CSPI CENTER FOR SCIENCE IN THE PUBLIC INTEREST
Publisher of *Nutrition Action Healthletter*

6049 '02 MAR 22 P1:17

March 21, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Petition for Rulemaking on Functional Foods and Request to Establish an Advisory Committee

To the Clerk:

Please find enclosed the original and four copies of the petition from the Center for Science in the Public Interest in the above referenced matter.

Please call (202) 332-9110, ext. 362 with any questions. Thank you.

Sincerely,

Patricia Zenich

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Research Assistant

02P-0122

CP 1

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

6050 '02 MAR 22 P1:17

Petition for Rulemaking on	)	
Functional Foods and	)	Docket No. _____
Request to Establish an	)	
Advisory Committee	)	
_____	)	

Submitted by the

Center for Science in the Public Interest

March 21, 2002

Center for Science in the Public Interest
1875 Connecticut Ave., NW
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Citizen Petition

I. Action Requested

The undersigned submits this petition under Sections 402(a), 403(a), and 701(a) of the Federal Food, Drug and Cosmetic Act (FDCA) to request that the Commissioner of the Food and Drug Administration (FDA):

- Develop and promulgate regulations or other guidance for industry on the safety-related information required on labels for functional foods;
- Develop an enhanced system to record and analyze reports of health problems associated with functional foods;
- Issue regulations to clearly establish the nature and extent of evidence companies need to adequately support structure/function claims;
- Require manufacturers of functional foods to provide notification of the use of novel ingredients to the FDA prior to marketing;
- Require manufacturers of food products making structure/function claims on labels or on labeling to provide notification to the FDA within 30 days after marketing begins;
- Require all foods with structure/function claims to carry the disclaimer currently required on dietary supplements that make such claims; and
- Establish an advisory committee to reevaluate the current labeling approaches for foods with novel ingredients to determine whether the distinctions between structure/function claims and health claims are understood by consumers and identify other changes needed to improve consumer understanding of health-related claims.

These requests are based on recommendations contained in the General Accounting Office (GAO) report entitled, *Food Safety: Improvement Needed in Overseeing the Safety of Dietary Supplements and Functional Foods.*[1] Although that report was issued more than one and a half years ago, the FDA has taken little action to implement the GAO's recommendations.

II. Statement of Factual Grounds

In July 2000, the GAO released a report concluding that the "FDA's efforts and federal laws provide limited assurances of the safety of functional foods and dietary supplements."[2] The GAO found, *inter alia,* that some functional food products do not contain the necessary safety-related information on their labels to protect consumers. The GAO also determined that the "FDA cannot effectively assess whether a functional food or dietary supplement is adversely affecting consumers' health because, among other things, it does not investigate most reports it receives of health problems potentially caused by these products."[3]

The GAO expressed further concern that the consumer is only provided limited assistance in making informed choices because the FDA does little to protect consumers against "inaccurate

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[1] GAO/RCED-00156 (July 2000) [hereinafter *GAO Report*].

[2] *Id.* at 4.

[3] *Id.* at 5. The GAO further recommended that the FDA clarify the boundary between conventional foods, including functional foods and dietary supplements, particularly the circumstances under which dietary supplements may be marketed in food form. The GAO explained that the failure to have a clear boundary means that "unsafe products could come to market because companies did not develop a sufficient level of evidence on their safety." While acknowledging that the FDA has been attempting to do this on a case-by-case basis, e.g. in its letters to Benecol and Hains, the GAO concludes that the FDA needs to clarify this boundary through regulations or guidance. *Id.* at 25-26.

and misleading claims." In particular, the GAO criticized the FDA for not clearly establishing "the nature and extent of evidence companies need to adequately support structure/function claims."[4]

Moreover, the GAO noted that "consumers may incorrectly view structure/function claims as claims to reduce the risk of or treat a disease. . . . Consequently, [the GAO believes] that consumers may attempt to treat a disease with a product not capable of producing this benefit."[5]

To address these concerns, the GAO recommended that the FDA:

- develop and promulgate regulations or other guidance for industry on the safety-related information required on labels for functional foods;
- develop an enhanced system to record and analyze reports of health problems associated with functional foods;

