

Two comments contended that changing a claim from "lowers cholesterol" to "maintains healthy cholesterol levels" does not change the effect of the product or its use. Some comments argued that "lowers cholesterol" claims should be permitted for cholesterol levels that are not "abnormal" or are below hypercholesterolemia.

FDA does not agree that claims concerning maintenance of normal cholesterol levels necessarily constitute implied disease claims. Although an elevated cholesterol level is a sign of hypercholesterolemia and an important risk factor for heart disease, a cholesterol level within the normal range is not a sign or risk factor for disease. Moreover, maintaining cholesterol levels within the normal range is essential to the structure and function of the body for reasons other than prevention of heart disease. Although many people think of cholesterol solely in terms of the negative role of elevated cholesterol in heart disease, normal cholesterol levels play a positive role in maintaining a healthy body. Cholesterol is a necessary constituent of cell membranes and of myelin, the sheath that coats nerves. Cholesterol is also required for the synthesis of steroid hormones, which are essential for life. Finally, cholesterol is required for the production of bile in the liver, making possible absorption of dietary fat and fat soluble vitamins. Thus, a claim that a dietary supplement helps

maintain cholesterol levels that are already within the normal range does not necessarily imply disease treatment. FDA also believes that Congress intended to permit dietary supplements to carry claims of this type under section 403(r)(6)(A) of the act.

The agency has concluded, however, that references to "healthy" cholesterol may be misleading to consumers because the phrase "healthy cholesterol" is now frequently used to refer to high density lipoproteins (HDL), a specific cholesterol fraction believed to be beneficial. To avoid this confusion, FDA has concluded that an appropriate structure/function claim for maintaining cholesterol would be "helps to maintain cholesterol levels that are already within the normal range."

FDA continues to believe that "lowers cholesterol," however qualified, is an implied disease claim. As many comments argued, lowering cholesterol is inextricably linked in the public mind with treating elevated cholesterol and preventing heart disease. The agency also believes that "promotes cholesterol clearance" is an implied disease claim because it is directed at lowering cholesterol rather than maintaining levels already determined to be within a normal range. FDA will review all cholesterol claims to determine whether the labeling as a whole implies that the product is intended to lower elevated cholesterol levels. In such cases, FDA would consider the labeling to create an implied disease claim.

(46.) A comment from a former Surgeon General of the United States argued that, given the importance of preventing cardiovascular disease, dietary supplements should be permitted to make claims for cholesterol reduction, because "our citizens deserve the opportunity to know when safe and effective dietary supplements are available to lower cholesterol." A comment from the Nutrition Committee of the American Heart Association argued that current scientific evidence does not support added benefits of dietary supplementation with nutritive substances for prevention of cardiovascular disease in the general population, and expressed concern that dietary supplements also carry risks.

FDA agrees that prevention of heart disease is an extremely important public health goal. Lowering cholesterol with certain drugs has been conclusively shown to be effective in reducing mortality from coronary artery disease. Indeed, the evidence linking the lowering of elevated cholesterol with preventing heart disease is so strong that identifying and using effective therapies to lower cholesterol in patients with elevated cholesterol levels has become of compelling importance. With this in mind, use of possibly ineffective therapies in persons with elevated cholesterol, which can delay or prevent effective treatment, poses significant public health risks. Although DSHEA requires that manufacturers who make structure/function claims have substantiation, manufacturers are not currently required to

submit that substantiation to FDA for premarket review, nor does FDA have the resources to inspect and review the quality of the substantiation in most cases. For this reason, FDA does not believe that permitting "lowers cholesterol" claims on dietary supplements without prior review serves the public health.

(47.) A few comments argued that FDA may not prohibit "lowers cholesterol" claims because the agency had earlier issued an advisory letter permitting such claims if the claim stated that the product was useful in the context of a healthy diet. One of these comments contended that the agency may not change its advice or guidance because it has cited no studies in this rulemaking to support the view that "lowers cholesterol" implies disease treatment.

FDA does not agree that it may not change its position on whether particular cholesterol claims imply disease treatment. The record and analysis in this rulemaking, as well as FDA's experience in implementing DSHEA, provide an ample basis for the conclusions that the agency has reached on cholesterol claims.

G. Conditions Associated With Natural States

(§ 101.93(q)(2)(iii))

The proposed rule stated that natural states such as aging, menopause, pregnancy, and the menstrual cycle, are not themselves diseases, but can be associated with abnormal conditions that are

diseases. FDA proposed in § 101.93(g)(2)(iii) to treat as a disease claim a statement that a product had an effect on a condition associated with a natural state if the condition presented "a characteristic set of signs or symptoms recognizable to health care professionals or consumers" as an "abnormality." FDA provided as examples of such abnormal conditions the following: Toxemia of pregnancy; premenstrual syndrome; hot flashes; and presbyopia, decreased sexual function, and Alzheimer's disease associated with aging.

In the July 8, 1999, FEDERAL REGISTER notice announcing a public meeting and reopening the comment period, FDA asked for additional comment on this provision of the proposed rule. The agency sought specific comment on the following three questions: (1) If FDA were to treat some conditions associated with natural states as diseases (e.g., toxemia of pregnancy and Alzheimer's disease) but not others (e.g., hot flashes, common symptoms associated with the menstrual cycle, and decreased sexual function associated with aging), what would be an appropriate principle for distinguishing the two groups? (2) For example, would it be appropriate to consider the severity of the health consequences if the condition were to go without effective treatment? (3) If so, how should "severity" be defined?

(48.) Although some comments from disease-specific organizations and health professionals supported this provision,

most of the comments strongly objected to classifying common conditions associated with natural states as diseases. None of the objecting comments argued that toxemia of pregnancy or Alzheimer's disease are not diseases. Almost all of these comments, however, contended that PMS, hot flashes, and various conditions associated with aging, such as decreased sexual function, are so common that they should be considered neither abnormal nor diseases. Some comments argued that any condition suffered by more than 50 percent of the population should be considered normal and not a disease, and gave as an example benign prostatic hypertrophy. Other comments cited prevalence rates for conditions such as PMS and hot flashes, and contended that the cited rates were too high for these conditions to be considered abnormal. A large number of comments asserted that the proposed rule would treat pregnancy, menopause, and aging as diseases. A few comments argued that if menopause, aging, and pregnancy are not diseases, then signs and symptoms associated with these states cannot be diseases. One comment argued that conditions related to natural states are not diseases but "health-related conditions" and that DSHEA permits statements about health-related conditions.

