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April 29, 1999

Mr. Donald R. Arbuckle
Acting Administrator and Deputy Administrator
Office of Management & Budget/OIRA
Room 350
Old Executive Office Building
Washington, D.C. 20503

Re: Docket No. 98N-0044 ("Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body;" Proposed Rule; 63 Fed. Reg. 23624 (April 29, 1998))

Dear Don:

The Food and Drug Administration's pending rulemaking on "Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body," 63 Fed. Reg. 23624 (April 29, 1998) ("Structure/Function Proposal), presents a number of issues of particular relevance to regulatory review by the Office of Information and Regulatory Affairs. Accordingly, I am attaching the comments filed with FDA on the proposed rule by Cargill Incorporated, Galagen Inc., and General Nutrition Corporation.

Although it appears that FDA's Structure/Function Proposal may not be finalized in its current form, we believe it is important to emphasize that FDA did not adequately address the Proposal's cost and benefit implications not only for companies, but, more importantly, for the national healthcare system. We are writing this letter to ensure that this issue receives appropriate analysis and consideration as these regulations are further developed by FDA, and reviewed by OMB.

As demonstrated in the attached comments, as currently drafted, FDA's Proposal adopts a relatively narrow approach to how much scientific information can be

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provided to the public about dietary supplements. The Proposal would unduly circumscribe the range of permissible "structure/function" claims for dietary supplements. FDA's limits will have the effect of restraining public access to accurate, meaningful information about safe and effective dietary products. This, in turn, will reduce incentives to conduct research into the beneficial health effects of dietary supplements and functional ingredients. If responsible, research-based companies are not able to use and communicate the results of their research, they will be less likely to undertake it. This cuts against the grain of the Dietary Supplement Health and Education Act of 1994, and also conflicts with First Amendment principles. See, e.g., Washington Legal Foundation v. Friedman, 1998 U.S. dist. LEXIS 11876 (D.D.C. July 30, 1998) (holding FDA may not completely suppress dissemination of truthful and non-misleading health information; Pearson v. Shalala, No. 98-5043 (D.C. Cir. Jan. 15, 1999) (First Amendment requires skepticism if FDA decides to "keep people in the dark for what the government perceives to be their own good").

By diminishing the flow of truthful, non-misleading information about dietary supplements, the current version of FDA's Structure/Function Proposal would handicap, rather than "empower," consumers to make preventive health care choices based on the scientific benefits of particular dietary supplements. This would thwart DSHEA's purposes, and reduce the public health benefits Congress sought to provide by enacting the legislation.

Specifically, please note the discussion of "benefit/cost analysis" and "regulatory alternatives" on pages 20-22 of the attached comments. Of special significance here is the fact that FDA has not considered the value of public health benefits to be gained (or lost) by virtue of granting (or denying) consumers access to accurate, meaningful health information about dietary supplements. As noted in the comments, this failure of analysis contrasts with other recent FDA regulations where the Agency did evaluate the public health impacts associated with consumers changing their behavior based on the extent and quality of information they are allowed to receive (e.g., recent regulations on tobacco, nutrition labeling, and ephedra).

FDA's discussion of "regulatory alternatives" is also problematic. As noted in the attached comments, FDA has stated that it does not consider its proposed prohibition of implied disease claims to be required as a matter of law. Indeed, FDA "considered treating a statement about a dietary supplement as a disease claim only if the statement included an express reference to a specified disease." 63 Fed. Reg. at 23630 (emphasis added). FDA rejected this reasonable alternative, however, in favor of a more restrictive approach, because the less burdensome approach "would be inconsistent with FDA's longstanding policy." Id. But the decision to choose a more burdensome regulatory alternative violates the letter and intent of DSHEA, and also

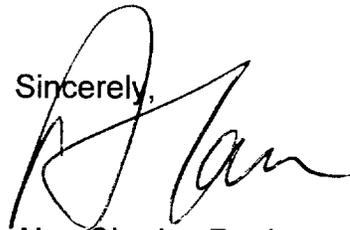
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contravenes the requirements of the Unfunded Mandates Reform Act and Executive Order 12866.

We hope this information will be useful in OIRA's deliberations, and we would be pleased to discuss it with you or the agency further.

Thank you for your consideration of these views.

Sincerely,

A handwritten signature in black ink, appearing to read "Alan Charles Raul". The signature is fluid and cursive, with a large initial "A" and "C".

Alan Charles Raul

ACR/syt
Enclosure

cc: Hon. Jane E. Henney
Hon. Tom Bliley
Hon. John D. Dingell
Hon. Dan Burton
Hon. Henry A. Waxman
Hon. David McIntosh
Hon. Dennis J. Kucinich

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September 28, 1998

BY FACSIMILE AND U.S. MAIL

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive
Room 1-23
Rockville, MD 20857

Re: Docket No. 98N-0044 ("Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body; Proposed Rule; 63 Fed. Reg. 23624 (April 29, 1998))

Dear Sir or Madam:

Attached herewith are the comments of Cargill Incorporated, GalaGen Inc., and General Nutrition Corporation in connection with the Food and Drug Administration's "Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body; Proposed Rule;" 63 Fed. Reg. 23624 (April 29, 1998).

Please contact the undersigned if you have any questions about these comments.

Sincerely,



Alan Charles Raul

ACR/syt
Enclosures

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9/28/98

COMMENTS OF
CARGILL INCORPORATED,
GALAGEN INC.,
AND
GENERAL NUTRITION CORPORATION
ON
FDA'S "STRUCTURE/FUNCTION" PROPOSAL (Docket No. 98N-0044)

Cargill Incorporated, GalaGen Inc. and General Nutrition Corporation are pleased to submit these comments on the Food and Drug Administration's ("FDA") "Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body; Proposed Rule and Dietary Supplements: Comments on Report of the Commission on Dietary Supplement Labels; Notice," 63 Federal Register 23624 et seq. (Apr. 29, 1998) ("FDA's Structure/Function Proposal").

