at 11.

⁴¹ *Id.* At 17.

⁴² \$7.84 billion*1.71=\$13.4 billion; \$14.7 billion*1.71=\$25.1 billion.

⁴³ Dobson DaVanzo & Associates, LLC, *The Economic Contribution of the Dietary Supplement Industry*, 17 (May, 2009), available at: <http://naturalproductsfoundation.org/clientuploads/NPF%20-%20Economic%20Impact%20Study.pdf>.

lost in other industries, for a total job loss of 2.29. Thus, if the Guidance results in the forced termination of between 55,720-104,475 workers in the dietary supplement industry, this will translate into an additional 71,878-134,772 jobs lost in other industries.⁴⁴ As a result, the Guidance will cause 127,598-239,247 jobs to be lost throughout the U.S. economy. In the current economic situation, many of these displaced workers will be unable to find other employment for an indefinite period of time.

iii. Decreases in Tax Revenues

The input-output model also estimated the amount of taxes paid to Federal, State, and local governments because of the dietary supplement industry. It assumes that the industry will directly pay many taxes such as payroll taxes, value-added taxes, corporate taxes, and others. Moreover, the industry will indirectly be responsible for other taxes paid by its employees (such as income taxes) and consumers (such as sales taxes). The model estimated that for every dollar of customer sales in the dietary supplement industry, approximately 23.5 cents in taxes was paid to the federal government and 20.9 cents was paid to state and local governments.⁴⁵

Similarly, a decrease in sales revenues in the dietary supplement industry under the Guidance will result in decreases in tax revenues to Federal, State, and local governments. Every one dollar loss in revenues in the dietary supplement industry will translate into a 23.5 cent loss in federal tax revenues and a 20.9 cent loss in state and local tax revenues. Thus, an annual loss of \$7.84 billion-\$14.7 billion in the dietary supplement industry translates into a loss of \$1.84 billion - \$3.54 billion in federal tax revenues and a loss of \$1.64 billion - \$3.07 billion in state and local tax revenues.⁴⁶

⁴⁴ $55,720 * 1.29 = 71,878$; $104,475 * 1.29 = 134,772$.

⁴⁵ Dobson DaVanzo & Associates, LLC, The Economic Contribution of the Dietary Supplement Industry, 19 (May, 2009), available at: <http://naturalproductsfoundation.org/clientuploads/NPF%20-%20Economic%20Impact%20Study.pdf>.

⁴⁶ $\$7.84 \text{ billion} * .235 = \1.84 billion ; $\$14.7 \text{ billion} * .235 = \3.54 billion ; $\$7.84 \text{ billion} * .209 = \1.64 billion ; $\$14.7 \text{ billion} * .209 = \3.07 billion .

IV. CONCLUSION

The FDA's Draft Guidance for the Dietary Supplement Industry regarding New Dietary Ingredient Notifications vastly broadens the definition of NDIs and increases the reporting requirements and recommendations for NDI notifications. As a result, the Guidance will impose significant burdens on dietary supplement manufacturers and distributors, consumers, and the greater U.S. economy. Manufacturers and distributors will spend a significant amount of time and money preparing NDI notifications and performing additional safety tests. Moreover, many dietary supplements will be rejected by the FDA under the stringent requirements of the Guidance, resulting in a significant loss of sales and the forced termination of many employees. As a result, consumers will encounter fewer dietary supplement options and higher prices for remaining products. The Guidance's impact will extend beyond the dietary supplement industry as employment, output, and tax revenues throughout the economy are affected. These losses will be especially devastating in the current economic climate.