In response to the questions in the July 8, 1999, FEDERAL REGISTER notice, many comments argued that the severity of the condition associated with a natural state was not an appropriate

principle for distinguishing diseases from nondiseases. These comments generally argued that the severity of the symptoms (rather than the severity of the consequences of going without effective treatment) was not an adequate basis to distinguish diseases from nondiseases. One comment from a food industry group argued that this was an inappropriate principle because "all natural states can have severe consequences if left unattended." This comment suggested that conditions that were "universal" should not be treated as diseases. This comment and one other also suggested that the distinguishing principle was whether the cause of the condition was "pathological."

FDA has reconsidered proposed § 101.93(g)(2)(iii), and has concluded that it is not appropriate, under DSHEA, to treat certain common, nonserious conditions associated with natural states as diseases. There are a wide variety of conditions representing impaired function of an organ or system that are associated with particular stages of life or normal physiologic processes. These stages and processes include adolescence, the menstrual cycle, pregnancy, menopause, and aging. (FDA notes that, contrary to the comments, the proposed rule would not have classified these stages or processes themselves as diseases; it classified only certain abnormal conditions associated with these stages or processes as diseases.) The conditions associated with these stages or processes can vary from common, relatively mild

abnormalities, for which medical attention is not required, to serious conditions that can cause significant or permanent harm if not effectively treated.

For example, pregnancy is associated with common and mild abnormalities such as morning sickness and leg edema that cause no permanent harm if left untreated, as well as with such serious conditions as hyperemesis gravidarum, toxemia of pregnancy, and acute psychosis of pregnancy, which can be life-threatening if not effectively treated. The menstrual cycle is commonly associated with mild mood changes, edema, and cramping that do not cause significant or permanent harm if left untreated, but also, more rarely, with serious cyclical depression that can result in significant harm if not effectively treated. Aging is almost invariably associated with characteristic skin and scalp changes, such as wrinkles and hair loss, which do not need medical attention. It is also, however, associated with serious diseases that will result in significant, often irreversible damage, many of which can be effectively treated. These diseases include osteoporosis, glaucoma, and arteriosclerotic diseases of coronary, cerebral, and peripheral vessels. Adolescence is commonly associated with mild acne, which does not cause significant or permanent harm if not treated, and, rarely, with cystic acne, which can produce severe physical and psychological scars if not effectively treated.

Whether all of these conditions represent diseases is, in part, a matter of definition and, in part, depends on the consequences of the conditions if not effectively treated, and on how commonly they occur, i.e., whether they may be considered "normal." Although most people consider the more serious or infrequent conditions referred to above to be diseases, views vary with respect to the common, milder conditions. FDA has reconsidered the position it took in the proposed rule and agrees with the comments that treating as diseases the common, mild symptoms associated with normal life stages or processes would not be consistent with the intent of DSHEA.

FDA does not believe that the frequency with which a condition associated with a natural state occurs is, by itself, sufficient to distinguish diseases from nondiseases. The severity of the consequences of disease, as well as the consequences of ineffective treatment, must also be considered. As noted above, whether common, minor conditions associated with natural states are diseases is a matter of debate, but FDA has decided not to treat them as diseases because the agency believes this approach is consistent with the intent of DSHEA. FDA does not, however, believe that DSHEA was intended to permit unreviewed claims about serious conditions that could cause significant or permanent harm, particularly where effective treatment is available. FDA also does not agree that "all

natural states can have severe consequences if left unattended." FDA has listed a large number of conditions associated with natural states that commonly do not have serious consequences even if not effectively treated. FDA also does not agree that it is helpful in this context to distinguish between diseases and nondiseases by asking which have a "pathological" basis. The term "pathological" is itself defined by reference to disease, namely, "caused by or involving disease; morbid" (Ref. 7).

Accordingly, for purposes of this rule, mild conditions commonly associated with particular stages of life or normal physiological processes will not be considered diseases. Therefore, § 101.93(g)(2)(iii) now states that a statement will be considered a disease claim if it claims that the product "has an effect on an abnormal condition associated with a natural state or process, if the abnormal condition is uncommon or can cause significant or permanent harm." Ordinarily, FDA would follow the suggestion in the comments that conditions associated with a stage of life or a normal physiological process be considered common if they occur in more than one-half of those experiencing that stage or process.

The following are examples of conditions about which structure/function claims could be made under § 101.93(g)(2)(iii): (1) Morning sickness associated with pregnancy; (2) leg edema associated with pregnancy; (3) mild mood

changes, cramps, and edema associated with the menstrual cycle; (4) hot flashes; (5) wrinkles; (6) other signs of aging on the skin, e.g., liver spots, spider veins; (7) presbyopia (inability to change focus from near to far and vice versa) associated with aging; (8) mild memory problems associated with aging; (9) hair loss associated with aging; and (10) noncystic acne. The following are examples of conditions that would remain disease claims: (1) Toxemia of pregnancy; (2) hyperemesis gravidarum; (3) acute psychosis of pregnancy; (4) osteoporosis; (5) Alzheimer's disease, and other senile dementias; (6) glaucoma; (7) arteriosclerotic diseases of coronary, cerebral or peripheral blood vessels; (8) cystic acne; and (9) severe depression associated with the menstrual cycle.

FDA has not included benign prostatic hypertrophy (BPH) on either of these lists, because the agency does not believe that BPH should be considered a consequence of aging. Like many other diseases, e.g., diabetes, prostate cancer, and heart disease, the incidence of BPH is much higher among older men. This does not mean that BPH or prostate cancer is caused by the aging process. Even if BPH were considered a direct consequence of aging, however, claims to treat or prevent it would still be treated as disease claims because failure to obtain effective treatment can cause significant or permanent harm.

FDA notes that it does not base the exclusion of the mild common conditions associated with natural states from § 101.93(g)(2)(iii) on the argument advanced by one of the comments that these are "health-related conditions" and that DSHEA permits structure/function claims about health-related conditions. FDA believes that a "health-related condition" is a state of health leading to disease. As FDA has said previously, "diseases" and "health-related conditions" are "so closely related that no bright-line distinction is practicable" (58 FR 2478, 2481 January 6, 1993). There is nothing in DSHEA, its legislative history, or in the definition of "disease or health-related condition" that would suggest that common conditions associated with natural states are "health-related conditions" within the meaning of section 403(r)(1)(B) of the act. Further, FDA does not agree that section 403(r)(6) of the act authorizes structure/function claims about "health-related conditions." Had Congress intended to authorize structure/function claims about "health-related conditions" it could easily have used that terminology, but did not.

(49.) Some comments concerned specific claims under proposed § 101.93(g)(2)(iii). One comment sought concurrence that the following are acceptable structure/function claims: "supports a normal, healthy attitude during PMS" and "supportive for menopausal women." Another comment argued that a statement

that a product provides nutrients that diminish the normal symptomatology of premenstrual syndrome or menopause is a permissible structure/function claim. Another comment asked whether "helps to maintain normal urine flow in men over 50 years old" is a permissible structure/function claim. One comment urged that only products proven safe when used as directed should be permitted for sale for enlarged prostate and that such products should recommend that a man see his physician. Another comment argued that the claim "for men over 50 years old," which FDA had proposed as an acceptable structure/function claim, is vague and ambiguous and is of no use to consumers.