We comprise life science research companies, functional food ingredient and product manufacturers committed to promoting standards of scientific research and substantiation through clinical research. We are working to create a positive regulatory environment that permits responsible companies to communicate the scientifically validated health benefits of dietary ingredients to consumers.

The September 17, 1998, issue of the New England Journal of Medicine, Vol. 339, Number 12, addresses a number of issues concerning scientific testing of dietary supplements. We wholeheartedly agree that manufacturers of dietary supplements and

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ingredients have the burden to test their products for safety and efficacy through clinical research and other appropriate scientific methods. Moreover, we agree that FDA must use its substantial authority under existing law to remove unsafe products from the marketplace. See 21 U.S.C. § 342(f). It appears that the editors of the New England Journal of Medicine, and other interested parties, may not be fully aware of FDA's specific statutory authority to move against unsafe dietary supplement products. FDA should publicize its responsibilities and utilize its statutory authority effectively in order to protect the public from unsafe items in the food supply, including any dangerous dietary supplements or ingredients. This important role can help assure the public that dangerous products will not go unregulated. Responsible manufacturers, as well as the public, stand to gain from the appropriate exercise of FDA's statutory authority.

Similarly, we hope that FDA will accept the New England Journal of Medicine's encouragement to promote the role of scientific research in substantiating the health benefits associated with consuming certain dietary supplements. The current draft of FDA's proposed regulation would have the opposite effect. It would create disincentives and erect regulatory barriers to conducting and publicizing scientific research into the link between dietary ingredients and health. FDA must stop treating all of these products like "snake oil"; once the Agency starts holding these products to reasonable standards of responsibility, the public will have a basis to distinguish those supplements and ingredients that are demonstrated to be safe, effective and useful in maintaining health and enhancing quality of life, from those that are not. The public is

the loser if FDA makes it hard for manufacturers to communicate their research publicly.

Executive Summary

DSHEA provided a new, more flexible framework for regulating dietary supplements. In DSHEA, Congress specifically recognized the link between ingestion of dietary supplements and prevention of chronic disease, improvements in public health, and reduction in long-term health care expenditures. Indeed, the public health benefits of dietary supplements were a key reason for enacting DSHEA. Surely, Congress did not intend that advances in scientific understanding would be withheld from the American public.

FDA's proposal, however, would discourage scientific investigation into how dietary supplements and ingredients impact the structure or function of the body. The proposal would thus impede public access to accurate, meaningful information about safe and beneficial dietary supplements and functional dietary ingredients. This would also reduce the incentives to conduct research into the beneficial health effects of dietary supplements by curtailing the ability of responsible companies to disseminate the results of their research. FDA's proposal essentially requires that structure/function claims be expressed in an oblique or elliptical fashion. This will only serve to confound the public; the public should not need to "decode" dietary supplement claims. It will also result in fewer consumers making the right decisions about what dietary supplements are appropriate for them. Overall public health will suffer as a consequence of FDA's restrictive approach.

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Impacts on the structure or function of the body inevitably play a role in maintaining or promoting health; therefore, beneficial structure/function impacts will always tend to provide implicit protection against disease. FDA's overbroad definition of "disease" would, therefore, have the effect of converting too many structure/function claims into "disease" claims. This, in turn, would unduly restrict the flow of truthful information under DSHEA.

FDA's Structure/Function Proposal appears to be illogical and contorted because the Agency has sought to exclude even the slightest "implicit" suggestion that dietary supplements and ingredients play a role in preventing disease. FDA also takes too narrow view of what is "health maintenance" versus "disease prevention." This restrictive approach cuts against the letter and spirit of DSHEA. It is neither consistent with the current state of the law as amended by DSHEA, nor with the state of existing science. Both clearly recognize the link between many beneficial dietary supplements and ingredients and long-term prevention of chronic disease.

All constitutional, statutory and public policy rationales favor allowing consumers access to meaningful health information. FDA's structure/function regulation should not preclude a dietary supplement from making "implicit" references to disease protection. To the contrary, structure/function claims for dietary supplements must be recognized as a subset of health-related claims. As such, they are allowed to characterize their beneficial impacts on disease. FDA must recognize that Congress would not have enacted statutory language specifically linking dietary supplements with disease

prevention if it had intended for FDA to prohibit any such references by administrative fiat.

Under the Unfunded Mandates Reform Act of 1995, and Executive Order 12866, FDA must not issue a final rule on structure/function claims until it conducts and considers a substantive benefit-cost analysis that identifies the benefits to public health of consuming beneficial dietary supplements and ingredients. The analysis must also identify the potential health benefits that are lost as a consequence of reduced consumer access to useful information about the health-related properties of dietary supplements and ingredients. If structure/function claims are forced to be relatively uninformative, this will be the unfortunate result, and the public will be the loser.

Finally, FDA must adopt a final rule that embodies, rather than rejects, the fundamental regulatory principles enacted in DSHEA:

- The Federal Government should take swift action against products that are unsafe or adulterated, [but] the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers.
- There is a growing need for emphasis on the dissemination of information linking nutrition and long-term good health.

I. BACKGROUND

As currently drafted, FDA's Structure/Function Proposal would deny consumers access to useful information about the health benefits of dietary supplements. This runs counter to both the letter and purpose of the Dietary Supplement Health and Education Act of 1994 ("DSHEA"), Pub. L. No. 103-417, 108 Stat. 4325 (amending the

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Federal Food, Drug and Cosmetic Act ("FDCA"), 21 U.S.C. § 321 et seq.). In DSHEA, Congress provided a new, more flexible framework for regulating dietary supplements. Congress legislated the new approach because FDA had unduly "limited" consumer access to healthful dietary supplements under the prior regulatory regime. 30 Weekly Comp. Pres. Doc. 2158 (Oct. 25, 1994) (President Clinton's statement on signing the DSHEA into law).

