

4160-01-F DMB

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. 98N-0044]

RIN 0910-AB97

Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing final regulations defining the types of statements that can be made concerning the effect of a dietary supplement on the structure or function of the body. The regulations also establish criteria for determining when a statement about a dietary supplement is a claim to diagnose, cure, mitigate, treat, or prevent disease. This action is intended to clarify the types of claims that may be made for dietary supplements without prior review by FDA and the types of claims that require prior authorization as health claims or prior approval as drug claims.

DATES: The final rule will become effective (insert date 30 days after date of publication in the FEDERAL REGISTER).

Display Date	1-5-00
Publishing Date	1-6-00
Certifier	SNReese

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SUPPLEMENTARY INFORMATION:

I. Introduction

In the FEDERAL REGISTER of April 29, 1998 (63 FR 23624), FDA proposed regulations to identify the types of statements that may be made without prior FDA review about the effects of dietary supplements on the structure or function of the body ("structure/function claims"), and to distinguish these claims from claims that a product diagnoses, treats, prevents, cures, or mitigates disease (disease claims). FDA received over 235,000 submissions in response to the proposed rule. Many of these were form letters, but over 22,000 were individual letters from the dietary supplement industry, trade associations, health professional groups, and consumers. Almost all the comments from the dietary supplement industry and from individuals, which made up the vast majority of the comments, objected to all or part of the proposed rule, arguing that it inappropriately restricted the structure/function claims that could be made for dietary supplements. Most of the comments from health professional

groups and groups devoted to particular diseases supported the proposed rule, or believed it did not go far enough in limiting structure/function claims for dietary supplements.

After reviewing the comments, FDA concluded that the comments had raised significant questions about some of the key provisions of the proposal such that a public meeting was warranted. In the FEDERAL REGISTER of July 8, 1999 (64 FR 36824), FDA announced a public meeting to be held on August 4, 1999, at which representatives of the dietary supplement industry, consumer groups, and health professionals were asked to address three major issues raised by the comments. The three issues, described in the FEDERAL REGISTER notice, were: (1) Whether to finalize the proposed definition of "disease" or retain a 1993 definition of "disease or health-related condition" that was in effect at the time the Dietary Supplement Health and Education Act (DSHEA) was enacted; (2) whether to modify one of the proposed criteria for assessing disease claims to permit structure/function claims related to certain conditions associated with natural states, such as hot flashes associated with menopause and decreased sexual function associated with aging; and (3) whether to permit implied disease claims structure/function claims. The July 8, 1999, notice also reopened the comment period until August 4, 1999, to receive written comments on these three issues.

This document addresses the comments received on the proposed rule, as well as comments received in response to the July 8, 1999, FEDERAL REGISTER notice. A few comments raised issues that are beyond the scope of this rule and generally will not be addressed in this document.

A. Highlights of the Final Rule

Like the proposed rule, the final rule contains criteria to determine when a labeling statement made about a dietary supplement constitutes a structure/function claim for which no prior FDA review is required and when it constitutes a disease-related claim that requires either authorization of a health claim or review under the drug provisions of Federal Food, Drug, and Cosmetic Act (the act). FDA has, however, made several important changes in the final rule in response to comments.

First, the agency has deleted the proposed definition of "disease." Rather than creating a new definition of disease, FDA will use the preexisting definition of "disease or health-related condition" in § 101.14(a)(5) (21 CFR 101.14(a)(5)) (formerly § 101.14(a)(6)), which was issued as part of the implementation of the health claims provisions of the Nutrition Labeling and Education Act (NLEA). This change has been made in response to the large number of comments that objected to the proposed definition and urged that FDA retain the NLEA definition.

Second, FDA has revised the criterion that applies to conditions associated with such natural states or processes as menopause, aging, adolescence, and pregnancy. The proposed rule stated that menopause, aging, and pregnancy are not themselves diseases but that certain conditions associated with them are diseases if they are recognizable to consumers or health professionals as abnormal. Many comments objected to classifying as diseases such common conditions as hot flashes, premenstrual syndrome (PMS), and decreased sexual function associated with aging. In response to these comments, FDA has revised proposed § 101.93(g)(2)(iii). Common conditions associated with natural states or processes that do not cause significant or permanent harm will not be treated as diseases under the final rule. For example, hot flashes, common symptoms associated with the menstrual cycle, ordinary morning sickness associated with pregnancy, mild memory problems associated with aging, hair loss associated with aging, and noncystic acne will not be treated as diseases under this provision. Uncommon or serious conditions like senile dementia, toxemia of pregnancy, severe depression associated with the menstrual cycle, and cystic acne will continue to be treated as diseases under the final rule.

Third, FDA has revised the criterion that relates to the use in labeling of the titles of publications that refer to diseases. In response to comments objecting that, as proposed, this

criterion would hamper manufacturers from providing consumers with information substantiating their claims, FDA has revised this criterion. Under the revised criterion, the use in labeling of a publication title that refers to a disease will be considered a disease claim only if, in context, it implies that the product may be used to diagnose, treat, mitigate, cure, or prevent disease. Highlighting, bolding, using large type size, or prominent placement of a citation that refers to a disease use in the title could suggest that the product has an effect on disease. Placing a citation to a scientific reference that refers to a disease in the title on the immediate product label or packaging will be considered a disease claim for that product. The agency will also consider whether the cited article provides legitimate support for the express structure/function statement made for that dietary supplement. Enhancing the bibliography with citations to scientific references that refer to a disease in the title and that have no reasonable relation to the statement made will be considered a disease claim. Similarly, the agency will consider whether citations are to bona fide research.

B. Background

DSHEA created a new regime for the regulation of dietary supplements. These products were previously regulated either as foods or as drugs, depending upon whether they had the attributes

of food and upon their intended uses. Before the passage of DSHEA, a dietary supplement for which a health-related claim was made was regulated either as a drug, which had to be shown to be safe and effective before marketing, or as a food, for which prior authorization to make a health claim was required if the claim concerned a disease or health-related condition. If the claim concerned a non-disease-related effect on the structure or function of the body and the claimed effect derived from a food attribute, such as nutritive value, the claim was considered a food claim, and prior authorization was not required. Under section 201(g)(1)(B) and (g)(1)(C) of the act (21 U.S.C. 321(g)(1)(B) and (g)(1)(C)), a drug is defined as "an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease," or "an article (other than food) intended to affect the structure or any function of the body." Section 505 of the act (21 U.S.C. 355) requires that new drugs (see section 201(p) of the act) be shown to be safe and effective for their intended uses before marketing. Under sections 403(r)(1)(B) and (r)(5)(D) of the act (21 U.S.C. 343(r)(1)(B) and (r)(5)(D)) and § 101.14, prior authorization is required to make a health claim for a dietary supplement. A health claim is a claim that "characterizes the relationship of any nutrient * * * in the food to a disease or health-related condition" (section 403(r)(1)(B) of the act; see § 101.14(a)(1)).