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[4] *Id.* at 5. The GAO also concluded that the FDA has taken no enforcement action against companies making "questionable claims," noting that FDA "has never asked a company marketing dietary supplements or functional foods with structure/function claims to voluntarily provide the agency with evidence supporting the claim, nor has FDA ever initiated an enforcement action to obtain access to the information through the courts." *Id.* at 21. Since publication of the GAO's report, the FDA has issued an "industry letter" to manufacturers of functional foods, reminding them of the legal requirements with which they must comply. Letter from Christine J. Lewis, Ph.D., Director, Office of Nutritional Products, Labeling and Dietary Supplements, FDA, Jan. 30, 2001 *available at* <www.cfsan.FDA.gov> [hereinafter *Industry Letter*]. In addition, the Agency has also released a series of warning letters to producers of foods with novel ingredients advising them that their products are adulterated and/or misbranded. Warning Letters from John B. Foret, Director of Compliance and Enforcement, CFSAN, FDA, *available at* <www.fda.gov/scripts/wlcgm/indexissuer.cfmm>, to Julia Sabin, President Smucker Quality Beverages, Inc. (June 8, 2001 ONPLDS 14-01); Cynthia Davis, Executive Vice President, US Mills, Inc. (June 5, 2001 ONPLDS 13-01); Doug Levin, CEO, Fresh Samantha, Inc. (June 4, 2001 ONPLDS 11-01); and Rodney C. Sacks, Chairman, Hansen Beverage Co. (June 4, 2001 ONPLDS 12-01).

[5] *Id.* at 5

- develop and promulgate regulations or other guidance for industry on the evidence needed to support structure/function claims.[6]

The GAO also recommended that Congress amend the FDCA to require functional food manufacturers to meet three requirements that are now only applicable to dietary supplements:

- "advance notification to FDA regarding ingredients that companies have determined are safe;"
- "notification to FDA regarding the use of structure/function claims;" and
- "disclaimers of FDA approval on product labels containing structure/function claims."[7]

The GAO further recommended that Congress establish an expert panel to:

> "reexamine the current approach to labeling, which distinguishes health claims from structure/function claims to determine whether the intended distinctions can be made clear and meaningful to consumers, or failing this, to identify other changes needed to improve consumers' understanding of health-related claims."[8]

The FDA should act on these GAO recommendations. Although the Agency has acknowledged the need for many of these actions in its Ten Year Plan for dietary supplements, it must also take action with respect to functional foods and establish firm time frames for the implementation of the GAO's recommendations. While the GAO directed some of its recommendations to Congress, rather than the FDA, the GAO did not state that the FDA lacked the authority to make these kinds of changes. Therefore, the FDA need not wait for Congress to

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[6] Structure/function claims should be based on universally recognized factual statements concerning known and substantively significant relationships regarding the effect of a substance on the structure or function of the body. The FDA should issue regulations setting forth a list of claims that may be used and establish a petition process for the approval of new claims.

[7] *GAO Report* at 26.

[8] *Id.*

act because the Agency already has statutory authority to take each of the steps suggested by the GAO in its recommendations to Congress.[9]

III. Statement of Legal Grounds

A. The FDA has legal authority to require safety-related information to appear on labels of products containing novel ingredients.

Under the Federal Food, Drug, and Cosmetic Act's misbranding provisions, a food is "misbranded" if its label is "false or misleading in any particular."[10] Congress further provided that in determining whether a product is misbranded because of misleading labeling, it is necessary to evaluate whether the label "fails to reveal facts material in light of . . . representations [made] or material with respect to consequences which may result from the use of the article."[11]

Under its general authority, the FDA has "authority to promulgate regulations for the efficient enforcement of this Act . . ."[12] Thus, Congress has given the FDA broad authority to require that manufacturers provide key additional information beyond what is already required to appear on product labels if the additional information is necessary to prevent consumers from being misled.[13] Safety information is key additional information for products containing

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[9] Because the notice and disclaimer requirements at issue were previously adopted pursuant to the Dietary Supplement Health and Education Act, the GAO may have assumed that amending a statute was the most obvious way in which the dietary supplement requirements could be extended to functional foods. But other mechanisms are available to the Agency.

[10] FDCA § 403(a), § 343(a).

[11] FDCA § 201(n), 21 U.S.C. § 321(n).

[12] FDCA § 701, 21 U.S.C. § 371.