DSHEA established the new regulatory policy for dietary supplements in response to a number of medical, economic and public policy findings. Specifically, Congress found that:

- (a) the benefits of dietary supplements to health promotion and disease prevention have been documented increasingly in scientific studies;
- (b) there is a link between the ingestion of certain nutrients or dietary supplements and the prevention of chronic diseases such as cancer, heart disease, and osteoporosis; and
- (c) the appropriate use of safe nutritional supplements will limit the incidence of chronic diseases, and reduce long-term health care expenditures.

21 U.S.C. § 321 note. Congress manifestly intended to "supersede" FDA's restrictive policy on dietary supplements and replace it with a less regulatory approach. Id. The Senate Report, No. 103-410, that accompanied the bill that was enacted as DSHEA chronicled "the history of Food and Drug Administration efforts restricting dietary supplements." Id. at 10 (report accompanying S.784). The Report states the following:

Despite a voluminous scientific record indicating the potential health benefits of dietary supplements, the Food and Drug Administration has pursued a heavy-handed enforcement agenda against dietary supplements for over 30 years. The Agency's approach has forced the Congress

to intervene on two previous occasions, and yet again with adoption of S.784.

Id. The Senate Report provided examples of FDA's restrictive policies on dietary supplements and then concluded that these "examples show the need for Congressional action to assure citizens have continued access to dietary supplements and information about their benefits." Id. at 11. Congress took action in DSHEA to "empower" "consumers . . . to make choices about . . . dietary supplements." 21 U.S.C. § 321 note. Congress specifically directed that "the federal government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers." Id.

FDA's Structure/Function Proposal is an unreasonable regulatory barrier in contravention of DSHEA. The Proposal will limit and slow the flow of accurate information to consumers in conflict with the mandate of Congress. The Proposal will also interfere with scientific progress because it curtails the ability of responsible companies to disseminate the results of their scientific research, and curtails the ability of consumers to receive information about the potential health benefits of dietary ingredients. **Simply stated, FDA's proposal would deny the public access to accurate, meaningful information about safe and beneficial dietary supplements.**

FDA should change course before finalizing its structure/function rule so as to conform to Congressional policy and scientific developments. The Agency must allow consumers broader access to meaningful information regarding the effect of dietary supplements on the structure or function of the body; and manufacturers and

distributors of dietary supplements should be allowed to make truthful and non-misleading statements regarding such effects. FDA's final rule must embody the findings of Congress in DSHEA. In order to do that, the Agency must recognize that the public can only derive the benefits of advances in nutrition research only if the fruits of that research can be effectively communicated to the public. By allowing relatively more information to be disseminated about dietary supplements, FDA's final rule would (1) enhance consumer choice, (2) benefit public health, (3) reduce long-term health care expenditures, and (4) increase incentives for research into the health benefits of dietary ingredients.

II. PRINCIPLES FOR REVISING FDA'S STRUCTURE/FUNCTION PROPOSAL

We recommend that FDA revise its Structure/Function Proposal in accordance with the following principles drawn from the findings and operative provisions of DSHEA, good scientific practice, and the interest of promoting the public health of American consumers.

- A. Dietary supplements can contribute to improving public health by lowering the long-term incidence of chronic disease.
- B. Dietary supplements can reduce long-term health care expenditures.
- C. Consumers should have relatively unrestricted access to dietary supplements, provided that unsafe or adulterated products must be removed from the market.
- D. FDA should err on the side of providing consumers with more, rather than less, access to truthful and accurate information about dietary supplements.

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- E. FDA should encourage the research and development of scientific information about dietary supplements, and support the dissemination of such information, provided that it is not misleading.
- F. FDA should not unreasonably expand the definition of "disease."
- G. Structure/function claims are a class of health-related claims that are exempted from FDA's prior authorization.
- H. Structure/function claims are implicitly health-related.
- I. Consumer should not have to "decode" relevant claims about dietary supplements.
- J. FDA should encourage structure/function claims to be expressed in a manner that is susceptible to meaningful and reliable substantiation.
- K. FDA should encourage the conduct and dissemination of scientific research regarding the beneficial properties of dietary supplements.
- L. FDA should encourage the development and commercial application of dietary ingredients with beneficial health-related properties.

III. GENERAL DISCUSSION

A. Overview of FDA's Structure/Function Proposal

Section 6 of DSHEA authorizes claims describing "the role of a nutrient or dietary ingredient intended to affect the structure or function in humans [or] characteriz[ing] the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function." 21 U.S.C. § 343(r)(6)(A). No prior FDA approval is required to make such structure/function claims. DSHEA not only authorizes these claims, it establishes structure/function claims as a category of health-related claims that are exempted from the requirement to obtain prior FDA approval.

DSHEA also directly states that making structure claims for a dietary supplement does not confer "drug" status. The law provides:

a food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with [the structure/function provision] is not a drug . . . solely because the label or the labeling contains such a statement.

DSHEA § 10; 21 U.S.C. § 321(g)(1).

FDA's Structure/Function Proposal is intended to implement Section 6 of DSHEA. The Proposal defines the types of statements that can be made concerning the effect of a dietary supplement on the structure or function of the body. The proposed regulations also establish criteria for determining when a statement about a dietary supplement is a claim to diagnose, cure, mitigate, treat or prevent disease (i.e., "disease claims").