Attachment A
Affidavit of Gretchen DuBeau

)
In re AGENCY INFORMATION COLLECTION)
ACTIVITIES; PROPOSED COLLECTION;)
COMMENT REQUEST; PREMARKET)
NOTIFICATION FOR A NEW DIETARY)
INGREDIENT)
)
)
)

Dkt. No. FDA-2011-N-0410

DECLARATION OF ALLIANCE FOR NATURAL HEALTH USA BY
GRETCHEN DUBEAU

I, Gretchen DuBeau, declare under penalty of perjury, and pursuant to 28 U.S.C. § 1746, that the following is true and correct to the best of my knowledge, information and belief:

1. I am the Executive Director of Alliance for Natural Health USA, 1350 Connecticut Avenue, NW, Washington, DC 20036 (“ANH”).
2. ANH is a United States division of an international, not-for-profit, non-governmental organization with headquarters in Washington, D.C. ANH is the successor to the American Association for Health Freedom, which, in turn, is the successor to the American Preventive Medical Association. ANH was founded in 2002.
3. ANH has a defined membership of 1,271 that consist of practitioners, medical doctors, scientists, business entities, consumers, and patients who variously manufacture, sell, distribute, recommend, and use dietary supplements.
4. As an alliance, ANH represents individuals and entities within the dietary supplement industry that are adversely effected by the FDA’s NDI Guidance

published June 3, 2011. *See Agency Information Collection Activities; Proposed Collection; Comment Request; Premarket Notification for a New Dietary Ingredient*, 76 Fed. Reg. 32214 (June 3, 2011)

5. ANH's corporate and individual members suffer substantial burdens not accounted for in FDA's analysis of burdens on industry but reflected accurately in the economic analysis performed by Dr. Joanna Shepherd Bailey appended to ANH-USA's comments in this proceeding. Although reluctant to sign individual affidavits and thus disclose their identities due to fear of FDA retaliation, ANH has contacted industry representative member corporations that were willing to disclose information concerning the burden imposed by the recently published NDI Guidance. The companies were chosen because they are representative of ANH members that manufacture, distribute, and sell dietary supplements.

6. The following information constitutes the information provided by the representative members directly to ANH:

- a. Between 40-75 percent of the 55,600 currently marketed dietary supplements will contain NDIs as defined by the NDI Guidance.
- b. Each product containing NDIs under the new NDI Guidance definition will require immediate NDI notification to the FDA.
- c. The typical hourly rate for employees with a science background that can provide the necessary information required in an NDI notification is \$30-\$40 per hour.

d. The NDI Guidance will impose significant costs upon industry to conduct the required safety studies. *See Attachment 1 (Cost Estimates for NDI Toxicology Studies).*

7. I have reviewed Dr. Joanna M. Shepherd Bailey's report entitled, *Economic Impact Statement of the FDA's Draft Guidance for the Dietary Supplement Industry regarding New Dietary Ingredient Notifications*. The report accurately presents the information I have provided to Dr. Shepherd Bailey based on my personal knowledge from interactions with ANH representative industry members.

Executed this 2nd day of August, 2011, in Washington, DC.



Gretchen DuBeau
Executive Director of
Alliance for Natural Health USA

Cost Estimate for NDI Toxicology Studies

7/26/2011

Study	Estimated Cost (\$)
Genotox Studies (3 study genotox battery)	
<i>Salmonella typhimurium</i> / <i>Escherichi coli</i> Plate Incorporation Mutation Assay in the Presence and Absence of Induced Rat Liver S-9 (Ames Test)	\$20,000
Lymphoma Mutagenesis in the L5178Y TK+/- Mouse with Colony Size Evaluation in the Presence and Absences of Induced Rat Liver S-9 with a Confirmatory Study	\$25,000
<i>In vitro</i> Chromosomal Aberration	\$22,500
Total:	\$67,500
Repeat Dose Studies	
14-Day dose range-finding oral study for max. tolerated dose (MTD) in rats	\$100,000
90-Day sub-chronic oral toxicity study (NOAEL) in rats	\$250,000
52-Week chronic toxicity (NOAEL) in rats	\$550,000
14-Day dose range-finding oral study (MTD) in dogs	\$150,000
90-Day sub-chronic oral toxicity study (NOAEL) in dogs	\$300,000
52-Week chronic toxicity (NOAEL) in dogs	\$650,000
2 -Year carcinogenicity study in mice	\$1,250,000
2-Year carcinogenicity study in rats	\$1,350,000
Total:	\$4,600,000
Reproduction Studies	
Pilot Teratology Study in Rats	\$40,000
Teratology Study in Rats	\$125,000
Pilot Teratology Study in Rabbits	\$50,000
Teratology Study in Rabbits	\$150,000
Two-Generation Study in Rats	\$650,000
Total:	\$1,015,000
Other Studies	
Repeat-Dose Tolerability study in Humans (30 patients)	\$888,000
ADME Study in Rats	\$65,000
Total:	\$953,000