FDA agrees that "supports a normal, healthy attitude during PMS" and "supportive for menopausal women" are appropriate structure/function claims. "Supports a normal, healthy attitude during PMS" is acceptable because PMS is generally a common, mild condition associated with a normal physiologic process. "Supportive for menopausal women" is acceptable because it is a general statement that does not refer to symptoms of any conditions at all. Claims about diminishing the normal symptomatology of premenstrual syndrome or menopause would also be acceptable structure/function claims, if they did not suggest, for example, prevention or treatment of osteoporosis, or another disease associated with these states. "Helps to maintain normal urine flow in men over 50 years old," however, is an implied

disease claim because, as many comments pointed out, the average or "normal" state in men over 50 years old is diminishing urine flow, in most cases due to BPH, so that the apparent "maintenance" really represents a claim of improvement (treatment).

H. Generally (§ 101.93(g)(2)(iv))

Under proposed § 101.93(g)(2)(iv), FDA stated that a statement would be considered a disease claim if it claimed explicitly or implicitly to have an effect on disease through one or more of the following factors: (1) The name of the product (e.g., "Carpaltum" (carpal tunnel syndrome), "Raynaudin" (Raynaud's phenomenon), "Hepatacure" (liver problems)). Names that did not imply an effect on a disease, such as "Cardiohealth" and "Heart Tabs," would not constitute disease claims; (2) statements about the formulation of the product, including a claim that the product contained an ingredient that has been regulated by FDA predominantly as a drug and is well known to consumers for its use in preventing or treating a disease (e.g., aspirin, digoxin, or laetrile); (3) citation of a publication or other reference, if the citation refers to a disease use. For example, labeling for a vitamin E product that included a citation to an article entitled "Serial Coronary Angiographic Evidence That Antioxidant Vitamin Intake Reduces Progression of Coronary Artery Atherosclerosis," would create a disease claim

under this criterion; (4) use of the term "disease" or "diseased;" or (5) otherwise suggesting an effect on disease by use of pictures, vignettes, symbols, or other means (e.g., electrocardiogram tracings, pictures of organs that suggest prevention or treatment of a disease state, or the prescription symbol (Rx)). The proposed rule stated that a picture of a body would not constitute a disease claim under this criterion.

(50.) A few comments stated that the phrase "has an effect on" in proposed § 101.93(g)(2)(iv) is vague and could be interpreted by the agency to mean almost anything. Some of these comments argued that disease claims should include only those that use the specific terms "diagnose," "prevent," "treat," "mitigate," or "cure."

FDA does not agree that the phrase "has an effect on" is inappropriately vague. FDA believes that it is necessary to use a phrase that encompasses synonyms for the terms "diagnose," "prevent," "treat," "mitigate," or "cure." If disease claims were limited to those that used the specific terms in the statute, it would be possible to make obvious and explicit disease claims simply by using terms that are similar in meaning to the statutory terms, e.g., "relieves arthritis pain" rather than "treats arthritis pain," or "eliminates the risk of cancer" rather than "prevents cancer."

I. Product Name (§ 101.93(g)(2)(iv)(A))

(51.) One comment observed that there is an inconsistency between the statement in the proposed rule that "Heart Tabs" does not imply an effect on a disease and § 101.14(a)(1), which states that:

Health claim means any claim made on the label or in the labeling of a food, including a dietary supplement, that expressly or by implication, including "third party" references, written statements (e.g., a brand name including a term such as "heart"), symbols (e.g., a heart symbol) characterizes the relationship of any substance to a disease or health-related condition * * *

and requested clarification.

FDA agrees, in part, and disagrees, in part, with the comment. FDA does not agree that § 101.93(g)(2)(iv)(A) and § 101.14(a)(1) are inconsistent. Section 101.14(a)(1) was issued in 1993 to implement the health claims provisions of NLEA. In § 101.14(a)(1), use of the term "heart" in a brand name and use of the heart symbol in labeling are offered as examples of health claims, if in the context of the labeling as a whole, the word or symbol suggests that there is a relationship between the product and a disease or health-related condition. Thus, according to the preamble to that final rule (58 FR 2478 at 2486), the heart

symbol might appropriately appear in the labeling of a food product if, in context, it did not suggest a relationship to heart disease, e.g, in conjunction with "Hey, Fudge Lovers." If, however, the heart symbol appeared alone on a food, without further explanation from context, consumers might conclude that the food was beneficial for reducing the risk of developing cardiovascular disease (id.).

Following the issuance of § 101.14(a)(1), Congress enacted DSHEA. DSHEA created a special regulatory regime for dietary supplements. That regime, while closely related to the regime for food, was not identical to the food regime. Section 403(r)(6) of the act specifies certain types of structure/function claims and general well-being claims that may be made for dietary supplements without first obtaining new drug approval or health claim authorization. The types of claims listed in section 403(r)(6) of the act are similar, but not identical to the claims permitted for foods under section 201(g)(1)(C) of the act. Under Nutrilab v. Schweiker, 713 F.2d 335 (7th Cir. 1983), conventional food claims are limited to structure/function effects that derive from the taste, aroma, or nutritive value of the food. Dietary supplement claims are not subject to that limitation. Had Congress intended the scope of the permitted claims to be identical, it could simply have declared that dietary supplements are "foods." In light of

Congress' intent to expand the types of claims authorized for dietary supplements in DSHEA, FDA interprets § 101.14(a)(1) as permitting dietary supplements to have brand names that include the word "heart" or other organs, if, in the context of the labeling as a whole, the name does not imply disease treatment or prevention.

FDA does agree, however, that under § 101.14(a)(1), a dietary supplement name that included the word "heart" could be a health claim, depending on the context. Thus, a dietary supplement could be called "HeartTabs" if its claim was "to maintain healthy circulation," or some other role related to the structure or function of the heart that did not imply treatment or prevention of disease. If, however, the product name was not qualified by any further claim in the labeling, the product could be considered, under § 101.14(a)(1), to be intended for treatment or prevention of cardiovascular disease.

FDA also believes that the heart symbol has become so widely associated with prevention of heart disease that its use in the labeling of a dietary supplement would be ordinarily considered an implied heart disease prevention claim. Consistent with the examples provided in the January 6, 1993, FEDERAL REGISTER document on health claims (58 FR 2486), however, there may be unusual cases in which, in context, the use of a heart symbol does not imply heart disease prevention.