FDA's Structure/Function Proposal does not properly implement the statutory mandate. It unduly restricts the ability of dietary supplement manufacturers and distributors to communicate accurate descriptions of the impacts of their dietary supplements on the human body. Impacts on the structure or function of the body inevitably play a role in maintaining or promoting health; therefore, beneficial structure/function impacts will always tend to provide implicit protection against disease. By construing the definition of "disease" too broadly, FDA would define too many structure/function claims as "disease" claims. This, in turn, would unduly restrict the flow of truthful information under DSHEA. Also, FDA proposes to construe any implicit impact on disease as a basis for turning an otherwise appropriate

structure/function claim into a disease claim. This is an unreasonable regulatory restraint on dietary supplements. As such, it violates DSHEA's mandate to liberalize consumers' access to accurate health information regarding dietary supplements.

In contrast with FDA, Congress did not back away from the link between dietary supplements and disease prevention. To the contrary, the statutory language of DSHEA contains numerous express findings by Congress that dietary supplements do in fact promote health and prevent disease. FDA must substantially reorient its Structure/Function Proposal in order to bring it into line with Congress' policy on dietary supplements. FDA's Proposal is so far off the mark that it fails to account for -- or even identify -- the very substantial benefits to public health offered by dietary supplements. By disregarding these benefits to public health -- which were the legislative findings that motivated Congress to adopt DSHEA -- FDA's Structure/Function Proposal fails to implement the statutory objectives of DSHEA. **FDA's Structure/Function Proposal would give rise to significantly greater public health benefits if it allowed consumers greater access to accurate information about dietary supplements. Congress has enacted this finding into law and FDA must now respect it.**

B. DSHEA Shifted the Line Between Drugs and Dietary Supplements

FDA's Structure/Function Proposal is an overzealous effort by the Agency to force dietary supplements on to the same playing field with drugs. FDA is drawing the line between dietary supplements and drugs under the Food, Drug, and Cosmetic Act, as amended by DSHEA, in the wrong place. Drugs are approved by FDA after extensive clinical trials demonstrate their safety and efficacy in diagnosing, curing,

mitigating, treating, or preventing disease, or affecting the structure or function of the human body. 21 U.S.C. § 321(g).

Dietary supplements may not make "disease claims," but they are entitled to make structure/function claims, *id.* § 343(r)(6)(A), provided that "the manufacturer of the dietary supplement has substantiation that such [structure/function] statement is truthful and not misleading." *Id.* § 343(r)(6)(B). In addition, the dietary supplement must bear a formal disclaimer that FDA has not evaluated the structure/function claim and that the product is not intended to diagnose, treat, cure, prevent any disease. *Id.* § 343(r)(6)(C).

It is inescapable that DSHEA shifted the line between drugs and dietary supplements in a number of ways. First, Congress embraced "the link between . . . dietary supplements and the prevention of chronic diseases such as cancer, heart disease, and osteoporosis" and recognized that "appropriate use of safe, nutritional supplements will limit the incidence of chronic diseases." 21 U.S.C. §321 note (emphasis added). Congress plainly understood that dietary supplements help protected against disease. As a result, the text, structure, and policy of DSHEA confirm that dietary supplements do not become "drugs" because they are intended to help prevent disease. **The health benefits of dietary supplements were a key reason for enacting DSHEA. Congress did not intend that advances in scientific understanding would be withheld from the American public.**

Second, Congress authorized dietary supplement manufacturers and distributors to make certain claims that, prior to DSHEA, would have automatically conferred

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"drugs" status. Specifically, Section 6 of DSHEA allows dietary supplements to be marketed based on their intended effect on the structure or function of the body. 21 U.S.C. § 343(r)(6); 21 U.S.C. § 321(g)(1) ("a food, dietary ingredient or dietary supplement for which a truthful and not misleading [structure/function] statement is made in accordance with § 403(r)(6) is not a drug . . . solely because the label or the labeling contains such a statement").

Congress expanded the universe of dietary supplements by allowing these products to make structure/function claims without thereby becoming "drugs." Congress struck a balance. Dietary supplement products that make structure/function claims must follow a specifically prescribed form: (1) the supplement may characterize its impact on the structure or function of the body; (2) the supplement may not claim to prevent disease; and (3) the supplement must contain a formal disclaimer of FDA evaluation and intent to prevent disease. Analyzing these provisions in the context of DSHEA indicates that Congress intended to allow dietary supplements that: (1) intend to affect the structure or function of the body; (2) help limit the incidence of chronic disease; and (3) do not expressly claim to prevent disease. DSHEA continues to reserve express disease claims for drugs, whereas dietary supplements can only be implicitly linked to protection against disease -- i.e., structure/function claims can accurately describing the beneficial impacts of the product on the structure or function of the body .

In finalizing its rule, FDA must be guided by the core regulatory principle articulated in DSHEA; "[T]he Federal Government should take swift action against

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products that are safe or adulterated, [but] the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing flow of safe products and accurate information to consumers." 21 U.S.C. § 321 note. In addition, Congress specifically found "there is a growing need for emphasis on the dissemination of information linking nutrition and long-term health." *Id.* Congress thus struck the balance in favor of liberalized access to dietary supplements, and to truthful information about them.

FDA's Structure/Function Proposal, however, does not reflect this balance. FDA's current interpretation of the structure/function provisions of DSHEA fails to implement the "design, objectives, and polic[ies]" behind the statute. See U.S. v. Two Plastic Drums, 984 F.2d 814, 818 (7th Cir. 1993). In fact, FDA's proposal does not respond at all to Congress' "[c]oncern over excessive regulation of dietary supplements" and Congress' signal to "shift toward a more permissive approach." Nutritional Health Alliance v. Shalala, 953 F. Supp. 526, 528 (S.D.N.Y. 1997), aff'd in part and vacated and dismissed in part, 144 F.3d 220 (2d Cir. 1998).