Attachment B
Curriculum Vitae

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ACADEMIC EMPLOYMENT:

Associate Professor of Law, Emory University School of Law, Fall 2008 – present

Assistant Professor of Law, Emory University School of Law, Fall 2005 – Fall 2008 (Visiting Assistant Professor in 2004).

Assistant Professor of Economics, Clemson University, 2002 - 2004.

Visiting Assistant Professor, Georgia State University, Department of Economics, 2002.

Instructor, Emory University, Department of Economics, 2000 - 2002.

Macroeconomic Research Team, Federal Reserve Bank, Atlanta, GA, 1998 - 1999.

PUBLICATIONS:

Law Journal Publications

- *The Partisan Price of Justice: An Empirical Analysis of Campaign Contributions and Judicial Decisions*, with Michael Kang, 86 NEW YORK UNIVERSITY LAW REVIEW 101 (forthcoming 2011)
- *Measuring Maximizing Judges: Empirical Legal Studies, Public Choice Theory, and Judicial Behavior*, UNIVERSITY OF ILLINOIS LAW REVIEW __ (forthcoming 2011)
- *Lawyers, Ignorance, and the Dominance of Delaware Corporate Law*, with William Carney and George Shepherd, HARVARD BUSINESS LAW REVIEW __ (forthcoming 2011)
- *Baseball's Accidental Racism: The Draft, African-American Players, and the Law*, with George Shepherd, CONNECTICUT LAW REVIEW __ (forthcoming 2011)
- *Legislatures, Judges, and Parole Boards: The Allocation of Discretion Under Determinate Sentencing*, with Nuno Garoupa and Dhammika Dharmapala, 62 FLORIDA LAW REVIEW 1037 (2010).
- *Are Appointed Judges Strategic Too?* 58 DUKE LAW JOURNAL 1589 (2009).
- *Money, Politics, and Impartial Justice*, 58 DUKE LAW JOURNAL 623 (2009).