(52.) Several comments agreed with proposed § 101.93(g)(2)(iv)(A) that product names that imply an effect on disease, including implying cure or treatment of a disease, should not be allowed. The comments, however, requested that the agency provide further guidance as to what types of product names are acceptable and what types are not. Some comments questioned whether product names such as "CarpalHealth," "HepatoHealth," "HepataCare," "CircuCure," or "Soothing Sleep" would be acceptable under proposed § 101.93(g)(2)(iv)(A). Other comments disagreed with the agency's examples and stated that it is difficult to distinguish the reasoning behind some of the examples cited. For example, a few comments stated that both "Cardiohealth" and "Heart Tabs" imply that the product prevents heart disease.

Two principles formed the basis for the distinctions in the proposed rule between product names that were considered structure/function claims and those that were considered disease claims. First, the name should not contain the name, or a recognizable portion of the name, of a disease. Second, the name should not use terms such as "cure," "treat," "correct," "prevent" or other terms that suggest treatment or prevention of a disease. Thus, "CarpalHealth" and "CircuCure" would be considered disease claims. In some cases, to determine whether a product name implies an effect on disease, the agency will need

to consider the context in which a term is presented in the labeling as a whole. Thus, "Soothing Sleep" could be considered a claim to treat insomnia, unless the labeling made clear that the product was intended only for occasional sleeplessness.

"HepataCare" and "HepataHealth" could also be considered disease claims because "Hepata" could be read as a reference to hepatitis, unless the labeling made clear that the product was intended for general liver health and not intended to treat or prevent hepatitis.

The agency notes that in the near future, FDA will issue for public comment a draft guidance to provide additional clarification and examples of claims that would and would not be considered disease claims under the final rule. FDA will include in the draft guidance examples of product names.

(53.) Another comment stated that proposed § 101.93(g)(2)(iv)(A) would prohibit the use of the name of the "dispensing institution" if it had the word "Cancer" in it because the agency would interpret the labeling as implying an effect on disease, when in fact the product was listing the institution where the product was dispensed, e.g., ABC Cancer Institute. Other comments were concerned that the proposed rule would prohibit the use of their company trade name, which includes the use of the word "prescription" and its abbreviation "Rx."

The agency reiterates that it will view the name in the context of the entire labeling to determine whether a disease claim is being made. However, a manufacturer may not circumvent the requirements of the act, DSHEA, or this final rule by using the name of an institution or the manufacturer to imply a disease claim.

The agency agrees that the use of the word "prescription" or its abbreviation "Rx" in the name of the product should not automatically be interpreted as a disease claim. Although these terms imply that the product is a prescription drug, some prescription drugs are intended for nondisease conditions. Therefore, if nothing else in the labeling suggests a disease use, the agency will not consider the use of "prescription" or "Rx" to be an implied disease claim. The agency notes, however, that the use of these terms on dietary supplement products may deceive consumers into thinking that they are purchasing a prescription drug without a prescription. Thus, use of the terms "prescription" or "Rx" is misleading and will misbrand the product under section 403(a)(1) of the act if, in the context of the labeling as a whole, the terms imply that the product is a prescription drug.

(54.) A few comments cited in a proposed rule published in the FEDERAL REGISTER of March 27, 1974 (39 FR 11298), in which FDA stated that it would challenge brand names only in situations

where clarifying language is incapable of rectifying FDA's concern with the brand name and that excision of a brand name should be a last resort and should be pursued only when all other methods of qualifying the name have failed.

The agency notes that the proposed rule cited in this comment was never finalized and was withdrawn on December 30, 1991 (56 FR 67440), as part of an FDA initiative to reduce the backlog of outstanding proposed rules that have never been finalized. The policies outlined in the March 27, 1974, FEDERAL REGISTER notice are not in effect.

(55.) Several comments sought a statement from FDA that if a product brand name becomes synonymous over time with use for prevention or treatment of a disease, it will still be permitted. As an example, the comments claimed that Kleenex has become synonymous with treatment of nasal congestion, but did not provide support for this assertion.

FDA does not believe that Kleenex is synonymous with treatment of nasal congestion and, absent any supportive data, has no reason to believe that consumers believe them to be synonymous. The agency would agree that Kleenex has become synonymous with "tissue," and that both are used in conjunction with nasal congestion. Neither tissue nor Kleenex, however, treat, prevent, or otherwise affect nasal congestion in any way. Because the agency was not presented with any specific examples

of, nor is it aware of any, names of products that are not intended to treat disease but that have become synonymous with disease treatment or prevention, it does not have reason to believe that there is a real basis for concern.

J. Product Formulation (§ 101.93(g)(2)(iv)(B))

(56.) Several comments questioned whether the inclusion of a dietary ingredient in the ingredient list of a dietary supplement would be interpreted as a disease claim under proposed § 101.93(g)(2)(iv)(B). They argued that to provide truthful labeling, this information must be included. Another comment stated that the proposal fails to distinguish between true claims and false claims. Several comments further argued that ingredient information may be of value to consumers to alert them to potential adverse effects or drug interactions. One comment urged that the presence of a constituent that is naturally occurring in a plant and is also regulated as a drug does not automatically classify the substance as a drug. The comment asserted that 45 percent of drugs are derived from plants, which, according to the comment, would classify a number of dietary ingredients as drugs.

Listing a dietary ingredient in the ingredient list of a dietary supplement will not be considered to imply an effect on disease unless the ingredient is one that has been regulated primarily by FDA as a drug and is well-known to consumers for its

use or claimed use in preventing or treating a disease. (In the proposed rule, the agency gave as examples aspirin, digoxin, and laetrile.) Very few dietary ingredients meet this test. The agency agrees that a certain percentage of drug products are derived from plants. However, only a handful of these drugs are well-known to consumers under the name of the plant or natural plant ingredient from which they were derived. Instead, they are known to consumers under a brand name or generic name, e.g., aspirin. Thus, FDA does not believe that listing dietary ingredients that happen to be related to well-known drugs will fall under this provision, except in unusual circumstances. In those cases where a manufacturer does add a drug ingredient that is well-known to treat or prevent disease to its product and label its presence, however, FDA may consider it a disease claim. The fact that the labeling is truthful does not necessarily mean that it falls within the scope of claims authorized by section 403(r)(6) of the act. For example, the agency believes that there are many dietary ingredients that could be shown to treat or prevent diseases, and for which it could thus be truthful to state that the product treats or prevents a specific disease. Under the act, however, if a manufacturer wants to label its product to treat or prevent disease, it must do so under the drug approval provisions or the health claim provisions of the act. It may not do so under section 403(r)(6) of the act. In drafting

section 403(r)(6) of the act to exclude disease claims, Congress made a judgment that the public health will be served by requiring premarket review of such claims.