DSHEA specifically authorized certain types of claims about the uses of dietary supplements, including some claims that formerly would have required review by FDA before the claim is made. Section 403(r)(6) of the act, added by DSHEA, allows dietary supplement labeling to bear, among other types of statements, a statement that "describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans" or that "characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function." Such statements are generally referred to as "structure/function claims." Because many of these claims would previously have been covered by the drug definition in section 201(g)(1)(C) of the act, section 201(g)(1) was amended by DSHEA to provide that a dietary supplement "for which a truthful and not misleading statement is made in accordance with section 403(r)(6) is not a drug under clause (C) solely because the label or the labeling contains such a statement."

Although a dietary supplement manufacturer who wishes to make a statement permitted under section 403(r)(6) of the act need not obtain prior review of the statement, the manufacturer must possess substantiation that the statement is truthful and not misleading, and must include in the statement the following disclaimer: "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." DSHEA also requires the manufacturer of a dietary supplement bearing a statement under section 403(r)(6) of the act to notify FDA, no later than 30 days after the first marketing of the dietary supplement with the statement, that such a statement is being made for the product. Regulations implementing these requirements were published in the FEDERAL REGISTER of September 23, 1997, and are codified at § 101.93 (21 CFR 101.93) (62 FR 49883 at 49886, September 23, 1997).

DSHEA did not alter the statutory treatment of dietary supplement claims related to disease ("disease claims"). Section 403(r)(6) of the act, specifically provides that statements permitted under that section "may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases," except that such statements may claim a benefit related to a classical nutrient deficiency disease, provided that they also disclose the prevalence of the disease in the United States. Consistent with the quoted provision, Congress did not modify section 201(g)(1)(B) of the act to exclude disease claims for dietary supplements from use as evidence of intended use as a drug, as it had done for section 201(g)(1)(C) of the act. Thus, dietary supplements "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" remain within the definition of a "drug." In enacting DSHEA, Congress also

maintained the requirement of prior authorization of a claim that characterizes the relationship of a nutrient in a dietary supplement to a disease (section 403(r)(1)(B) and (r)(5)(D) of the act). An interested person may submit a petition to FDA requesting the agency to issue a regulation authorizing the health claim (see § 101.70 (21 CFR 101.70)). The petitioner must demonstrate, among other things, that the use of the substance at levels necessary to justify the claim is safe and that there is "significant scientific agreement" among qualified experts that the claim is supported by the totality of publicly available scientific evidence (§ 101.14(b)(3)(ii) and (c)). The agency notes that for health claims to be used on conventional foods, an interested person may submit to FDA a notification of an authoritative statement by one of certain designated scientific bodies concerning the substance-disease relationship to which the claim refers (see section 403(r)(3)(C) of the act). Unless FDA issues a regulation modifying or prohibiting the claim, or a Federal district court finds that applicable statutory requirements have not been met, the claim may be used 120 days after the notification has been submitted (see section 403(r)(3)(C)(ii) and (r)(3)(D) of the act). This alternative authorization procedure does not apply to dietary supplements by statute, but FDA has proposed to extend it to dietary supplements by regulation (see 64 FR 3250, January 21, 1999).

Although FDA believes that dietary supplements have potential benefits for consumers, dietary supplements labeled with unproven disease claims, i.e., those that have not met the requirements for health claim authorization or new drug approval, can pose serious risks. Such claims may encourage consumers to self-treat for a serious disease without benefit of a medical diagnosis or treatment. They may also cause consumers to substitute potentially ineffective products for proven ones, foregoing or delaying effective treatment for serious and life-threatening illnesses. Reliance on disease prevention claims may encourage consumers to feel sufficiently protected from developing serious diseases (e.g., cancer or human immunodeficiency virus (HIV) infection) that they delay or forego regular screening, and forfeit the opportunity for early medical treatment that may be critical to survival. Finally, use of dietary supplements to treat disease may increase the risk of adverse reactions due to the interaction of the dietary supplement with other compounds a consumer is taking for that disease or for other conditions, e.g., prescription medications.

This final rule is intended to apply only to structure/function claims and disease claims within the meaning of section 403(r)(6) of the act. DSHEA, generally, and section 403(r)(6) of the act, specifically, apply only to dietary supplements for human consumption and were enacted to provide a

unique regulatory regime for these products. Thus, this rule is neither intended to apply to products other than dietary supplements for human consumption nor to interpret other provisions of the act.

The final rule establishes criteria for determining whether a statement made about a dietary supplement is acceptable as a structure/function claim under section 403(r)(6) of the act. The rule is neither intended to establish whether any particular structure/function claim is appropriate for any specific product, nor whether the claim would be permitted under other provisions of the act. Like the labeling of any other FDA-regulated product, the labeling of dietary supplements must comply with all applicable requirements of the act and regulations. For example, an otherwise acceptable structure/function claim might nevertheless be false or misleading for other reasons, causing the product to be misbranded under section 403(a)(1) of the act.

C. The Proposed Rule

The proposed rule defined criteria for determining when a statement about a dietary supplement is a claim to diagnose, cure, mitigate, treat, or prevent disease ("disease claim"), and thus requires prior approval as a drug or prior authorization as a health claim. The proposed rule included a definition of "disease," which was to replace a definition of "disease or health-related condition" issued for implementation of the health

claims regulations, and 10 criteria for identifying express or implied disease claims. FDA proposed to treat a statement about a dietary supplement as a disease claim if the statement claimed, explicitly or implicitly, that the product: (1) Has an effect on a specific disease or class of diseases; (2) has an effect, using scientific or lay terminology, on one or more signs or symptoms that are recognizable to health care professionals or consumers as being characteristic of a specific disease or of a number of different specific diseases; (3) has 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; (4) has an effect on disease through one or more of the following factors: (a) The name of the product; (b) a statement about the formulation of the product, including a claim that the product contains an ingredient that has been regulated by FDA as a drug and is well known to consumers for its use in preventing or treating a disease; (c) citation of a publication or reference, if the citation refers to a disease use; (d) use of the term "disease" or "diseased;" or (e) use of pictures, vignettes, symbols, or other means; (5) belongs to a class of products that is intended to diagnose, mitigate, treat, cure, or prevent a disease; (6) is a substitute for a product that is a therapy for a disease; (7) augments a particular therapy or drug action; (8) has a role in

the body's response to a disease or to a vector of disease; (9) treats, prevents, or mitigates adverse events associated with a therapy for a disease and manifested by a characteristic set of signs or symptoms; or (10) otherwise suggests an effect on a disease or diseases.