C. The Fundamental Problem with FDA's Proposal Is Its Over-Broad Prohibition of Implicit Impacts on Disease

In contrast with Congress' desire to promote consumers' access to accurate information about the health benefits of dietary supplements, FDA's Structure/Function Proposal deprives the public of meaningful information. FDA would prohibit any implicit references to disease and claims that refer to "signs or symptoms" of a disease with the disease itself. See 63 Fed. Reg. at 23625-26. **The current draft makes a point of**

requiring dietary supplement claims to be unuseful to the consumer. For example, FDA's proposal indicates that it would be acceptable for a dietary supplement to state that it "helps maintain a healthy cholesterol level," but not to state that it "lowers cholesterol." 63 Fed. Reg. at 23626. If a consumer's cholesterol levels are higher than ideal, but not in the disease range, it is simply not helpful for FDA to prohibit language that speaks in terms of "lowering" cholesterol as opposed to "maintaining healthy" levels. A person whose cholesterol levels are within the ideal range may have no need for a dietary supplement that "helps maintain" healthy cholesterol levels. Rather, a consumer needs to know whether the dietary supplement will actually "lower" his or her cholesterol levels to bring the person within the healthy range. Therefore, FDA's proposed language is itself vague and misleading. In the case of cholesterol, the consumer is rightfully interested in the concept of "lowering," not "maintaining" certain levels. Moreover, DSHEA requires that structure/function claims be substantiated. How can a dietary supplement manufacturer substantiate "maintaining a healthy cholesterol level?" The manufacturer's substantiation data will necessarily demonstrate that its product lowers cholesterol levels.

Moreover, DSHEA authorizes truthful and accurate statements about the effect of a dietary supplement on the structure or function of the body. Assume, for example, that a manufacturer produces a dietary supplement whose effect on the structure or function of the body is that it inhibits the production of cholesterol in the liver. FDA's proposed prohibition of a claim that the product "lowers" cholesterol is not only counterfactual, it is also in conflict with DSHEA's specific authorization for truthful

structure/function claims. The manufacturer should be able to communicate this information under DSHEA, provided that the manufacturer does not claim that its cholesterol-lowering product treats, prevents or mitigates disease.

Another example of FDA's unhelpful approach to providing accurate information to consumers involves the impacts of certain dietary supplements on the structure or function of the prostate gland. FDA proposes to disallow claims telling consumers what they want to know, that the product "improves urine flow in men over 50 years old." Instead, FDA proposes to allow statements that the dietary supplement would "help[] promote urinary tract health." 63 Fed. Reg. at 26326. **FDA's requirement that structure/function claims be oblique or elliptical will confound consumers. It will result in fewer consumers making the right decisions about dietary supplements and overall public health will suffer as a consequence.**

FDA's churlish approach to providing health information to consumers not only contravenes the letter and spirit of DSHEA, it also trenches on First Amendment concerns. In DSHEA, Congress directed FDA to err on the side of providing consumers with accurate and truthful health information about dietary supplements. This comports with the First Amendment to the Constitution, which guarantees the right of consumers to receive -- and manufacturers to express -- non-misleading information. See Washington Legal Foundation v. Friedman, 1998 U.S. Dist. LEXIS 11876 (D.D.C. July 30, 1998) (FDA may not completely suppress dissemination of truthful and non-misleading health information). Applying these principles generously is especially appropriate where Congress has found that the ingestion of dietary supplements

contributes to improvements in public health. In essence, there are a powerful constitutional, statutory, and public policy reasons for FDA to revise its Structure/Function proposal in favor of allowing consumers to receive more useful health information.

D. FDA Should Promote Research and Development and Reliance on Nutrition Science

FDA's Structure/Function Proposal should promote rather than deter the conduct of, and reliance on, scientific research into dietary supplements, functional foods and other beneficial dietary ingredients. But if manufacturers of dietary supplements cannot communicate relevant information to consumers about the actual impacts of their products on the structure or function of the body, there will be no incentive for manufacturers to conduct scientific research to establish such effects. FDA's Structure/Function Proposal will discourage nutrition science and clinical research because the more scientific information a manufacturer knows and says about its product, the more likely it is that FDA will classify the product as a drug. Any reference to scientific research regarding the health properties of a dietary supplement could be considered by FDA as indicia of "drug" status under the current draft. FDA might be free to conclude that a manufacturer's scientific research provides the "context" to infer a disease claim. See 63 Fed. Reg. at 23626.

The Proposal's inherent hostility to scientific research regarding dietary supplements cannot be squared with DSHEA. In establishing an Office of Dietary Supplements within the National Institutes of Health, for example, Congress sought to:

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"(1) to explore more fully the potential role of dietary supplements as a significant part of the efforts of the United States to improve health care; and

(2) to promote scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions.

42 U.S.C. § 287c-1(b). Congress also ordered that "consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements." 21 U.S.C. § 321 note (emphasis added). **It is impossible to read DSHEA as anything but a strong endorsement for conducting and disseminating scientific research on dietary supplements and individual nutrients. See, generally, 42 U.S.C. § 287c-1(c)(2),(4).** FDA's Proposal would not advance these objectives.

The report of the Dietary Supplement Commission also "states that incentive mechanisms should be developed to encourage the dietary supplement industry to invest in research on these products." 63 Fed. Reg. at 23636. The report also states that "the public interest would be served by more research to assess the relationships between dietary supplements and the maintenance of health and/or prevention of disease." *Id.* FDA said it "agree[d] that additional research should be undertaken in the public and private sectors to assess the relationships between dietary supplements and the maintenance of health and/or prevention of disease," *id.*, but its Structure/Function Proposal goes in the opposite direction.