FDA agrees that it is important to inform consumers about potential adverse effects or drug interactions for specific dietary supplement ingredients. In fact, dietary supplement labeling, like the labeling of other FDA-regulated products, is required to include all facts that are material in light of consequences that may result from use of the product or representations made about it (sections 403(a)(1) and 201(n) of the act). This provision is not intended in any way to preclude truthful adverse event or drug interaction information from appearing in a dietary supplement's labeling.

(57.) A dietary supplement manufacturer asked FDA to clarify the effect of § 101.93(4)(ii) on a dietary ingredient found in common food(s), whose biological activity is first characterized in a food context, but which is subsequently approved as a drug. The comment asked whether, if indole-3-carbinol, a compound discovered in broccoli and other vegetables, were to be approved as a breast cancer drug, claims to the effect that a vegetable-based dietary supplement product contains indole-3-carbinol would be permitted as structure/function claims under the proposed rule. The comment claimed that the proposed rule would classify such claims as disease claims even if the

biological activity of this dietary ingredient were first identified in the food context.

Where an ingredient has been approved as a drug, section 201(ff)(3) of the act prohibits marketing of the ingredient as a dietary supplement unless the ingredient itself was previously marketed as a food (including a dietary supplement), or unless a food containing the ingredient was previously marketed for the presence of the ingredient. In the example provided in the comment, the isolated ingredient indole-3-carbinol could not be marketed as a dietary supplement, unless a food containing the ingredient had been marketed for the presence of the ingredient before the drug was approved or was the subject of substantial investigations that had been made public. However, to avoid a conflict between this provision and section 201(ff)(3) of the act in a situation where the ingredient was marketed as a food first, FDA has revised § 101.93(g)(2)(iv)(B) to exclude claims about an ingredient that is an article included in the definition of "dietary supplement" under section 201(ff)(3) of the act.

(58.) One comment misunderstood § 101.93(g)(2)(iv)(B) and believed that this provision only applies to the listing of OTC drug ingredients recognized by consumers.

This provision is not limited to the listing of OTC drug ingredients. For purposes of § 101.93(g)(2)(iv)(B), the agency may consider as a disease claim a claim that the product contains

an ingredient that has been regulated by FDA as a drug, whether marketed over-the-counter or by prescription, and that is well known for its use in preventing or treating a disease.

K. Citation of Publication Titles (§ 101.93(g)(2)(iv)(C))

(59.) Many comments objected to this proposed criterion or sought clarification. Many comments said that the proposed criterion undermines DSHEA by prohibiting the use of most journals, is not required by DSHEA, or is contrary to section 403B of the act (21 U.S.C. 343-2), which, the comment said, exempts scientific publications from labeling rules and is intended to allow consumers to be more informed by reading scientific studies. Other comments said that Congress intended to encourage the dissemination of scientific research and truthful, non-misleading information, so FDA should not prohibit titles of scientific studies. Some comments stated that the issue should not be whether a publication's title refers to a disease use, but rather whether, on balance, the entire presentation, including the product label, package insert, and other labeling, represents a disease claim. These comments supported the use of complete citations to scientific literature, including the titles of scientific articles. Some comments suggested that the proposal contradicted earlier FDA positions. One comment referred to the September-October 1998 issue of FDA Consumer which, the comment stated, suggested that consumers

contact companies to obtain scientific articles that the company might have to substantiate a claim. Another comment said the proposal was contrary to FDA policy to recognize and accept valid science. Several comments questioned how to provide substantiation of labeling claims, in compliance with 403(r)(6)(B) of the act, if the supporting articles cannot be cited. One comment stated that there will be more fraud and deception in the marketplace because companies will not cite scientific support for their statements. Several comments stated that the proposed rule will restrict access by consumers and the medical community to important new research results and discourage companies from investing in research. A dietary supplement manufacturer suggested revising the provision to permit companies to cite "bonafide" textbooks and peer-reviewed scientific journals that mention a disease in the title. Another dietary supplement manufacturer suggested revising this provision to permit citation of a publication or reference if the citation "is necessary to present a balanced discussion of the documented mechanism by which a nutrient or dietary ingredient acts to maintain the structure or function of the body."

FDA agrees that in enacting DSHEA, Congress intended to encourage the dissemination of scientific research and truthful, non-misleading information. FDA also agrees that consumers can benefit from reviewing the scientific support used to

substantiate a statement made for a dietary supplement under section 403(r)(6) of the act. In keeping with these goals, FDA has modified § 101.93(g)(2)(iv)(C) to narrow the circumstances under which citation to a scientific reference will be considered a disease claim. Based on Congress' explicit prohibition in section 403(r)(6) of the act of claims to affect disease, however, FDA does not believe that Congress intended to permit scientific references to be used in a way that constitutes an implied disease claim. Consequently, § 101.93(g)(2)(iv)(C) has been revised to state that citation of a title referring to a disease will be treated as a disease claim, if, in the context of the labeling as a whole, the citation implies treatment or prevention of a disease, e.g., through placement on the immediate product label or packaging, inappropriate prominence, or lack of relationship to the product's express claims.

The agency continues to believe that placing a citation to a scientific reference that mentions a disease in the title on the immediate product label or packaging should be considered a disease claim for that product, because of the unusual and unnecessary prominence of such placement. For citations to scientific references that refer to a disease use in the title and that are included in other types of labeling (i.e., other than the product label or packaging) the agency will consider the context in which the citation is presented. FDA agrees with the

comments that the totality of all available labeling should be considered to determine the context. One element that the agency will look at is the prominence of the citation in the labeling. If, for example, the citation is simply listed in the bibliography section of the labeling among other titles, it will generally not suggest an implied disease claim. On the other hand, 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. The agency will also consider whether the cited article provides legitimate support for a 403(r)(6) of the act statement that appears in the labeling of the 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.

FDA also agrees that it is important to provide a balanced discussion of the scientific literature regarding the claim. FDA encourages manufacturers to cite references that provide a balanced discussion of the evidence supporting a structure/function claim.

The agency believes that the final rule strikes a reasonable balance between encouraging the dietary supplement industry to

inform consumers about the substantiation for their claims and preventing abuses of section 403(r)(6) of the act.

(60.) Several comments challenged the basis for the proposed restriction on scientific references. One comment from industry said the proposed restriction on titles is outside DSHEA because the act refers to statements. The comment said titles could be prohibited if they were misleading, but said the rule should not contain a blanket prohibition.