Claims that did not fall within the proposed criteria for disease claims and that otherwise complied with the notification and disclaimer provisions of § 101.93(a) through (e) were to be eligible for use as structure/function claims. The proposed rule also provided examples of claims that would be permitted as structure/function claims and those that would require prior review as disease claims under each of the 10 criteria.

The basis for the proposed rule was the agency's experience in implementing section 403(r)(6) of the act, and the final report (the report) of the President's Commission on Dietary Supplement Labels (Ref. 1), which included a number of recommendations for distinguishing structure/function and disease claims and suggested that FDA issue further guidance on acceptable structure/function claims.

II. Comments

A. General Comments

(1.) Many comments focused on the impact of the rule on consumers. Many comments opposing the proposed rule said that consumers should be able to receive truthful and non-misleading

information and that the proposed rule would curtail or restrict such information or restrict the focus of dietary supplements to preventive care and wellness. Some comments added that DSHEA, through the dissemination of truthful and non-misleading information on health promotion and disease prevention, makes consumers responsible for their own health. Other comments said that FDA should let the public educate itself. Other comments suggested that FDA simply adopt a "truthful and non-misleading" standard. Some comments added that full disclosure of all pertinent information (such as the preliminary status of scientific studies substantiating the claim) would be sufficient. Another comment questioned whether consumers would, as the preamble to the proposed rule stated, benefit from not having to search for information and from getting appropriate information. The comment argued that consumers would receive less information under the rule and would have to search more extensively for information.

Many comments supporting the proposed rule, including comments from nutrition counselors and health professionals, said that the proposal would reduce confusion among patients, prevent consumers from being misled, diminish the number of inappropriate disease claims, and help consumers decide when to seek medical attention. One comment added that, while it supported the need for consumers to have choice regarding dietary supplements, the

choice should be made based on accurate information that is supported by appropriate scientific investigations. One comment argued that in the absence of valid effectiveness data, which does not exist for most dietary supplements, it is not possible to provide "truthful" information about the effects of these products. Some comments said that the proposal would protect consumers from harmful or potentially harmful products and save consumers from needless suffering and financial loss; others expressed concern that inappropriate statements would expose consumers to potentially harmful drug-supplement interactions, create "false hopes," and lead consumers to stop complying with advice from health care professionals or to avoid proven treatments.

FDA agrees that DSHEA encourages the dissemination of truthful and non-misleading information about the uses of dietary supplements to affect the structure or function of the body, and encourages full disclosure of information about claims authorized by the statute. To the extent that truthful and non-misleading information is being withheld from consumers in the context of structure/function claims for dietary supplements, it is the statute that, in the first instance, precludes certain information from being included in such claims. Section 403(r)(6) of the act permits dietary supplement labels to carry structure/function claims without meeting the requirements for

drug approval or health claim authorization, but precludes them from carrying unreviewed claims that the product diagnoses, treats, mitigates, cures, or prevents disease. (The statute does not ultimately prevent dissemination of information about disease uses to the consumer in labeling claims or otherwise. Instead, it requires that claims about disease uses meet certain standards of substantiation and undergo agency review.) This final rule differentiates between structure/function claims authorized by section 403(r)(6) of the act and disease claims that may not be made in dietary supplement labeling under the authority of section 403(r)(6). The agency notes that, in response to comments, the final rule classifies many more claims as structure/function claims than would have been so classified under the proposed rule, thus increasing the amount of information available to the consumer without prior FDA review.

The agency also declines to adopt a "truthful and non-misleading" standard instead of the final rule. Section 403(a)(1) of the act already subjects all food claims, including structure/function claims on dietary supplements, to the "truthful and non-misleading" standard, so promulgating the same standard through regulations is unnecessary. In addition, section 403(r)(6)(B) of the act already requires dietary supplement manufacturers to have substantiation that their statements are truthful and non-misleading. Finally a

fundamental problem with this approach is that a "truthful and non-misleading" standard, unlike the final rule, would not provide any criteria for differentiating between structure/function claims and disease claims.

(2.) Some comments focused on product safety. One comment said that regulation of claims is unnecessary because dietary supplements are safe. Similarly, another comment claimed that "one million peer-reviewed studies" showed that dietary supplements provide benefits, whereas a recent medical journal reported deaths and other injuries to patients who use prescription drugs. Other comments declared that dietary supplements are safer than most regularly-used drug products. In contrast, other comments argued that the safety of many dietary supplements is unknown, and that risks have been documented with some supplements. Some comments claimed that dietary supplements pose risks because they can cause consumers to avoid or delay more effective treatment. One comment stated that there is a substantial potential for public harm because of the unknown or unregulated source materials for many dietary supplements, the variety of suppliers, and the lack of regulatory production standards and quality control.

Although this final rule may not appear to be a safety measure because it addresses the labeling of dietary supplements rather than their composition, protecting consumer health and

safety is one of its major purposes. 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.

FDA also believes that the safety and the effectiveness of products intended to promote health, including both dietary supplements and drugs, cannot be viewed independently of each other. FDA agrees that prescription drugs can and do cause adverse reactions. It is important to remember, however, that "safety" is relative. Products that are capable of treating diseases have powerful effects on the body and frequently carry risks. Before prescription drugs are marketed, both their risks and their benefits must be carefully investigated and documented in adequately designed clinical trials. Prescription drugs are permitted to be marketed only when the agency concludes that their documented benefits outweigh their known and potential

risks. Those with significant risks are approved for marketing only if the benefits warrant those risks. And they are marketed as "prescription" drugs to ensure that health professionals manage their risks. Even over-the-counter (OTC) drugs are evaluated for both benefits and risks and are permitted to be marketed only when their established benefits outweigh their risks. There is no comparable testing and approval process for dietary supplements marketed with structure/function claims. The manufacturer must have substantiation of the structure/function claim, but this substantiation is not reviewed before the product is marketed with the claim. Contrary to the suggestion in the comment, few dietary supplements have been the subjects of adequately designed clinical trials.