[13] Frederick H. Degnan, *The Food Label and the Right-to-Know,* 52 Food, Drug L. J. 49, 51 (1997).

ingredients known to interact with particular medications, exacerbate pre-existing conditions or become dangerous when used over an extended period of time.[14]

In carrying out its mandate to prevent misbranding, the FDA may require "special labeling" for food "where information is necessary to ensure that consumers are aware of special health risks associated with consumption of a particular product."[15] Thus, although the FDA does not consider "protein products intended for use in weight reduction . . . inherently unsafe," it requires such products to carry a warning statement that provides in pertinent part that "very-low-calorie protein diets may cause serious illness or death."[16] The label further further warns "Not for use by infants, children or pregnant or nursing women."[17]

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[14] E.g., FDA has issued a public health advisory on the risk of drug interactions with St. John's wort and drugs used to treat HIV infection and to prevent the risk of organ transplant, as well as drugs used for heart disease, depression, seizures and contraception. FDA, Public Health Advisory, Subject: Risk of Drug Interactions with St. John's Wort and Indinavir and Other Drugs, Feb. 10, 2000. Ginkgo can act as a blood thinner. Taking it with other anticoagulants may increase the risk of excessive bleeding or stroke. A. Fugh-Berman, *Herb-drug interactions,* 355 Lancet 134 (1998). National Institutes of Health (NIH) investigators determined that garlic supplements can cause potentially harmful side effects when combined with a type of medicine used to treat HIV/AIDS. Piscitelli et. al (2002) Garlic-Saquinavir Interaction. Clin Infect Dis 34:234-238. Most recently, the FDA has begun to investigate reports of liver toxicity associated with the use of kava that have led to the withdrawal of kava-containing products from several European countries. U.S. FDA, *Letter to Health Care Professionals about FDA Seeking Information on Liver Injury and Kava Products.* Dec. 19, 2001, *available at* <www.cfsan.gov/~dem/ds-ltr27.htm>.

[15] 61 Fed. Reg. 3117 (Jan. 30, 1996) (Final rule permitting use of Olestra).

[16] *Id.* at 3160. The FDA's authority to issue such warnings was upheld in *Council for Responsible Nutrition v. Goyan,* No. 80-1124 (D.D.C. Aug. 1, 1980), *reprinted in* Food, Drug Cosm. L. Rep. (CCH) ¶ 38,057.

[17] 21 C.F.R. § 101.17(d)(l).

Similarly, the FDA requires products containing Olestra to state:

> **This Product Contains Olestra.** Olestra may cause abdominal cramping and loose stools. Olestra inhibits the absorption of some vitamins and other nutrients. Vitamins A, D, E and K have been added.[18]

Moreover, the FDA has used its authority to require warning statements on the labels of iron-containing products including both dietary supplements and drugs. The warning statements are required to help prevent accidental overdoses of iron-containing products by children.[19]

The FDA has also required that a variety of specific information about particular ingredients be disclosed to alert consumers who may have special dietary or medical concerns. For example:

- Products containing the artificial sweetener aspartame must state:

  "PHENYLKETONURICS: CONTAINS PHENYLALANINE.[20]

- Sulfite levels exceeding a threshold of ten parts per million must be declared on food labels.[21]

- Any food whose reasonably foreseeable consumption may result in a daily ingestion of 50 grams of sorbitol or 20 grams of mannitol must state: "Excess consumption may have a laxative effect."[22]

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[18] 61 Fed. Reg. at 3159-60.

[19] 62 Fed. Reg. 2218, 2249 (Jan. 15, 1997) (Final Rule on Iron Containing Supplements and Drugs: Label Warning Statements and Unit-Dose Packaging Requirements) (codifed at 21 C.F.R. § 101.17(e).

[20] 21 C.F.R. §§ 172.804(d)(2).

[21] 21 C.F.R. § 101.100(a)(4).

[22] 21 C.F.R. §§ 184.1835(e), 180.25(e).

The courts have upheld the FDA's authority to impose such labeling requirements.[23] Given the potential harm that may occur to consumers who eat products that contain novel ingredients that may interact with their medicines, exacerbate existing medical conditions, or cause other health problems, the agency surely would have the authority to require warnings to alert consumers to these risks.

B. The FDA has the authority to develop an enhanced system to record and analyze health problems associated with functional foods.