- *The Influence of Retention Politics on Judges' Voting*, 38 THE JOURNAL OF LEGAL STUDIES 169 (2009).
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- *Tort Reform's Winners and Losers: The Competing Effects of Care and Activity Levels*, 55 UCLA LAW REVIEW 905 (2008).
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- *The Demographics of Tort Reform*, with Paul H. Rubin. 4 THE REVIEW OF LAW & ECONOMICS 591 (2008).
- *Blakely's Silver Lining: Sentencing Guidelines, Judicial Discretion, and Crime* 58 HASTINGS LAW JOURNAL 533 (2007).
- *Tort Reform and Accidental Deaths*, with Paul H. Rubin. 50 THE JOURNAL OF LAW & ECONOMICS 221 (2007).
 - reprinted in ROUNDTABLE VIEWPOINTS: BUSINESS LAW (2008)
 - subject of Op-Ed, *Tort Reform Saves Lives*, WALL STREET JOURNAL by Rubin, Oct. 8, 2005.
- *Deterrence versus Brutalization: Capital Punishment's Differing Impacts Among States*, 104 MICHIGAN LAW REVIEW 203 (2005).
 - Featured in front page article: Adam Liptak, *Does Death Penalty Save Lives? A New Debate*, THE NEW YORK TIMES, November 18, 2007.
 - subject of Op-Ed, *Why Not All Executions Deter Murder*, THE CHRISTIAN SCIENCE MONITOR, Dec. 14, 2005.
- *An Empirical Study of Public Defender Effectiveness: Self-Selection by the "Marginally Indigent,"* with Judge Morris B. Hoffman and Paul H. Rubin. 3 OHIO STATE JOURNAL OF CRIMINAL LAW 223 (2005).
 - subject of Op-Ed, *Free-Market Justice*, THE NEW YORK TIMES, by Hoffman, Jan. 8, 2007.
- *Murders of Passion, Execution Delays, and the Deterrence of Capital Punishment*, 33 THE JOURNAL OF LEGAL STUDIES 283 (2004).
- *Does Capital Punishment Have a Deterrent Effect? New Evidence from Postmoratorium Panel Data*, with Paul Rubin and Hashem Dezhbakhsh. 5 AMERICAN LAW AND ECONOMICS REVIEW 344 (2003)
 - reprinted in BEZPIECZNE PANSTWO. NOWE TRENDY W POLITYCE KARN (2006).
 - reprinted in ECONOMICS, LAW AND INDIVIDUAL RIGHTS (2008)
- *Police, Prosecutors, Criminals, and Determinate Sentencing: The Truth about Truth-in-Sentencing Laws*, 45 THE JOURNAL OF LAW & ECONOMICS 505 (2002).
- *Fear of the First Strike: The Full Deterrent Effect of California's Two- and Three-Strikes Legislation*, 31 THE JOURNAL OF LEGAL STUDIES 159 (2002).
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Other Academic Publications

- *Public Choice and the Law*, with Paul H. Rubin in THE ELGAR COMPANION TO PUBLIC CHOICE ____ (Michael Reksulak, Lauralliam F. Shughart II eds., 2011, forthcoming)
- *Diversity, Tenure, and Dissent*, LEGAL WORKSHOP: DUKE LAW SCHOOL SYMPOSIUM ISSUE: EVALUATING JUDGING, JUDGES, AND JUDICIAL INSTITUTIONS (2010)
- *Elected Judges as Politicians*, LEGAL WORKSHOP, DUKE LAW SCHOOL (2010)
- *Judicial Opposition as Politics*, 166 JOURNAL OF INSTITUTIONAL AND THEORETICAL ECONOMICS 88 (2010).
- *The Economics of Capital Punishment*, in CRIMINAL LAW AND ECONOMICS 207 (Nuno Garoupa ed., 2010)
- *Delaware Corporate Law: Failing Law, Failing Markets*, with William J. Carney & George B. Shepherd in THE LAW AND ECONOMICS OF CORPORATE GOVERNANCE: CHANGING PERSPECTIVES (Alessio M. Paces, ed., 2010, forthcoming)
- *The Economics of Crime*, with Erling Eide and Paul H. Rubin, 2 FOUNDATIONS AND TRENDS IN MICROECONOMICS 291 (2006).
- *The Relationship between Prison Populations and Crime: Causes and Impacts*, 5 CRIMINOLOGY AND PUBLIC POLICY 285 (2006).
- *The Deterrent Effect of Capital Punishment: Evidence from a Judicial Experiment*, with Hashem Dezhbakhsh, 44 ECONOMIC INQUIRY 512 (2004).
- *Antitrust and Market Dominance*, with William G. Shepherd and George B. Shepherd, 46 THE ANTITRUST BULLETIN 835 (2002).

Books

- *THE ECONOMICS OF INDUSTRIAL ORGANIZATION*, with William G. Shepherd (2003).

CONGRESSIONAL TESTIMONY:

- *Testimony on Crime and Deterrence: Hearing on H.R. 2934, The Terrorist Penalties Enhancement Act of 2003. Before the House Judiciary Committee; Subcommittee on Crime, Terrorism, and Homeland Security*, 108th Cong. (2004).