E. FDA Should Encourage Meaningful Substantiation

The Dietary Supplement Commission Report also suggests that FDA should provide guidance on the substantiation of structure/function claims. 63 Fed. Reg. at 26635. FDA's proposal should be revised to reflect this sound idea. See also Comments of the Staff of the Bureau of Consumer Protection of the Federal Trade Commission (submitted to FDA Docket No. 98N-0044 (Aug. 27, 1998)). DSHEA requires substantiation for structure/function claims, and the public would be well served by the establishment of more regimented and consistent criteria for substantiation. Indeed, FDA's reluctance to propose guidance for substantiation has the effect of diminishing the role that dietary supplements can play in promoting public health. Consumers will not be able to rely as extensively and confidently on products whose beneficial impacts on the structure or function of the body are not well substantiated. Thus, FDA should propose substantiation standards for notice and comment, prior to finalizing a structure/function rule.

In addition to these policy considerations, FDA should modify its criteria for structure/function claims in order to assure that they are capable of logical and objective substantiation. As noted above, the oblique, or elliptical, claims that FDA proposes to allow do not easily lend themselves to substantiation. For example, how can a manufacturer substantiate "maintaining health cholesterol levels" if its product actually reduces borderline-high cholesterol levels? If FDA allowed straightforward and meaningful structure/function claims, the corresponding substantiation would not be awkward or incongruous. Rather, substantiation should constitute objective

documentation of the claim -- i.e., proof that the dietary supplement does in fact bring about the claimed effects on the structure or function of the body. Often, this will entail the raising or lowering of some clinical marker. FDA's proposal to treat references to "laboratory or clinical measurements" as indicia of a dietary supplement's "drug" status is thus counter-productive. 63 Fed. Reg. at 23625. The inability to refer to such measurements will deter clinical research and impede reliable substantiation of structure/function claims.

F. Benefit/Cost Analysis

FDA's Structure/Function proposal is legally flawed because of its failure to implement the Unfunded Mandates Reform Act of 1995's requirement for a benefit/cost analysis. It also does not appropriately implement Executive Order 12866's requirement for such analysis. FDA's analysis was essentially limited to the costs of changing labels, as opposed to taking account of the public health benefits to be gained by providing for improved access to useful information (as well as the potential public health benefits that would be lost by reducing access to such information).

The proposed rule utterly fails to consider the public health benefits associated with ingesting dietary supplements as well as the losses to public health that could result from consumers failing to take appropriate dietary supplements due to uninformative structure/function claims. FDA's failure to assess and consider such benefits (and costs) stands in contrast with the specific finding of DSHEA that "appropriate use of safe nutritional supplements will limit the incidence of chronic diseases, and reduce long-term health care

expenditures." 21 U.S.C. § 321 note. Moreover, Senate Report 103-410 states that "[v]itamins and minerals can improve health and save lives" and documents the important protective benefits of various specifically named herbs, amino acids and other dietary supplements. Senate Report 103-410 at 5-9.

FDA must not issue a final rule on structure/function claims until it conducts and relies on a benefit-cost analysis that identifies the benefits to public health of ingesting dietary supplements and the dis-benefits (or costs) of reduced consumer access to those supplements. In other words, **FDA must assess the public health impacts associated with consumers modifying their consumption patterns for dietary supplements based on the extent and quality of information they are allowed to receive.** FDA has performed and relied on such analyses in other rulemakings: e.g., in the recent tobacco regulation, 61 Fed. Reg. 44395, 44568 et seq. (Aug. 28, 1996) (compliance with regulation would "reduc[e] underage tobacco use" and prevent early deaths); nutrition labeling regulations, 58 Fed. Reg. 2927, 2935 et seq. (Jan. 6, 1993) (analysis "examined the health benefits from consumer response to food labeling"); and the proposed ephedra regulation, 62 Fed. Reg. 30677, 30705 et. seq. (June 4, 1997) (analyzing "number of people who consume the relevant products [or] . . . modif[y] their use of these products"). In connection with the ephedra proposal, FDA even noted that its regulation would "lead to utility losses for some customers." 62 Fed. Reg. at 30710. FDA has engaged in no similar analysis here, but it must.

If FDA fails to perform this analysis for dietary supplements, neither the public nor Congress will be able to assess the damage to public health resulting from an

excessively narrow structure/function regulation that deprives consumers of meaningful health information about dietary supplements.

G. Regulatory Alternatives

FDA's Proposal indicates that the Agency "considered treating a statement about a dietary supplement as a disease claim only if the statement included an express reference to a specified disease." 63 Fed. Reg. at 23630 (emphasis added). FDA's analysis of this issue demonstrates that the Agency concedes it would be perfectly lawful under FDCA and DSHEA to allow implicit references to disease in structure/function claims for dietary supplements. In other words, the position advanced by these Comments is a legal and potentially viable regulatory option. FDA explains that it "did not adopt this option . . . [because] it would be inconsistent with FDA's long standing policy . . . [and] inconsistent with the interpretation of 'disease claims' that FDA has used in administering Section 403(r)(6) of the Act prior to issuing this proposed rule." *Id.*

This admission demonstrates precisely how FDA has failed to give effect to DSHEA. The 1994 statute expressed the specific purpose of superseding FDA's long-standing policies and interpretations regarding dietary supplements. Accordingly, in its final regulation, **FDA must adopt Congressional policy on dietary supplements in lieu of the Agency's superseded one. This means that implicit references to diseases should be allowed for dietary supplement structure/function claims. FDA has no alternative but to follow the Congressional policy clearly articulated in DSHEA.**

IV. SPECIFIC COMMENTS ON FDA'S STRUCTURE/FUNCTION PROPOSAL

A. Structure/Function Claims Are a Subset of Health-Related Claims

FDA's Proposal improperly distinguishes between other health-related claims and structure/function claims. In fact, the structure/function claims that are authorized for dietary supplements in 21 U.S.C. § 343(r)(6) constitute a subset of the claims authorized by in 21 U.S.C. § 343(r)(1)(B). These two statutory subsections must be read together. They can be paraphrased as follows:

for purposes of making a health claim (i.e., "characteriz[ing] [its] relationship . . . to a disease or a health-related condition"), a dietary supplement may "describ[e] the role of a nutrient or dietary ingredient intended to affect the structure or function in humans [or characterizes the documented mechanism] by which a nutrient or dietary ingredient acts to maintain such structure or function."