The comment is apparently referring to section 403(r)(6) of the act, which prescribes the terms under which a "statement" may be made for a dietary supplement. FDA believes that the comment's reading is too literal, however. A "statement" does not have to be a declaratory sentence but rather is fairly read to include other kinds of statements, such as citations of scientific authority. In keeping with DSHEA's purpose to broaden the scope of labeling claims that may be made for dietary supplements without subjecting them to regulation as drugs, FDA believes that Congress intended "statement" to refer to any claim made that recommends or suggests a particular use of a dietary supplement. In addition to being under inclusive, a narrower interpretation would not benefit the dietary supplement industry because it would limit the scope of claims authorized under section 403(r)(6) of the act.

(61.) A few comments stated that the agency did not provide any support for the assumption that citations are disease claims rather than substantiation for a claim.

FDA believes that a citation of a title that refers to a specific disease can serve both as a disease claim and as substantiation for a claim. A citation of a publication title that links the product to a particular disease could lead consumers to believe that the product can be used to diagnose, prevent, mitigate, treat, or cure a disease, even if the title also provides substantiation for the product claims.

As stated above, citation of a scientific reference will not be treated as a disease claim if, in the context of the labeling as a whole, the reference lacks prominence and if it is appropriate support for the product claim.

(62.) One comment sought clarification of the effect of this provision on multi-ingredient products. The comment asked whether a disease claim for the entire product would be created if the labeling cited an article about only one ingredient of a multi-ingredient product.

Generally, if a citation is presented in the product labeling in such a way as to imply that a specific ingredient can treat or prevent disease, the product, as a whole, will be considered to be intended to treat or prevent disease.

(63.) A few comments requested FDA to clarify how proposed § 101.93(g)(2)(iv)(C) would operate. The comments questioned whether they would have to delete a citation from a list or redact the reference to a disease from the title of the article.

One comment asked whether an article that contains a reference to a disease can be cited if the title is not used in the citation. The comments further questioned whether they can provide the entire article, with the title on it, if requested by a consumer. Some comments asked FDA to clarify that a label may cite a title that appears in a publication whose name includes a disease (such as the publication titled Cancer) or to clarify how scientific studies may be cited. One comment requested that the agency issue further guidance to clarify what is and is not covered by § 101.93(g)(2)(iv)(C).

FDA does not expect a manufacturer to redact portions of the citation or delete a citation from a list of references or bibliography if it is appropriate to include the reference to substantiate a claim. As described above, if the citation to a scientific reference refers to a disease, the agency will consider the context in which the citation is presented, including its prominence in the labeling and whether there is a reasonable relationship between the reference and the express claim. In most cases, the unredacted reference title can be included in the product labeling without subjecting the product to regulation as a drug, as long as the prominence of the reference does not suggest that it is being used to imply disease treatment or prevention. Under revised § 101.93(g)(2)(iv)(C), the only reason a publication title would be considered a disease

claim regardless of prominence would be if the reference is not reasonably related to substantiating the product's express claim. In that case, FDA believes that the reference would be a disease claim, even if the name of the disease is redacted, because the only purpose of including the reference would be to suggest use of the product for treatment or prevention of the disease discussed in the reference.

With regard to citation of titles from journals whose official names include the name of a disease, the same considerations of appropriate prominence and reasonable relationship to the product's express claims apply. FDA expects that accepted conventions of scientific citation will be used for all citations that appear in labeling.

Finally, if specific information about an unlabeled use of a product is requested by a consumer, and the request is not solicited by the manufacturer, providing articles that are responsive to the request will not be considered a disease claim.

FDA will issue further guidance on § 101.93(g)(2)(iv)(C), if necessary.

(64.) Several comments sought modifications to proposed § 101.93(g)(2)(iv)(C). One comment suggested revising the provision to permit companies to cite articles or references that use "intermediate terms" (which the comment said were terms or

phrases that have disease-related endpoints) on the label or labeling.

Whether a citation that refers to a disease-related endpoint will be considered a disease claim under the rule will depend on the context in which the disease-related endpoint is referred to and whether the reference implies that the product has an effect on disease. For example, the title of an article that states that a product was shown to maintain cholesterol levels that were already within the normal range, with no reference to a disease, would be considered a structure/function statement about maintenance rather than a disease claim. However, if the title of the article states that the product was shown to lower elevated cholesterol levels, this implies that the product can be used to have an effect on the disease states hypercholesterolemia and heart disease, because heart disease is associated with high cholesterol levels.

(65.) A trade association suggested that the title should not be considered to be a disease claim unless it uses the terms "treat," "cure," "mitigate," "prevent," or "diagnose."

As stated elsewhere in this document, FDA believes that a disease claim can be made explicitly or implicitly using terms other than those listed in the comment. For example, depending on how it was used in a product's labeling, a scientific reference entitled "Using Ingredient X For Diabetes" could

constitute a claim that the product can diagnose, mitigate, treat, cure, or prevent diabetes, without using any of these specific terms.

(66.) A few comments argued that citation of articles that refer to a disease use should be permitted because consumers have access to these articles in connection with the sale of dietary supplements under section 403B(a) of the act.

As stated above, FDA has revised the proposed rule's treatment of citations to scientific articles. Under the final rule, such citations will not always be considered disease claims. FDA does not agree, however, that section 403B of the act applies to the citation of titles in product labeling. Although section 403B of the act exempts certain publications from the labeling provisions of the act, section 403B(a)(2) states that the exemption applies only when, among other requirements, the publication is "used in connection with the sale of a dietary supplement to consumers when it * * * does not promote a particular manufacturer or brand of a dietary supplement." If the reference or the title of the reference was disseminated by a particular manufacturer of the dietary supplement discussed in the reference, the agency would conclude that it was being used to promote that manufacturer's brand of the dietary supplement. Therefore, the exemption in section 403B of the act would not apply.

Furthermore, to qualify for the exemption in section 403B of the act, a publication must be "an article, a chapter in a book, or an official abstract * * * reprinted in its entirety" and must be "displayed or presented, or * * * displayed or presented with other such items on the same subject matter, so as to present a balanced view of the available scientific information of a dietary supplement." A citation to an article alone could not meet these requirements.

L. Use of Disease or Diseased (§ 101.93(g)(2)(iv)(D))

(67.) Many comments agreed with proposed § 101.93(g)(2)(iv)(D), stating that the terms "disease" or "diseased" should classify a statement as a disease claim. Several comments urged that a statement referring in a general way to the concept of "health promotion and disease prevention" not cause the statement to be considered a disease claim, as long as no specific disease was mentioned. One comment asked that the agency permit general discussions of the concept of disease prevention, citing the following example from the U.S. Public Health Service Healthy People 2000 initiative: "Better dietary and exercise patterns can contribute significantly to reducing conditions like heart disease, stroke, diabetes, and cancer, and could prevent 300,000 deaths."