This does not mean that dietary supplements are unsafe or that they do not have benefits. Some have already been shown to be safe and to have benefits, and the safety and effectiveness of others are likely to be shown in the future. At this time, however, many marketed supplements have not been the subjects of adequate studies to establish whether or not they are safe or effective, or the nature of the benefits they may provide.

(3.) Many comments asserted that FDA had no authority to issue the proposed rule because it was inconsistent with DSHEA and congressional intent, in that it restricted rather than increased the amount of information given to consumers. Some

comments said that Congress enacted DSHEA to reverse FDA's "overly restrictive" approach towards health claims and to increase the dissemination of truthful and non-misleading health information and that Congress repeatedly expressed its displeasure with FDA's regulatory approach. One comment said FDA must determine whether a proposed action is consistent with its statutory authority before it takes any regulatory action. The comment cited excerpts from congressional documents "condemning the agency's repeated penchant" for restricting statements on dietary supplement labels and labeling, and said that, given congressional intent and the act's language, FDA has no authority to proceed with rulemaking without a grant of authority from Congress. One comment cited section 403B of the act (21 U.S.C. 343-2) as evidence that Congress, by exempting certain publications from the definition of labeling, barred FDA from restricting in "any way whatsoever" the dissemination of such publications and information.

FDA agrees that DSHEA was intended to authorize the dissemination of more truthful and non-misleading information in dietary supplement labeling without the need for prior agency review. In response to comments that the proposed rule was too restrictive, FDA has modified the final rule to incorporate many of the changes requested by the comments, including a return to the preexisting definition of "disease or health-related

condition," and a less restrictive interpretation of the types of structure/function claims that can be made about conditions associated with such natural states as aging, pregnancy, and the menstrual cycle. The final rule classifies many more claims as structure/function claims than the proposed rule would have.

The agency does not agree, however, that section 403(r)(6) of the act authorizes dissemination of any and all information about dietary supplements without prior review. That section authorizes statements about the effects of dietary supplements on the structure or function of the body, but not statements that claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases. Section 403B of the act exempts from being considered labeling certain balanced, third-party publications that are physically separate from product labeling and do not promote a particular brand or product. This provision does not authorize dietary supplement manufacturers to ignore the restrictions in section 403(r)(6) of the act on what structure/function claims may be made by a manufacturer about its product on the product label and in materials that are indisputably part of the product's labeling.

The agency also disagrees with the assertion that separate congressional authority is needed for this rulemaking. FDA issued the proposed rule, and this final rule, to implement section 403(r)(6) of the act. No independent authority to issue

these regulations is necessary because section 701(a) of the act (21 U.S.C 371(a)) expressly gives FDA "the authority to promulgate regulations for the efficient enforcement of this Act, except as otherwise provided in (section 701 of the act) * * *." The proposed rule identified section 701(a) of the act as being part of the agency's legal authority (see 63 FR 23624 at 23628 and 23631), and there is no exception in the act that restricts or limits, either expressly or impliedly, the agency's ability to issue regulations to implement section 403(r)(6) of the act. Therefore, the rule is authorized by law and consistent with FDA's statutory authority.

(4.) Some comments contended that FDA did not provide a sufficient justification for issuing the rule. Two comments challenged FDA's assertion that the rule would reduce substantial confusion among manufacturers. The comments referred to statements in the preamble to the proposed rule which said FDA received approximately 2,300 notifications of structure/function claims and sent objection letters to approximately 150 notifications. One comment said the low objection rate did not indicate "substantial confusion" among manufacturers, while the other comment hypothesized that, if FDA objected to a small number of claims in each notification, the number of objectionable claims was very small. Other comments contended that the Commission report did not support the proposed rule.

These comments were divided in their reasons. Some comments argued that the Commission exceeded its statutory mandate under section 12 of DSHEA or failed to perform its statutory obligations. Thus, the comments stated, FDA cannot base any regulation on the Commission's findings, guidance, or recommendations and has no authority to proceed with the rulemaking. Other comments stated that FDA relied on statements from individual Commission members rather than the report itself, that the report did not suggest that FDA issue regulations, and that the report did not suggest that FDA issue a new definition of disease. One comment said that the Commission did not support a need for regulations. Another comment noted that the Commission did not recommend regulations and asserted that FDA had publicly said that DSHEA is self-implementing.

FDA does not agree that there is insufficient support for this rule. FDA's experience, the Commission report, and FDA's authority under section 701(a) of the act to issue regulations implementing statutory requirements provide more than adequate support for the rule. The preamble to the proposed rule referred to substantial confusion among manufacturers and consumers, rather than manufacturers alone. Comments received from other sources, particularly physicians, dieticians, and health professional organizations, agreed that consumers are confused and misled by claims. In addition, the number of objection

letters is not the sole indicator of manufacturer confusion, for three reasons. First, manufacturers and consumers have asked FDA to provide clarification on structure/function and disease claims, and such requests for clarification would not necessarily have resulted in an objection letter from FDA. Second, the agency has repeatedly said that the absence of an objection letter does not necessarily indicate acceptance of the claim. Third, there are apparently a large number of marketed dietary supplement products making claims for which FDA has not received 30-day notification letters under section 403(r)(6) of the act. (In the proposed rule, FDA estimated that approximately 22,500 dietary supplement labels carried structure/function claims. FDA had received 2,300 notifications at the time of the proposed rule. While some notifications contain more than one claim, they do not average 10 claims per notification.)

FDA also does not agree that the Commission report was necessary to provide support for this rule. The proposal was based not only on the Commission report, but also on the agency's experience in reviewing 30-day notification letters submitted under section 403(r)(6) of the act (63 FR 23624 at 23625). Although FDA believes the rule is consistent with the views expressed in the Commission report, the Commission report was not a necessary prerequisite for the agency to issue the rule. FDA issued the proposal under section 403(r)(6) of the act (section 6

of DSHEA) and the rulemaking authority of section 701(a) of the act, not under section 12 of DSHEA. FDA takes no view on whether the Commission met its statutory obligations in issuing its report. To the extent that the report is beyond the Commission's authority, FDA's experience and section 701(a) of the act provide adequate support for the rule. Thus, whether or not the Commission exceeded its mandate is irrelevant to the validity of the rule.