This means that DSHEA amended the Food, Drug, and Cosmetic Act to allow a subset of § 343(r)(1)(B) health-related claims to be made for dietary supplements (in addition to traditional nutrients) without advance approval. DSHEA specified, however, that only structure/function health-related claims could be made without FDA's prior authorization (which continues to be required for traditional nutrients). DSHEA also imposed certain other conditions on structure/function claims.

Based on this analysis, FDA's proposal to preclude structure/function claims from making any contextual references to "disease" is inconsistent with the very design of the statute. Structure/function claims for dietary supplements should be allowed to

characterize the relationship between the dietary supplement or ingredient and disease.

B. Disease Claims

The proposal correctly states that § 403(r)(6) of DSHEA authorizes only those structure/function claims "that are not also disease claims." However, there is a crucial distinction between the terminology of Section 6 of DSHEA (21 U.S.C. § 343(r)(6)(C)) and the terminology used in FDCA's definition of drug (21 U.S.C. § 321(g)). The general FDCA definition of "drug" speaks in terms of articles (other than food) that are "intended for use" in the diagnosis, cure, mitigation, treatment or prevention of disease or "intended to affect" the structure or any function of the body. 21 U.S.C. § 321(g) (emphasis added). DSHEA, however, specifically authorized dietary supplements to affect the structure or function of the body -- without thereby becoming drugs -- so long as the structure/function statement does not "claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases." 21 U.S.C. § 343(r)(6)(C) (emphasis added).

In other words, Congress authorized dietary supplements to "intend to affect" the structure or function of the body, provided that the product (1) does not expressly claim to prevent, etc. disease and (2) the product bears an express, formal disclaimer of an intent to prevent, etc. disease. This language can only be understood as authorizing structure/function claims that imply some protection against disease if the product eschews any express claim to prevent disease. Any other reading of this language

would conflict with these express findings Congress incorporated in the statutory text of DSHEA:

* * *

(2) . . . the benefits of dietary supplements to health promotion and disease prevention have been documented increasingly in scientific studies;

(3)(A) There is a link between the ingestion of certain nutrients or dietary supplements and the prevention of chronic diseases such as cancer, heart disease and osteoporosis;

* * *

(5) . . . appropriate use of safe nutritional supplements will limit the incidence of chronic diseases, and reduce long-term health care expenditures;

* * *

(8) Consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements;

* * *

21 U.S.C § 321 note (emphasis added).

Congress would not have enacted statutory language specifically linking dietary supplements with disease prevention if it intended that FDA could just prohibit any references to that linkage by administrative fiat.

This analysis is consistent with the report of the Dietary Supplement Commission. It stated that structure/function claims "should not refer to specific diseases, disorders, or classes of diseases and should not use drug-related terms such

as 'diagnose', 'treat', 'prevent', 'cure' or 'mitigate.'" 63 Fed. Reg. at 23625 (quoting Dietary Supplement Commission Report at 38-39) (emphasis added).

FDA stretches the reach of "disease" claims by prohibiting structure/function claims "if, in context, an effect on disease were expressed or implied." 63 Fed. Reg. at 23626. This radically inflates the realm of "disease claims" because it relies on vague and expansive terms like: "context" and mere "effects" on disease rather than the prescribed statutory terms (i.e., no claims to prevent, treat, etc. disease); and because it precludes "implied" as well as express effects on disease.

C. Implied Claims

The Proposal states that "FDA agrees with the Commission that an acceptable structure/function claim must not imply prevention or treatment of disease." 63 Fed. Reg. at 23625. FDA is not accurately citing the Commission Report in this regard. The Report actually states that "some members [of the Commission] believe statements of nutritional support [i.e., structure/function claims] may imply disease prevention." Dietary Supplement Commission Report at 36. This is the opposite of FDA's reading. FDA appears to be relying on the Report's statement that "at least one member believes that statements of nutritional support may neither expressly nor implicitly claim such usage." Id. This "at least one member" language is hardly a ringing endorsement for FDA's position on implied claims.

FDA should follow the Report's actual guidance that structure/function claims "should not refer to specific diseases" and should "not use drug-related terms." Accordingly, FDA's proposal to reject structure/function claim that "expressly or

implicitly claim[s] an effect on a disease or class of diseases," 63 Fed. Reg. at 23625, cannot be justified in light of either DSHEA statute or the Dietary Supplement Commission Report.

D. Over-Broad Definition of Disease and Over-Reliance on "Signs and Symptoms"

FDA's definition of disease is too broad. We strongly support the concept that maintaining a normal or healthy function must not be considered a disease claim. The medical community recognizes a continuum -- or "grades of health" -- ranging from "positive health" to "dead." See James M. Humber and Robert F. Almeder, eds., What Is Disease? (Humana Press 1997) at 13. Disease is a pathological departure from "normal," and not all departures from "normal" are pathological. Id. at 277. Thus, FDA's definition of disease should not be extended to cover any and all deviations from, impairments of, or interruptions of the normal structure or function of the body. The concept of disease should be qualified by some notion of "pathology."