The FDA has the authority to develop appropriate systems for analyzing health problems associated with functional foods. Section 903(c) of the Act specifically authorizes the FDA to collaborate with other science-based federal agencies to enhance the scientific and technical expertise available to the Secretary with respect to "the development, clinical investigation, evaluation and postmarket monitoring of emerging medical therapies, including . . . advances in nutrition and food science."[24]

C. The FDA has the authority to issue regulations or guidance on the evidence needed to support structure/function claims.

The FDA has explicit authority under Section 701(a) to issue regulations "for the efficient enforcement" of the FDCA. In addition, it is specifically authorized to develop guidance

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[23] E.g., Council for Responsible Nutrition v. Goyan (No. 80-1124 D.D.C. Aug. 1, 1980), *reprinted in* Food, Drug Cosm. L. Rep. (CCH) ¶ 38,057, National Nutritional Foods Association v. Novitch, 589 F. Supp, 798 (S.D.N.Y. 1984) (both courts upheld the FDA's authority to require labels on low-calorie protein products to alert consumers to the health risks associated with use of those products). *See also,* Cosmetic, Toiletry and Fragrance Assoc., Inc. v. Schmidt, 409 F. Supp. 57, 64 (D.D.C. 1976)(upheld FDA warnings on all foods, drugs and cosmetics sold in aerosol cans to avoid puncturing or incinerating the cans and to avoid storing them above 120 degrees Fahrenheit).

[24] 21 U.S.C. § 393(c).

documents with public participation.[25] Indeed, as the court noted in *Pearson v. Shalala,*[26] under the Administrative Procedure Act, the FDA cannot provide a reasoned explanation for determining whether a health claim is supported by "significant scientific agreement" unless it defines the criteria being used. The court, therefore, required the FDA to "explain what it means by significant scientific agreement, or at a minimum, what it does not mean." [27] Similarly, the FDA must explain the level of evidence needed to support structure/function claims before it can take enforcement action against particular products for insufficient substantiation.

D. The FDA can impose premarket notification requirements for novel ingredients under existing statutory authority.

Under its § 701(a) authority to promulgate regulations, the FDA has recently proposed mandatory premarket notification requirements for products of biotechnology (PNB). In explaining its decision to propose those requirements, the FDA listed a number of concerns that are also raised with respect to functional foods that contain novel ingredients.[28]

In the Preamble to the PNB proposal, the FDA explained that "premarket [n]otification will help to ensure that all market entry decisions by the industry are made consistently and in full compliance with the law."[29] Similarly, the FDA has stated its concern "that some of the herbal and

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[25] FDCA § 701(h)(1)(A), 21 U.S.C. § 371(h)(l)(A).

[26] 164 F.3d 650 (D.C. Cir. 1999).

[27] *Id.* at 660.

[28] 66 Fed. Reg. 4706, 4708-09 (Jan. 18, 2001) (Proposed Rule on Premarket Notification Concerning Bioengineered Foods) [Hereinafter *PNB Proposal*].

[29] *PNB* at 4712. The FDA explained that "because breeders using rDNA technology can introduce genetic material from a much wider range of sources than previously possible, there is a greater likelihood that the modified food will contain substances that are significantly different from, or are present in food at a significantly higher level than, counterpart substances

other botanical ingredients that are being added to conventional foods may cause the food to be adulterated because these added ingredients are not being used in accordance with an approved food additive regulation and may not be GRAS for their intended use."[30]

The FDA can also impose premarket notification requirements for novel ingredients to ensure products are not misbranded. As the FDA acknowledged in the preamble to the PNB proposal, existing common or usual names might not be appropriate for some substances produced by this technology.[31] Similarly, with respect to functional foods, the FDA needs to evaluate the common or usual names for various botanical ingredients to ensure that they accurately reflect the ingredient's composition. For example, herbs vary depending on the species being used, the part of the plant from which they are taken and the strength of the extract. It would, therefore, be false and misleading to consumers to identify an ingredient as "ginseng," when there is Siberian Ginseng, Red Panax Ginseng and American ginseng, all of which have different properties and any one of which may be contained in a product.

Moreover, the FDA needs to determine whether instructions for use are required and whether the manufacturer needs to specify the amount and frequency with which the functional food should be consumed to produce desired effects. Finally, warning labels might be needed in

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historically consumed in food." Such ingredients may not be Generally Recognized as Safe (GRAS) and may require regulation as food additives. Therefore, "FDA should be made aware of the intended marketing of the modified food and have access to relevant information to evaluate whether the [substance] is a food additive. . . ." *Id.* at 4709.