With regard to the issues raised about the consistency of the agency's approach with the Commission report, it is true that the Commission did not specifically recommend regulations, but the Commission did express the view that FDA guidance on claims under section 403(r)(6) of the act would be "appropriate and helpful in clarifying the appropriate scope" of such claims (the report, p. 38).

As to the agency's public statements that DSHEA is self-implementing, the comment took those statements out of context. When DSHEA was passed, there was confusion in the industry about whether the types of statements permitted by section 403(r)(6) of the act could be made under the authority of the statute alone, in the absence of implementing regulations. To clear up this confusion, at least one agency official publicly said that DSHEA was "self-implementing." Agency statements to this effect were intended to clarify that manufacturers were not required to wait

for FDA to issue implementing regulations before making claims under section 403(r)(6) of the act; however, they were in no way intended to imply that the agency lacked authority to issue implementing regulations.

Contrary to the suggestion in one of the comments, FDA did not rely on the views of individual Commission members, but on the official 7-point "guidance" developed by the Commission "as to what constitutes an acceptable statement of nutritional support of the structure function type" (the report at pp. 38 and 39). The criteria developed by FDA are highly consistent with the Commission's guidance. FDA also agrees that the Commission did not make any findings or recommendations on the definition of disease. As described elsewhere in this rule, the final rule does not modify the existing definition of disease found in FDA's health claims regulations.

(5.) One comment said that FDA should have admitted that there is and will be some overlap between disease and structure/function claims and that the agency should have drafted a rule to prevent extreme overlap between structure/function claims and drug or health claims.

FDA disagrees with this comment. In the proposed rule, FDA recognized that section 403(r)(6) of the act leaves open questions concerning the distinction between structure/function claims and disease claims. Diseases cause, and can be

characterized as, abnormalities in the structure or function of the body. It would therefore be possible to describe almost all products intended to treat or prevent disease in terms of their effects on the structure or function of the body, without mentioning the disease itself.

The language of DSHEA, however, does not support treating those structure/function claims that are also disease claims as statements permitted under section 403(r)(6) of the act. As noted above, section 403(r)(6) of the act contains two passages that indicate Congress' intent to exclude from the scope of structure/function claims any claim that is also a disease claim. Section 403(r)(6) of the act provides that structure/function statements "may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases." It also requires structure/function claims to be accompanied by a disclaimer stating that the product "is not intended to diagnose, treat, cure, or prevent any disease."

In light of the statutory framework, FDA concluded in the preamble to the proposed rule that section 403(r)(6) of the act authorizes claims related to the effect of a product on the structure or function of the body only if they are not also disease claims. FDA's conclusion was consistent with the policy guidance offered by the President's Commission on Dietary

Supplement Labels. In the report the Commission offered general guidance on structure/function claims, including the following:

3. Statements indicating the role of a nutrient or dietary ingredient in affecting the structure or function of humans may be made when the statements do not suggest disease prevention or treatment.

(The report, p. 38)

Accordingly, FDA believes that it is appropriate to define the universe of permitted structure/function claims by first identifying those claims that should be considered disease claims. Remaining claims about the effect of a dietary supplement on the structure or function of the body may be acceptable structure/function claims under section 403(r)(6) of the act, provided that they are consistent with the requirement in section 201(ff)(1) of the act that a dietary supplement be "intended to supplement the diet."

(6.) Some comments, particularly those received at the public hearing or during the reopened comment period, argued that it is difficult or impossible to draw principled distinctions between structure/function claims and disease claims. Some of these comments said that section 403(r)(6) of the act, which is premised on such a distinction, is not scientifically based.

Other comments argued that it is not necessary or practical to draw clear lines between disease claims and structure/function claims, and that dietary supplement labeling should instead focus on educating consumers about the conditions for which a product may be used. According to these comments, if there are disease conditions that might be implied by a particular claim, the labeling should, for example, inform consumers of the symptoms of such conditions, the importance of seeking medical attention for them, and their health-related consequences. Other comments argued that consumers reading the labels of dietary supplements will incorrectly assume that the information provided therein has been reviewed by the government and that the claims, express or implied, are supported by the kind of scientific evidence that supports drugs with similar claims.

FDA agrees that it may be very difficult to draw clear lines between structure/function claims and disease claims. Despite the difficulty, implementing section 403(r)(6) of the act requires the agency to draw these lines. FDA would not be carrying out its statutory obligations if it abdicated responsibility for distinguishing between the two types of claims, and instead permitted dietary supplements to disseminate information about specific disease states. FDA agrees that scientifically valid information about diseases is helpful to consumers, if it is delivered consistently and accurately, but

does not agree that section 403(r)(6) of the act authorizes such dissemination. FDA strongly believes that the dissemination of such information on dietary supplement labels increases the likelihood that consumers will believe that the supplements are intended to treat or prevent the diseases described in the labeling. Therefore, it is important that any disease claims in dietary supplement labeling continue to be subject to prior FDA review to evaluate the safety and effectiveness of the product for the use described or suggested by the claim.

The agency also notes that there may be important health-related consequences associated with taking a dietary supplement, even if the product does not bear disease claims. For the labeling of a dietary supplement to be considered truthful and non-misleading (see sections 403(a) and (r)(6) and 201(g)(1) of the act), it must include all information that is material in light of the claims made for the product and the consequences that may result from its use (see section 201(m)) of the act.

(7.) Many comments discussed the rule's effect on scientific research. Some comments argued that the proposal would discourage scientific research on dietary supplements. One comment contended that such research might prompt FDA to consider a dietary supplement to be a drug. Another comment said the proposal would "chill" the availability of third-party information on dietary supplements.

The agency disagrees with the comments. The comments provided no evidence, and the agency is aware of none, that establishing criteria for distinguishing structure/function claims and disease claims will adversely affect the conduct or use of scientific research. In the agency's experience, establishing regulatory standards has generated more research rather than less. As described below, some comments from pharmaceutical companies and from patient organizations expressed the contrary concern that allowing dietary supplements to make disease claims without FDA review would undermine incentives for rigorous scientific research. The agency also notes that nothing in this rule would treat scientific research or the publication of research results in a scientific journal as evidence that a product is marketed as a dietary supplement or is a drug.