FDA agrees that general statements about health promotion and disease prevention may be acceptable, as long as the

statements do not imply that a specific product can diagnose, mitigate, cure, treat or prevent disease. Accordingly, FDA has revised § 101.93(g)(2)(iv)(D) to permit general statements about disease prevention that do not refer explicitly or implicitly to a specific disease or class of diseases or to the specific product or ingredient. For example, the statement "a good diet promotes good health and prevents the onset of disease" would not be considered a disease claim. On the other hand, the claim "Promotes good health and prevents the onset of disease" would refer implicitly to the product and would constitute a disease prevention claim. FDA also believes that the particular statement offered by one of the commenters would constitute a disease claim. The example cites four specific diseases. If that statement were included in the labeling for a dietary supplement, a consumer would reasonably assume that the statement applies to the product and that taking that dietary supplement contributes to preventing the diseases listed. If, however, the statement said "better dietary and exercise patterns can contribute to disease prevention and better health," FDA would not consider it a disease claim.

M. Pictures, Vignettes, and Symbols (§ 101.93(g)(2)(iv)(E))

(68.) Many comments agreed that certain pictures, vignettes, and symbols can explicitly or implicitly convey that the product has an effect on disease. A few comments agreed that a diseased organ should be considered a disease claim. They argued, however,

that a picture of a healthy heart, healthy artery, or other healthy organ should be permitted because such pictures do not in and of themselves depict a disease. A few comments stated that a healthy electrocardiogram (EKG) tracing should not be considered a disease claim. One comment requested that the agency clarify whether a picture of an organ is permitted if the claims are appropriate and within the scope of permitted structure/function claims. The comment offered as an example a statement that a product maintains cardiovascular health accompanied by a picture of a heart and circulatory system.

FDA agrees that in most cases, a picture of a healthy organ would not be considered a disease claim, if, in the context of the labeling as a whole, it did not imply treatment or prevention of disease. As described in response to comment 51 of section II.I of this document, however, there may be symbols for organs, like the heart symbol, that have become so widely recognized as symbols for disease treatment or prevention, their use in labeling would constitute an implied disease claim. FDA also believes that a picture of a healthy EKG tracing is an implied disease claim. Because most consumers cannot distinguish a healthy EKG tracing from an unhealthy one, both types may be viewed as references to diagnosis or treatment of unhealthy heart conditions.

N. Membership in Product Class (§ 101.93(g)(2)(v))

Some product class names are so strongly associated with use to treat or prevent a specific disease or class of diseases that claiming membership in the product class implies disease treatment or prevention. Under proposed § 101.93(g)(2)(v), a statement would have been considered a disease claim if it claimed that the product belonged in a class of products recognizable to health care professionals or consumers as intended for use to diagnose, mitigate, treat, cure, or prevent a disease. The preamble provided the following examples of class names that would imply disease treatment or prevention: Claims that the product was an "antibiotic," a "laxative," an "analgesic," an "antiviral," a "diuretic," an "antimicrobial," an "antiseptic," an "antidepressant," or a "vaccine." These examples were not intended to constitute an exclusive list of product class names that convey disease claims. Under the proposed rule, claiming that a product was in a class that is not recognizable to health care professionals or consumers as intended for use to diagnose, mitigate, treat, cure or prevent disease would not have constituted a disease claim under this criterion. The preamble provided as examples of acceptable structure/function claims: Claims that the product was an "energizer," a "rejuvenative," a "revitalizer," or an "adaptogen." In light of the agency's decision that claims for

relief of "occasional constipation" should not be considered disease claims, the term "laxative" will not be considered a disease claim under the final rule, as long as the remainder of the labeling makes clear that the product is not intended to treat chronic constipation.

(62.) Most of the comments on proposed § 101.93(g)(2)(v) were generally supportive, but some wanted to ensure that the provision would be applied in specific ways. One comment urged that "appetite suppressant" be treated as a disease claim, while another comment urged that "tonic" be treated as a structure/function claim.

FDA does not agree that "appetite suppressant" should be considered a disease claim. As discussed elsewhere in this document, although obesity is a disease, overweight is not. An appetite suppressant may be intended for ordinary weight loss, rather than as a treatment for obesity. Therefore, "appetite suppressant" would only be considered a disease claim in a context where it implies use for obesity. FDA agrees that "tonic" is not a disease claim. "Tonic" is commonly understood as a general term for anything that refreshes, and, by itself, would not be considered to constitute a disease claim.

(70.) Some comments stated that various class names should be allowed when they describe the mechanism by which a supplement has its effect, or when they are present in a product and it is

truthful and not misleading to name them. One comment offered as examples of class names that might be used to describe a product's mechanism of action: A statement that a product that is soothing to the stomach achieves its effects as a result of its "carminative (antispasmodic) properties" or as a result of its "anti-inflammatory effect on the gastrointestinal tract." This comment stated that it is not membership in a given class of compounds that should make a product a drug, but rather the intended use of the product. One comment asked whether this criterion precludes a statement that daily consumption of vitamins and minerals may prevent the onset of disease or other physical ailments.

Nothing in this provision would preclude a manufacturer from truthfully declaring the ingredients contained in a product. In fact, FDA regulations require the ingredients in a dietary supplement to be listed on its label. (See § 101.4(a)(1) and (g) (21 CFR 101.4(a)(1) and (g)), and § 101.36). The rationale for § 101.93(g)(2)(v) is that certain product class names (not particular ingredients) are so strongly associated with use to diagnose, treat, mitigate, cure, or prevent disease that claiming membership in the class would constitute a disease claim. FDA does not believe that claiming membership in a product class is necessary in order to provide an accurate list of the ingredients present in a product.

FDA agrees that dietary supplements may carry statements that characterize "the documented mechanism of action by which a nutrient or dietary ingredient acts to maintain * * * structure or function," but only to the extent that such a statement does "not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases" (section 403(r)(6) of the act). In the examples provided in the comment, FDA is unaware of evidence establishing that the claims actually describe "documented" mechanisms by which the products "maintain" a calm stomach. Nevertheless, assuming that these statements met the other requirements of section 403(r)(6)(A) of the act, FDA would not consider the term "antispasmodic" to constitute a disease claim because the agency does not believe that it is closely associated with treatment or prevention of gastrointestinal disease. The term "anti-inflammatory" is, however, strongly associated with treatment of certain serious gastrointestinal diseases, and would constitute a disease claim.

FDA agrees with the statement that it is not membership in a given class of compounds that makes a product a drug, but rather the intended use of the product. This criterion sets forth FDA's conclusion that claiming membership in certain product classes that are strongly associated with use to treat or prevent disease is evidence that the product is intended to treat or prevent disease.