The consequence of FDA's over-broad definition of disease would be to force more structure/function claims into the "drug" realm. This further compounds the problem created by FDA's desire to prohibit dietary supplements from bearing any "implicit" or "contextual" references to disease.

FDA should not define "disease" as any non-pathological deviation from, impairment of, or interruption of the normal structure or function of the body. By FDA's proposed definition, "disease" should be defined as "any condition that is not a normal function of the body" and "should not refer to specific diseases" and should "not use drug-related terms." Accordingly, FDA's proposal to reject structure/function claim that "expressly or

Growing tired too easily, carrying a few extra pounds, or not being as strong as the next guy, could be considered a departure from normal or impairment of an organ.

FDA further stretches the proposed definition of disease by relying inordinately on "signs or symptoms" that are characteristic of a disease. 63 Fed. Reg. at 23625. It may be possible to express or characterize almost any impact on a structure or function of the body in terms of various laboratory measurements. Some of these measurements, such as cholesterol levels, will represent a continuum ranging from an optimally healthy condition to a sub-optimal condition, to a borderline condition, to a disease condition.

Therefore, FDA should not adopt its proposed definition of disease. Instead, FDA should apply the current definition of disease in § 101.14(a)(6) to structure/function claims for dietary supplements. This approach would be consistent with the statutory design that establishes structure/claims for dietary supplements as a subset of health-related claims.

E. Contextual and "Implicit" Disease Claims

For the reasons discussed above, FDA should not preclude structure/function claims from carrying implicit or contextual references to protection against disease. As previously noted, **Congress specifically recognized and intended that the ingestion of dietary supplements would be linked with the prevention of disease.** Therefore, **FDA should not disqualify structure/function claims that could be understood as involving references to particular diseases.** 63 Fed. Reg. at 23626.

FDA should also not preclude implicit claims regarding possible effects on a natural state that presents a characteristic set of "signs or symptoms" recognizable to health care professionals or consumers as constituting an abnormality of the body. First, this exceedingly vague prohibition of a broad potential range of implicit health impacts should be rejected. Second, FDA should not preclude references to "signs or symptoms" because DSHEA itself only prohibits express claims of preventing disease, not references to "signs or symptoms." Finally, FDA should restrict its interpretation of disease claims to actual diseases, not mere abnormalities. There is no agreement in the medical community that abnormalities, absent more, constitute disease. Nothing in DSHEA can be construed as granting FDA additional authority to extend its "disease" jurisdiction to cover "departures from normal." For further elaboration of this point, we would refer you to the excellent comments filed by two Mayo Clinic physicians. See FDA Comment submitted by Tu T. Nguyen, MD, and Joseph A. Murray, MD.

V. OUR COMMENTS ON SPECIFIC PROPOSED REVISIONS TO C.F.R. SECTIONS

Section 101.14. Health Claims: General Requirements Disease or Health-Related Condition: Our position is that no revision in the definition of disease should be made. The current definition is adequate, and the proposed definition is too broad.

Section 101.93(g). Definition of Disease: Our position is that the current definition of disease in existing Section 101.14 should be adopted here as well (with appropriate conforming changes).

Section 101.93(g)(2). **Disease claims:** Our position is that implicit claims should not be precluded.

Section 101.93(g)(2)(i): Our position is the reference to "has an effect" on a specific disease should be narrowed to cover only the effects on disease prescribed in the statute (i.e., prevent, treat, etc.).

Section 101.93(g)(2)(ii): Our position is the provision regarding effects on "signs or symptoms" that are "characteristic" of diseases should be eliminated.

Section 101.93(g)(2)(iii): Our position is the provision regarding "an effect on a consequence of a natural state that presents a characteristic set of signs or symptoms recognizable to health care professionals or consumers as constituting an abnormality of the body" should be eliminated.

Section 101.93(g)(2)(iv)(C): Our position is the reference to "citation" of scientific publications or references should be eliminated.

Section 101.93(g)(2)(v): Our position is the reference to "belong[ing] to a class of products that is intended to diagnose, mitigate," etc. disease should be eliminated as too vague and too broad.

Section 101.93(g)(2)(vi): Our position is the reference to "a substitute for a product that is a therapy for a disease" should be eliminated as too vague and too broad.

Section 101.93(g)(2)(viii): Our position is the reference to "a role in the body's response to a disease or to a vector of diseases" should be eliminated as too vague and too broad.

Cargill, GalaGen, General Nutrition Comments on S/F Proposal

Section 101.93(g)(2)(x): Our position is the reference to "otherwise suggest an effect on a disease or diseases" should be eliminated as too vague and too broad. In particular, the reference to a mere "effect on a disease" does not conform to the statutory language.

**ROUTING SLIP
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DATE OF CORRESPONDENCE: 04/29/99

DATE INTO FDA: 05/05/99

TO: DON ARBUCKLE, ADMIN., OMB, OFFICE OF INFORMATION & REGULATORY AFFAIRS

FROM: ALAN C RAUL, SIDLEY & AUSTIN

SYNOPSIS: COMMENTS ON FDA'S RULEMAKING ON REGULATIONS ON STATEMENTS MADE FOR DIETARY SUPPLEMENTS CONCERNING THE EFFECT OF THE PRODUCT ON THE STRUCTURE OR FUNCTION OF THE BODY (DOCKET 98N-0044).

LEAD OFFICE: HFA-305

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COORDINATION:

SIGNATURE REQUIRED:

REFERRALS FROM HF-40

ASSIGNED TO	ACTION	DUE DATE
----- HFA-305	----- NECESSARY ACTION	-----



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16-70