(8.) Several comments addressed the relationship between dietary supplements and drug products, and the effects of this regulation on drug products and drug development. Some comments suggested that the proposal represented an attempt by FDA to regulate dietary supplements in a manner that benefits pharmaceutical interests or to regulate dietary supplements in a manner that is similar to European regulatory systems that apply drug requirements to such products.

In contrast, other comments expressed concern over the negative effects of DSHEA and the proposed rule on incentives for

pharmaceutical drug development. One comment asked FDA to provide an "unambiguous demarcation" that would preserve research and development incentives for drug products and permit evaluation of opportunities in the dietary supplement marketplace. According to this comment, section 403(r)(6) of the act, and DSHEA generally, were intended to create "parity" between the dietary supplement and food industries without undermining research and development incentives for the pharmaceutical industry and to address a perceived failure by FDA to implement the health claims provision for dietary supplements in section 403(r)(5)(D) of the act. The comment contended that section 403(r)(6) of the act is intended to provide a limited statutory safe harbor for certain dietary supplements that might otherwise be subject to regulation under the health claim rules for food or as unapproved new drugs, but it does not permit any and all structure/function statements for dietary supplements. Thus, the comment said FDA should have "parallel interpretations" of sections 201(g)(1)(C) and 403(r)(6) of the act. The comment suggested that FDA enforce the requirement of a "documented mechanism" imposed in section 403(r)(6)(A) of the act, which permits claims that "characterize the documented mechanism by which a nutrient or dietary supplement acts to maintain" structure or function and that FDA limit claims to "maintaining," rather than "promoting" or "improving" structure or function.

FDA does not agree that this rule was designed to benefit the pharmaceutical industry or to establish rules that are consistent with European regulation of dietary supplements. As noted above, some pharmaceutical companies believe that the rule will harm them by permitting competition by products that have not had to undergo rigorous testing or review. Other pharmaceutical companies already produce dietary supplements and expressed the same reservations about the rule as other dietary supplement manufacturers. There was also no attempt to model this rule after European regulation of dietary supplements.

FDA recognizes the importance of maintaining incentives for research and product innovation. By establishing criteria for determining when a statement may be a disease claim, the final rule indirectly contributes towards preserving the incentives for pharmaceutical research and development by ensuring that products marketed for treatment or prevention of diseases must all meet the same regulatory standards. As stated below, FDA believes that if the rule were to permit dietary supplements to carry implied disease claims, the incentives for new drug development could be significantly undermined.

FDA agrees with the comment that the structure/function provisions of sections 403(r)(6) and 201(g)(1)(C) of the act are similar in scope. FDA also agrees that to make a statement about the mechanism by which a dietary supplement maintains structure

or function, the mechanism of action must be "documented." FDA does not agree, however, that this is the only provision under which a dietary supplement may claim to maintain healthy structure or function. Maintenance claims also can be made under the provision that authorizes statements that "describe the role" of a supplement "intended to affect the structure or function" of the body (section 403(r)(6)(A) of the act).

In response to the comment asking FDA to limit claims to "maintaining," rather than "promoting" or "improving," structure/function, the agency agrees that "improving" often suggests some abnormality or deficiency that can be treated, so a claim to "improve" a structure or function of the body would be more likely to be a disease claim. On the other hand, a claim to improve memory or strength would be a permitted structure/function claim, unless disease treatment were implied. Use of the term "promote" may be acceptable under the portion of section 403(r)(6)(A) of the act which authorizes claims that "describe[] the role of a * * * dietary ingredient intended to affect the structure or function." Whether a claim for "promoting" structure or function is a disease claim will depend on the context and nature of the claim. For example, a claim that a product "helps promote digestion" would be a structure/function claim because it does not refer explicitly or implicitly to an effect on a disease state, but a claim that a

product promotes low blood pressure would be considered a disease claim. Both the preamble to the proposed rule and the Commission recognized that statements using the word "promote" can be appropriate when the statements do not suggest disease prevention or treatment or use for a serious health condition that consumers cannot evaluate (see 63 FR 23624 at 23626).

(9.) A few comments objected to the statement that a dietary supplement bearing an appropriate structure/function claim may be subject to regulation as a drug if there is other evidence that it is intended for the diagnosis, cure, mitigation, treatment, or prevention of disease. One comment argued that many dietary supplements are used for medicinal purposes and it would be "easy" for FDA to find evidence that they were intended for this purpose based on consumer use of the product.

Although FDA's longstanding interpretation of section 201(g)(1)(B) of the act authorizes the agency to rely on evidence outside the labeling and advertising of a product to establish its intended use, FDA does not rely on such evidence alone except in unusual circumstances. For example, the courts have suggested that if the agency seeks to rely solely on evidence that consumers use a product for a particular purpose to support a finding of intended use for that purpose, consumers must use the product predominantly or nearly exclusively for that purpose. (See, e.g., Action on Smoking and Health (ASH) v. Harris, 655

F.2d 236, 239-240 (D.C. Cir. 1980); National Nutritional Foods (NNFA) v. Weinberger, 512 F.2d 688, 702 (2d Cir. 1975), cert. denied, 423 U.S. 827 (1975).) The fact that some consumers used a dietary supplement for medicinal purposes would not by itself be sufficient to establish intended use as a drug, if use for medicinal purposes was not the predominant use.

FDA reiterates, however, that in appropriate circumstances, FDA may find that a dietary supplement for which only structure/function claims are made in labeling may nevertheless be a drug if there is other evidence of intended use to prevent or treat disease.

(10.) Some comments discussed the "disclaimer" statement required by section 403(r)(6)(C) of the act. The disclaimer reads as follows: "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." One comment said the disclaimer resolves any consumer confusion between dietary supplement claims and drug claims. Another comment said the proposed rule showed that FDA was implicitly rejecting the disclaimer's meaning because the proposed rule would restrict the amount of information flowing to consumers. One comment said the disclaimer reflects Congress' understanding of a tension between structure/function and disease claims, while another comment asserted that the disclaimers required on a label are an attempt

to decrease the amount of space on a label for a structure/function claim.