Although this provision does not itself treat as a disease claim a statement by a vitamin manufacturer that the product prevents the onset of a disease, such a statement would be considered a disease claim under § 101.93(g)(2)(I), which covers statements that a product has an effect on a specific disease or class of diseases. In addition, a general statement that a product prevents the onset of disease would be considered a disease claim under § 101.93(g)(2)(iv)(D), as noted in the discussion of that provision. Claiming membership in the class of vitamins or minerals would not constitute a disease claim under this criterion.

(71.) A food manufacturers' trade association and an individual manufacturer opposed the provision, arguing that it goes beyond the intent of DSHEA and would prohibit the use of any term associated with a drug product.

FDA does not agree that this provision goes beyond the intent of DSHEA nor that it would prohibit the use of any term associated with a drug product. DSHEA precludes statements under section 403(r)(6) of the act from claiming to treat or prevent disease. This provision constitutes FDA's conclusion that some drug class names (but not all terms associated with drug products) are so strongly associated with disease prevention or treatment that claiming membership in the class constitutes a

claim that the product, like other members of the class, treats or prevents disease.

(72.) One pharmaceutical company argued that proposed § 101.93(g)(2)(v) would violate DSHEA, because DSHEA specifically defines as a dietary supplement an article that is approved as a new drug under section 505 of the act, if it was, prior to approval, marketed as a dietary supplement.

FDA agrees that the dietary supplement definition includes the provision cited by the comment (section 201(ff)(3)(A) of the act), but believes that the definition and § 101.93(g)(2)(v) are not inconsistent. Section 101.93(g)(2)(v) would treat as a disease claim a labeling statement that the supplement is a member of a product class when that class is so recognizable for its disease treatment or prevention use that the labeling statement would be understood as a disease claim for the supplement. The criterion would not treat inclusion of an ingredient in a dietary supplement as a disease claim merely because the ingredient had been approved under section 505 of the act nor would it preclude listing the ingredient in the Supplement Facts panel or ingredient list.

0. Substitute for Disease Therapy (§ 101.93(g)(2)(vi))

Under proposed § 101.93(g)(2)(vi), a statement would have been considered a disease claim if it explicitly or implicitly claimed that the product was a substitute for another product

that is a therapy for a disease. FDA offered "Herbal Prozac" as an example of such a claim. A claim that did not identify a specific drug, drug action, or therapy (e.g., "use as part of your weight loss plan") would not constitute a disease claim under this criterion.

(73.) There was general support for the provision, particularly for considering terms that make a direct connection with an approved drug, like "Herbal Prozac" and "Herbal Phenfen," disease claims. Several organizations noted that associating dietary supplements with regulated drug products is deceptive and dangerous because it can signal to consumers that because the product is "herbal" it is safer. Several medical associations, however, objected to the interpretation that "use as part of your weight loss plan," is nonspecific and would be acceptable. They maintained that the term implies treatment of a disease, obesity. A comment from a manufacturer also strongly objected to the statement in the proposal that "Use as part of your weight loss plan" would be an acceptable structure/function claim. The comment contended that the legislative history of the act shows that Congress intended weight loss claims to be treated as disease claims. Finally, the comment argued that even if FDA decides to permit weight loss claims as structure/function claims, the legislative history of the act and case law require that FDA classify products containing "antinutrients" as drugs.

FDA agrees with these comments that obesity is a disease, and that obesity claims are not acceptable structure/function claims. Being overweight, i.e., being more than one's ideal weight but less than obese, however, is not a disease. FDA believes that it is commonly understood that "weight loss plans" relate to a broad range of overweight statuses. Therefore, weight loss plans are not so narrowly associated with disease treatment that a reference to use as part of a weight loss plan should be considered a disease claim.

FDA does not agree that either the legislative history of the act or the case law interpreting section 201(g) of the act or DSHEA require a determination that FDA classify as drugs products making weight loss claims. The legislative history of section 201(g)(1)(C) of the act shows that Congress added the structure/function definition of "drug" in part to capture obesity claims that were not covered by section 201(g)(1)(B) because obesity was not, at that time, considered a disease. FDA believes that the legislative history in fact supports FDA's view that weight loss claims are properly considered structure/function claims. Although obesity claims are now covered by section 201(g)(1)(B) of the act because obesity is now considered a disease, section 201(g)(1)(C) was added to cover conditions, like overweight, that are not considered diseases, but that affect the structure or function of the body.

Structure/function claims under section 403(r)(6) of the act are closely related to structure/function claims under section 201(g)(1)(C) of the act and therefore should encompass weight loss claims.

FDA also does not agree that cases cited by the comment compel the conclusion that weight loss products must be regulated as drugs. In Nutrilab v. Schweiker, 713 F.2d 335 (7th Cir. 1983), American Health Products Co. v. Hayes, 574 F. Supp. 1498 (S.D.N.Y. 1982), aff'd, 744 F.2d 912 (2d Cir. 1984), and United States of America v. Undetermined Quantities Of "CAL-BAN 3000", 776 F. Supp. 249 (E.D.N.C. 1991), the courts held that certain weight loss products were drugs under section 201(g)(1)(C) of the act because they were labeled to affect the structure or function of the body, and did not qualify for the "food" exception to section 201(g)(1)(C). At the time these cases were decided, the only issue was whether these products were "foods" or "drugs." Since then, however, DSHEA created a new statutory category of products, dietary supplements. Section 403(r)(6) of the act, which was added by DSHEA, permits structure/function claims to be made for dietary supplements without subjecting them to regulation as drugs, even if they could not qualify for the "food" exception in section 201(g)(1)(C) of the act. Therefore, these cases do not establish that dietary supplements making weight loss claims must be regulated as drugs. To the contrary,

because the products were held to be drugs under section 201(g)(1)(C) of the act rather than section 201(g)(1)(B), these cases support treatment of weight loss claims for dietary supplements as structure/function claims authorized under section 403(r)(6) of the act.

Finally, FDA does not agree that, under United States v. Ten Cartons, More or Less, of an Article * * * Ener-B Vitamin B-12, 72 F.3d 285 (2d Cir. 1995), dietary supplements making weight loss claims must necessarily be regulated as drugs. The court in Ener-B held that a dietary supplement that makes a structure/function claim may nevertheless be regulated as a drug, under certain circumstances. In that case, the court found that FDA could regulate a product as a drug, based on its method of intake (nasal administration). Nothing in that case suggests that FDA must regulate dietary supplements making weight loss claims as drugs.

(74.) Several comments reiterated that general statements about the nature of a product or its mechanism of action should not be disease claims, or should be structure/function claims as long as they are truthful and not misleading. One comment objected to the provision as duplicative of proposed § 101.93(g)(2)(v). Another comment sought to delete the provision, arguing that dietary supplement manufacturers have the