[30] *See Industry Letter, supra* note 4.

[31] *Id.* at 4710.

cases where a novel ingredient has been associated with interactions with particular prescription medicines or medical conditions or where a particular ingredient should not be consumed over extended time periods.[32]

E. FDA has the authority to require notification of structure/function claims.

Under § 701(a), the FDA also has the authority to enact regulations requiring food producers using structure/function claims to notify the Agency. As the GAO explained, "the absence of notification requirements for functional foods making structure/function claims limits FDA's ability to identify inappropriate claims."[33] Identifying inappropriate claims is essential to preventing the sale of potentially dangerous products.

The FDA has explained how notification requirements for structure/function claims appearing on dietary supplements protects the public health. The same rationale applies to foods making structure/function claims.

> "Because structure/function claims are not subject to the new drug approval standard or the health claim authorization standard and do not undergo FDA review before marketing, FDA believes it is important to ensure that such claims do not promote products for disease treatment or prevention claims. Disease treatment or prevention claims can pose serious risks to consumers if they induce consumers to substitute ineffective or less effective treatments for proven ones, especially if the disease involved is serious or life- threatening. Therefore, the Agency believes that ensuring that such claims cannot be made without a demonstration of safety and effectiveness will protect and promote public health."[34]

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[32] *See* note 12 *supra* and accompanying text.

[33] *GAO Report* at 26

[34] 65 Fed. Reg. 999, 1003 (Jan. 6, 2000) (Final Rule on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body).

The FDA, should, therefore, exercise its authority to require notification of such claims within 30 days of marketing to carry out the general mandate of the act to prevent the sale of adulterated and misbranded products.[35]

F. FDA has the authority to require that functional foods carry the disclaimer that must appear on supplement labels.

Under its § 701(a) rulemaking authority, the FDA should also require that functional foods making structure/function claims carry the same disclaimer as dietary supplements to alert consumers to the fact that the FDA has not verified the accuracy of the claim and that the product is not intended for use as a drug. That disclaimer states: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."[36] As the GAO concluded in its report: "the absence of disclaimer requirements for structure/function claims on functional foods limits consumers' ability to distinguish FDA-authorized claims from other claims that have not been reviewed and authorized."[37]

Congress did not preclude the FDA from extending the disclaimer requirements to foods. In fact, Congress anticipated that some food manufacturers would use the disclaimer in conjunction with structure/function claims on their products. Thus, Congress provided that a food or dietary

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[35] *PNB Proposal* at 4708. Although the GAO recommended that foods that bear labeling with structure/function claims notify FDA within 30 days after marketing, ideally such notification should take place *prior* to marketing.

[36] FDCA § 403(r)(6)(C), 21 U.S.C. § 353(r)(6)(C).

[37] *GAO Report* at 26.

supplement making claims in accordance with Section 403(r)(6) of the FDCA -- which requires use of the disclaimer -- is not a drug.[38]

G. FDA has the authority to create an advisory committee on functional foods.

As discussed earlier, the GAO recommended that Congress establish an advisory committee to evaluate various issues relating to consumer understanding of health and structure/function claims. Although GAO urged Congress to mandate this step, the FDA already has the authority to set up an advisory committee to address these issues.

Under the Federal Advisory Committee Act (FACA) either Congress *or* the "head of an agency" may establish an advisory committee so long as specified procedural requirements are followed.[39] Thus, the FDA need not and should not wait for Congressional authorization to begin establishing an advisory committee.

IV. Conclusion

In light of the growth of the functional food market, the FDA should take prompt action to adopt the GAO's recommendations. It is particularly important that the Agency adopt notification and disclaimer requirements for functional foods. This is the best way in which the FDA can prevent the marketing of products with illegal ingredients before they reach consumers and to ensure that consumers are alerted to the fact that the FDA has not reviewed the accuracy of the claims.

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[38] FDCA § 201(g)(D).

[39] 5 U.S.C.A. App. 2 § 9.

V. Environmental Impact

This petition is subject to a categorical exclusion under 21 C.F.R. § 25.30(h) and, therefore, CSPI is not required to prepare an environmental assessment.

VI. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

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Director of Legal Affairs

Ilene Ringel Heller
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