Section 403(r)(6) of the act requires dietary supplement manufacturers who wish to make a structure/function statement to include the disclaimer, and, since 1997, FDA regulations regarding the disclaimer have been codified at § 101.93. However, the disclaimer's role does not eliminate the need for this final rule to establish criteria for determining whether a statement is a disease claim. Section 403(r)(6) of the act provides that a statement for a dietary supplement that is made under section 403(r)(6) "may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases." Had Congress thought the disclaimer, alone, was sufficient to distinguish between structure/function claims and disease claims, it would not have enacted the restriction against disease claims in section 403(r)(6) of the act.

FDA does not agree with the assertion that the disclaimer, which is expressly required by the act, is a scheme to decrease the space for structure/function claims on a label. FDA believes that the disclaimer is intended to make sure that consumers understand that structure/function claims, unlike health claims and claims that appear on the labels of drugs, are not reviewed by FDA prior to marketing, and to caution consumers that dietary supplements bearing such claims are not for therapeutic uses.

(11.) Several comments sought additional statements or language on product labels. One comment supported the marketing of dietary supplements and other substances whose effectiveness has not been established and that have no appreciable toxicity as long as the product's label stated that effectiveness had not been proven. Another comment said precautions, such as adverse reactions and contraindications to certain diseases and medications, are important information for labels. The comment also sought a description of a dietary supplement product's contents as a percentage of a person's recommended daily intake (RDI) and in actual units.

FDA declines to revise the rule as suggested by the comments. With regard to the marketing of dietary supplements with a label statement that the product's effectiveness has not been proven, the agency advises that dietary supplements that do not do what they claim to do are misbranded. The act forbids false and misleading labeling and advertising claims and requires businesses to have substantiation for any structure/function claims they make for dietary supplements in labeling (see section 403(a) and (r)(6)(B)) of the act). The presence of a disclaimer indicating that effectiveness has not been established cannot vitiate these statutory obligations. Therefore, it would be inappropriate for FDA to sanction the use of effectiveness disclaimers.

Although the act does not prescribe any specific statements concerning adverse reactions or contraindications that dietary supplements must carry, the agency notes that dietary supplement labeling, like the labeling of all other FDA-regulated products, is required to include all information that is material in light of consequences that may result from the use of the product or representations made about it (see sections 403(a)(1) and 201(n) of the act).

As for requiring information on the percentage of RDI and actual units for dietary ingredients in dietary supplements, FDA agrees that such information is useful. In fact, FDA's nutrition labeling regulations for dietary supplements generally require the percentage of the RDI or daily reference value (DRV) that a dietary supplement contains to be given for dietary ingredients that have an RDI or DRV (see § 101.36(b)(2)(iii) (21 CFR 101.36(b)(2)(iii))). In addition, the amount in units must be given, regardless of whether an RDI or DRV has been established (see § 101.36(b)(2) and (b)(3) (21 CFR 101.36(b)(2) and (b)(3))). This information can be found on the Supplement Facts panel of dietary supplements.

(12.) One comment objected to referring to structure/function statements as "claims." The comment said that, under section 403(r)(6) of the act, such statements must be

truthful and non-misleading, so they should be called "statements" instead of "claims."

FDA has traditionally used the term "claim" to refer to any statement made by a manufacturer that recommends or suggests a particular use of a product. This term is used for all products regulated by FDA, including drugs, foods, devices, and dietary supplements. Use of the term "claim" is not intended to suggest that a statement is untrue or misleading in any way.

(13.) One comment said that any substance used with "pharmacologic intent" should be classified as a drug or biologic in order to ensure the efficacy, potency, and purity of medicines. The comment explained that such substances have a potential for therapeutic benefit as well as harm, and suggested that existing and new dietary supplements that are marketed with health-related claims be required to provide scientific evidence of their safety and efficacy as a condition of their being marketed as a drug or biologic.

FDA declines to adopt the comment's suggestion. Section 403(r)(6) of the act expressly authorizes certain structure/function claims for dietary supplements. Many of these claims may be said to be "health-related." (The agency is uncertain what is meant by "pharmacologic intent.") Thus, the act does not require all substances with health-related claims to be classified as a drug or biologic.

Regarding safety and effectiveness evidence for dietary supplements that bear health-related claims, FDA agrees that such evidence should continue to be required where the claim is a health claim within the meaning of § 101.14(a)(1) or a claim that subjects the product to regulation as a drug under section 201(g)(1)(B) of the act. With regard to health-related claims that are authorized by section 403(r)(6) of the act, section 403(r)(6)(B) does require manufacturers to have substantiation for their claims. However, the act does not generally require dietary supplement manufacturers that make claims for their products under section 403(r)(6) of the act to provide a premarket demonstration of safety and effectiveness to FDA.

(14.) One comment recommended that FDA not finalize the proposed rule because it claimed that the proposal's criteria were based on a subjective evaluation of claims and not on objective information from market research studies to determine whether consumers are confused by the claim. The comment also argued that FDA did not provide data and information regarding consumer confusion, and that all interested parties should be able to evaluate and comment on any data before FDA finalizes the proposal. The comment asserted that a significantly revised and limited final rule could provide a basic regulatory definition of disease and a "construct" for structure/function claims so that detailed regulatory criteria would be unnecessary.

The act does not require market research studies to determine whether a particular statement is a structure/function claim or disease claim, and it would be both impractical and inefficient to require such studies to decide the status of every possible claim that could be made under section 403(r)(6) of the act. FDA also does not believe that market research studies are necessary to provide a reasonable basis for the agency's determinations concerning the meaning of labeling claims. The agency has extensive experience in interpreting such claims. The agency has, however, modified the second criterion in § 101.93(g)(2)(ii) to eliminate reference to recognition of signs and symptoms by consumers or health professionals because many comments objected that this standard would appear to require consumer testing. FDA has replaced the recognition standard with an objective standard.

(15.) One comment said that it would be inappropriate for FDA to issue any regulation that restricted the scope of statements of nutritional support related to a nutrient content claim or claims pertaining to a classical nutrient deficiency-related disease. The comment said that claims such as "calcium builds strong bones" are acceptable and that FDA should clarify this fact in the final rule.

FDA agrees that dietary supplements may carry structure/function statements concerning the relationship of

nutrients and the structure or function of the body, such as "calcium builds strong bones." The preamble to the proposed rule also specifically acknowledged that although statements under section 403(r)(6) of the act generally may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases, "such statements may claim a benefit related to a classical nutrient deficiency disease, provided that they also disclose the prevalence of the disease in the United States" (63 FR 23624). The final rule codifies this exception at § 101.93(g)(2), which states that "FDA will find that a statement about a product claims to diagnose, mitigate, treat, cure, or otherwise prevent disease (other than a classical nutrient deficiency disease) * * *" (emphasis added). Classical nutrient diseases are also specifically excluded from the definition of disease in § 101.93(g)(1). Thus, because the final rule already contains the exception, no change to the rule is necessary.