EDUCATION:

- Emory University, Atlanta, GA, Ph.D. in Economics; Fields of Specialization: Law & Economics & Econometrics (study at Emory School of Law), 2002. Woodruff Scholar.
- Baylor University, Waco, TX, BBA in Economics and International Business, 1997 (GPA: 4.0; Summa Cum Laude)

TEACHING EXPERIENCE:

- Torts; Law and Economics; Analytical Methods for Lawyers; Statistics for Lawyers; Economics and Public Policy; Econometrics; Statistics; Accounting for Lawyers, Finance for Lawyers, Advanced Microeconomics; Introduction to Microeconomics

SELECTED SCHOLARLY PRESENTATIONS:

University Presentations

- University of Chicago Law School, Law & Economics Faculty Workshop (2011)
Products Liability Reform and Business Activity
- University of Texas School of Law, Center for Law, Business, and Economics (2011)
Products Liability Reform and Business Activity
- Northwestern University School of Law, Searle Center Policy Roundtable (2010)
Offer-of-Judgment Rules and Civil Litigation
- Economics Institute of the Academy of Sciences of the Czech Republic and Charles University Dept. of Economics, Prague (2010)
The Partisan Price of Justice
- University of Illinois College of Law, Conference to Honor Tom Ulen (2010)
Measuring Maximizing Judges
- George Mason Robert A. Levy Fellows Workshop in Law & Liberty (2010)
The Partisan Price of Justice
- University of Chicago Law School, Law & Economics Faculty Workshop (2009)
The Business of Judicial Elections
- Northwestern University School of Law, Law & Political Economy Colloquium (2009)
The Business of Judicial Elections
- Georgetown University Law School, Law & Economics Faculty Workshop (2009)
The Business of Judicial Elections
- Northwestern University School of Law, Judicial Behavior Workshop (2009)
Are Appointed Judges Strategic Too?
- Duke Law School, Workshop on Judicial Behavior (2009)
Are Appointed Judges Strategic Too?
- University of Southern California School of Law, CLEO Faculty Workshop (2007)
The Influence of Retention Politics on Judges' Decisions
- University of North Carolina School of Law, Faculty Colloquium (2007)
The Influence of Retention Politics on Judges' Decisions
- NYU School of Law, Comparative Law & Economics Forum (2007)
The Influence of Retention Politics on Judges' Decisions
- University of Michigan School of Law, Law & Econ Colloquium (2007)
The Demographics of Tort Reform
- Northwestern University School of Law, Law & Econ Colloquium (2006)
The Demographics of Tort Reform
- Florida State University School of Law, Law & Econ Colloquium (2006)
Cross-Monitoring and Corporate Governance
- Stanford Law School, Law & Econ Colloquium (2006)
Tort Reform and Accidental Deaths
- Univ. of Illinois College of Law, Comparative Law & Economics Forum (2005)
Tort Reform and Accidental Deaths
- George Mason University, Law & Econ Colloquium (2005)
Tort Reform and Accidental Deaths

- University of Georgia, Law & Econ Colloquium (2005)
Deterrence versus Brutalization: Capital Punishment's Differing Impacts Among States
- University of Alabama, Department of Economics Faculty Colloquium (2004)
Diversity, Segregation, and Crime: An Industrial Organization Analysis of Competition
- University of Toronto School of Law, Law & Economics Colloquium (2004)
Deterrence versus Brutalization: Capital Punishment's Differing Impacts Among States
- Georgetown University Law School, Olin Law & Economics Workshop (2004)
Capital Punishment and Deterrence: Evidence from a Judicial Experiment
- Georgia Tech University, Department of Economics Faculty Colloquium (2001)
Police, Prosecutors, Criminals, and Determinate Sentencing