(16.) Many comments suggested that FDA issue a guidance document instead of regulations. Some of the comments stated that regulations are neither desirable nor necessary. Others stated that a guidance document would be appropriate because it would permit new information to support new structure/function claims or because it would enable FDA to conduct consumer research and industry outreach programs before imposing new rules. Some comments also requested separate guidance documents

for specific claims or recommended that FDA create or use advisory committees to help draft guidance documents. Two comments said that the Commission report only provided guidance and suggestions, so FDA did not have to issue the proposed rule. Another comment said that publishing a guidance document would consume fewer agency resources and that a rule is unnecessary because the industry already knows the permissible scope of statements for dietary supplements.

FDA disagrees with the comments. The final rule creates uniform, enforceable requirements for structure/function claims. By doing so, the final rule establishes a "level playing field" for all members of the dietary supplement industry, and permits rational use of FDA's limited enforcement resources. In contrast, guidance documents, although they represent FDA's best advice on a particular matter, are not binding on any party. Relying solely on guidance documents would not be as effective in achieving consistency in the regulation of structure/function claims on dietary supplements and would lead to case-by-case enforcement.

FDA does, however, intend to issue a guidance document to provide additional information regarding structure/function and disease claims. The guidance document would complement, rather than substitute for, the final rule.

As for those comments stating that a guidance document would permit new information to support new structure/function claims or that outreach programs are necessary, FDA notes that interested persons may generate such information regardless of the rule. FDA may also conduct research or other programs or consult advisory committees or other persons if such actions would be helpful. In short, gathering more information or conducting research and other programs is not dependent on whether FDA issues a guidance document instead of a rule.

(17.) A few comments stated that FDA should enforce existing laws and regulations, remove unsafe products from the market, take action against dietary supplements that make "extravagant, unsubstantiated" claims, or promote educational activities instead of issuing regulations. One comment suggested that FDA resources would be better spent reviewing notices sent to the agency instead of issuing regulations. Another comment suggested that FDA continue to clarify issues on a case-by-case basis.

FDA disagrees with the comments. Regulations offer several important advantages that case-by-case clarification, individual enforcement actions, and educational activities generally cannot. For example, when FDA develops a regulation, it provides notice, obtains public comment, considers alternatives, and evaluates the rule's potential impacts, costs, and benefits. Individual

enforcement actions and educational activities are not subject to these considerations.

Regulations also establish uniform, industry-wide requirements in a single administrative proceeding (rulemaking). In contrast, individual enforcement actions focus on distinct facts that may not lend themselves to uniform application to an entire industry. Moreover, enforcement actions are resource-intensive and require multiple steps, such as inspections, warning letters, and sometimes litigation, before they are completed. Educational activities may deal with general topics and provide valuable opportunities for discussing issues with FDA, but they do not create uniform requirements.

Regulations are also easier to locate because they are published in the FEDERAL REGISTER when they are issued, are codified and published in the Code of Federal Regulations (CFR) and can be found in libraries and on government Internet sites (such as the Government Printing Office's website at www.gpo.gov). In contrast, agency correspondence and results of individual enforcement actions are not as widely available and may be difficult for some regulated entities and consumers to obtain.

Thus, when it comes to establishing uniform, industry-wide requirements, conserving agency resources, and providing public

notice and an opportunity to comment, regulations are preferable to individual enforcement actions and educational activities.

(18.) A comment suggested that FDA adopt an approach like hazard analysis critical control point (HACCP) instead of issuing the rule.

FDA disagrees with the comment. HACCP is best suited for issues relating to how a product is manufactured. Here, the principal issue is the claims made for a product rather than how the product is made.

(19.) A comment stated that FDA lacks the expertise to determine whether a botanical is a drug or a dietary supplement. The comment explained that botanicals can be used for medicinal purposes, but that they can also be used for promoting general well being and supporting the structure or function of the body. According to the comment, FDA declared Yellowdock, an herb, to have medicinal purposes only, when the herb also had a long history of use as a food source.

The comment may have misinterpreted the rule. The focus of this rule is not on whether a substance has a history of use as a food but on claims made in the product's labeling. The rule defines the types of statements that may be made concerning a dietary supplement's effect on the structure or function of the body. FDA has many years of experience in regulating and interpreting health-related product claims.

established lists of ingredients and botanical products that are safe and permitted for therapeutic purposes. The comment suggested that FDA consider assembling a committee to establish a similar list for the United States.

A list of dietary ingredients and botanical products and their therapeutic uses might provide valuable information. Nevertheless, section 403(r)(6) of the act permits only structure/function claims for dietary supplements that are not also disease claims, and so such a list would not be relevant to this rulemaking.

(21.) Two comments suggested that FDA list examples of structure/function claims in order to reduce confusion. Another comment would have FDA describe both disease claims and structure/function claims.

FDA intends to issue a guidance document that will provide examples of claims that would and would not be considered disease claims. This final rule also includes many examples of structure/function and disease claims.

B. Permitted Structure/Function Statements (§ 101.93(f))

Proposed § 101.93(f) stated that dietary supplement labels and labeling may bear structure/function statements that are not disease claims within the meaning of proposed § 101.93(g) and

that otherwise comply with the notification and disclaimer provisions of § 101.93(a) through (e). FDA is revising § 101.93(f) on its own initiative to make it clear that a dietary supplement may bear a disease claim if it is the subject of an authorized health claim, but that otherwise disease claims will subject the product to regulation as a drug.

C. Definition of Disease (§ 101.93(g)(1))

To assist in describing what constitutes a disease claim, the proposed rule contained a definition of "disease." The proposed definition was based on standard medical and legal definitions of the term (Refs. 2, 3, 4, and 5). Proposed § 101.93(g)(1) defined "disease" as:

any deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms, including laboratory or clinical measurements that are characteristic of a disease.

The proposed definition would have replaced an earlier definition issued in 1993 as part of the regulations implementing the health claims provisions of NLEA. The implementing regulations require dietary supplement manufacturers to obtain