Conferences and Meetings

- American Law & Economics Association Annual Meetings, New York, NY (2011)
The Partisan Price of Justice
- Southeastern Association of Law Schools Annual Meetings, Hilton Head, SC (2011)
Teaching Empirical Methods to Law Students
- American Law & Economics Association Annual Meetings, Princeton, NJ (2010)
The Business of Judicial Elections
- American Law & Economics Association Annual Meetings, San Diego, CA (2009)
Are Appointed Judges Strategic Too?
- Conference on New Institutional Economics, Max Planck Institute, Germany (2009)
Judicial Opposition as Politics
- Conference on Empirical Legal Studies, New York, NY (2007)
Tort Reform's Unintended Consequences
- American Law & Economics Association Annual Meetings, Boston, MA (2007)
The Demographics of Tort Reform
- European Association of Law and Economics Annual Conference, Madrid (2007)
The Demographics of Tort Reform
- Law and Society Association Annual Meetings, Baltimore, MD (2006)
Cross-Monitoring and Corporate Governance
- Canadian Law and Economics Association Annual Meetings, Toronto, CA (2006)
Cross-Monitoring and Corporate Governance
- American Law & Economics Assoc. Annual Meetings, New York, NY (2005)
Blakely's Silver Lining: Sentencing Guidelines, Judicial Discretion, and Crime
- American Economics Association Annual Meetings, Washington, D.C. (2005)
Blakely's Silver Lining: Sentencing Guidelines, Judicial Discretion, and Crime
- National Academy of Sciences, National Research Council Semi-Annual Meeting, Washington, D.C. (2004)
Capital Punishment and Deterrence
- American Law & Economics Assoc. Annual Meetings, New York, NY (2005)
Deterrence versus Brutalization: Capital Punishment's Differing Impacts Among States
- Southern Economics Association Annual Conference, New Orleans, LA (2004)
Deterrence versus Brutalization: Capital Punishment's Differing Impacts Among States
- American Law & Economics Assoc. Annual Meetings, Chicago, IL (2004)
Capital Punishment and Deterrence

- American Law & Economics Assoc. Annual Meetings, Toronto, CA (2003)
Major League Baseball, Market Regulations, and the Export of Employment
- American Law & Economics Assoc. Annual Meetings, Washington, D.C. (2001)
The Deterrent Effect of California's Two- and Three-Strikes Legislation

OTHER PROFESSIONAL ACTIVITIES:

- Peer-Reviewer (Referee) for: JOURNAL OF LEGAL STUDIES, JOURNAL OF LAW, ECONOMICS AND ORGANIZATION, JOURNAL OF EMPIRICAL LEGAL STUDIES, REVIEW OF LAW & ECONOMICS, INTERNATIONAL REVIEW OF LAW & ECONOMICS, SUPREME COURT ECONOMIC REVIEW, ECONOMICA, JOURNAL OF INDUSTRIAL ORGANIZATION, MANAGERIAL & DECISION ECONOMICS, CONTEMPORARY ECONOMIC POLICY, PUBLIC FINANCE REVIEW.
- Statistical Expert in the Areas of Damage Computation, Employment Law, Healthcare Law, and Competition Policy
- Other Professional Recognition for my research includes:
 - Television interviews on CNN Sunday; National Fox News; The O'Reilly Factor on the National Fox News Network; and CBS, ABC, and FOX local affiliates.
 - Op-Eds in *The Wall Street Journal*, *The New York Times*, and *The Christian Science Monitor*.
 - Print interviews include the *The New York Times*, *Chronicle of Higher Education* and *The Atlanta Business Chronicle*.
 - Radio interviews include BBC: Five Alive; WJR in Detroit, MI; KRLD in Arlington, TX; WLW in Cincinnati, OH; KTSA in San Antonio, TX; CHED in Edmonton, Canada; WRVA in Richmond, VA; CJME in Saskatoon, Canada; NTR in Saskatoon, Canada; WMVZ in Detroit, MI; KXNT in Las Vegas, NV; and KRLA in Los Angeles, CA.
 - Research also cited in the National Center for Policy Analysis: Executive Alert; The Weekly Standard; and The National Journal.
 - Research also requested for use by the Senate Judiciary Committee; U.S. Naval Academy; House of Representatives (Rep. Bob Goodlatt); Attorney General of Alabama; New York State Assembly (Stephen Kaufman); and the Chief of Criminal Appeals Division of Chicago (Renee Goldfarb).