

January 13, 2000

MEMORANDUM

Re: Final Rule Concerning “Structure or Function” Claims for Dietary Supplements

On January 6, 2000, FDA published a final rule defining the scope of claims that can be made concerning the effect of a dietary supplement on the “structure or function” of the body. 65 Fed. Reg. 999 (January 6, 2000). The regulation defines “structure/function” claims relying on statutory language, and makes its central focus the classification of prohibited “disease claims” which lie outside the boundaries of permissible “structure/function” claims for dietary supplements. The final rule varies in a number of significant respects from the proposed rule published in the Federal Register on April 29, 1998. 63 Fed. Reg. 23623 (April 29, 1998). Because of FDA's renewed emphasis on implied disease claims, however, it is unclear whether this final regulation, as implemented by FDA, will prove an advance, a retreat, or the initiation of trench warfare on structure/function claims.

This memorandum discusses the final rule, highlighting key elements of FDA's explanation of each provision, as provided in the preamble to the rule and in the document entitled, “FDA Finalizes Rules for Claims on Dietary Supplements” issued by the FDA press office, and compares those comments and provisions, where applicable, to the corresponding provisions of the proposed regulation.

Because this is a final rulemaking, objections to the rule must be submitted in the form of a petition for reconsideration and stay. Under FDA's procedural rules, any such petition must be submitted within 30 days of the rule's January 6, 2000 publication date in order to initiate a reversal of the FDA position.

A. Background

Section 403(r)(6) of the FD&C Act, as adopted under the Dietary Supplement Health and Education Act of 1994 (DSHEA), authorizes manufacturers complying with a premarket notification procedure to include “statements of nutritional support” in dietary supplement labeling. Historically, similar “structure/function” claims have been authorized under Section 201(g)(1)(C) for conventional “foods” and ingredients of dietary supplements having “nutritive value” (*e.g.*, vitamins, minerals) and thus meeting the established definition of “food.” *Nutrilab, Inc. v. Schweiker*, 713 F.2d 335, 338 (7th Cir. 1983) (defining “food” to include articles consumed primarily for “taste, aroma, or nutritive value”). Section 201(g)(1)(C) authorizes claims that a “food” is intended to “affect the structure or any function of the body of man . . .” 21 U.S.C. § 321(g)(1)(C). Under the rubric of “statements of nutritional support,” Section 403(r)(6) effectively authorizes structure/function claims for all other dietary ingredients, including herbal, botanical, and other ingredients having no conventional nutritive value at the levels consumed.

Section 403(r)(6) specifically authorizes statements:

claiming a benefit related to a classical nutrient deficiency disease that discloses the prevalence of the disease in the United States,

describing the role of a nutrient or dietary ingredient intended to affect the structure or function in humans,

characterizing the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, or

describing general well-being from consumption of a nutrient or dietary ingredient.

21 U.S.C. § 343(r)(6).

Section 403(r)(6) functions as a safe harbor, insulating conforming claims from regulation as unapproved “health claims” under Section 403(r)(1)(B) of the FD&C Act. In addition, compliance with Section 403(r)(6) provides an exclusion from Section 201(g)(1)(C) of the Act, classifying non-food structure/function claims as drug claims. Section 403(r)(6) provides no safe harbor from “drug” regulation where dietary supplement claims suggest that the product is “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals . . .” 21 U.S.C. §§ 321(ff); 343(r)(6); *cf.* 21 U.S.C. § 201(g)(1)(B).

Moreover, FDA states that, consistent with Section 201.128 of FDA rules, a dietary supplement bearing a structure/function claim complying with Section 403(r)(6) may nonetheless be regulated as a “drug” where the agency has “other evidence” that the product is intended for drug use. Section 201.128 provides that the “intended use” of a product may be determined from “expressions” of the manufacturer or “circumstances surrounding the distribution of the article” including, “labeling claims,” “advertising matter,” “oral or written statements,” and the manufacturer’s knowing sale of the product for a “drug” use that is not labeled or advertised. 21 C.F.R. § 201.128.

B. The “Structure/Function” Claim Designation

The regulation amends 21 C.F.R. § 101.93 (which currently governs only Section 403(r)(6) premarket notification requirements), expanding the rule to define the scope of Section 403(r)(6) “statements of nutritional support” concerning the role or mechanism by which a dietary ingredient effects or maintains the structure or function. FDA formally would adopt “structure/function claim” to describe these claims. This reflects the agency’s view that the statutory term, “statement of nutritional support,” is not accurate for all relevant claims because some dietary supplements have no “nutritional value.” *See* 62 Fed. Reg. 49859, 49863 (September 23, 1997).

The choice of the “structure/function” terminology indicates that Section 403(r)(6) authorizes the same *types* of claims for dietary supplements as have been authorized historically for conventional “food” under Section 201(g)(1)(C) of the FD&C Act. Accordingly, the final rule provides useful guidance for the construction of structure/function claims for “conventional food” as well as dietary supplements.

The rule does not define claims describing “general well-being” from consumption of a nutrient or dietary ingredient, or claims concerning benefits related to a classical deficiency disease. With regard to “well-being” claims, this apparently reflects the agency’s recognition that such claims do not constitute “structure/function” claims. Both types of claims are permitted provided they are stated in a truthful and nonmisleading manner and otherwise comply with Section 403(r)(6).

C. Scope of Permitted Structure/Function (“S/F”) Claims

The final regulation does little more than restate the language of Section 403(r)(6) in defining the “structure/function” statements that are permitted under Section 403(r)(6). The rule states that structure/function claims may

“describe the role of a nutrient or dietary ingredient intended to affect the structure or function in humans or that characterize the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function . . .”

65 Fed. Reg. at 1050 (21 C.F.R. § 101.93(f)).

D. Scope of Prohibited “Disease Claims”

1. Definition of “Disease”

Section 403(r)(6) explicitly excludes from the scope of “statements of nutritional support,” “claims to diagnose, mitigate, treat, cure, or prevent a *specific disease or class of diseases.*” In addition, Section 201(ff) makes clear that dietary supplements are regulable as Section 201(g)(1)(B) “drugs” when such claims are made. 21 U.S.C. 321(g)(1)(B).

In 1990, the Nutritional Labeling and Education Act (“NLEA”) was passed. Regulations adopted in 1993 under that Act defined “disease” as:

“damage to an organ, part, structure, or system of the body such that it does not function properly (*e.g.*, cardiovascular disease), or a state of health leading to such dysfunctioning (*e.g.*, hypertension); except that diseases resulting from essential nutrient deficiencies (*e.g.*, scurvy, pellagra) are not included in this definition.”

21 C.F.R. § 101.14(a)(5) (formerly 21 C.F.R. § 101.14(a)(6)).

The April 29, 1998 proposal would also have amended Section 101.14 of FDA regulations, expanding significantly the definition of “disease or health-related condition,” and thus the reach of health claims regulation. “Disease” would have been defined identically for purposes of defining “health claims” and prohibited “disease claims” under Section 403(r)(6). This means that all Section 403(r)(6) “disease claims” potentially would have also subjected traditional foods to enforcement as making unapproved “health claims,” as well as Section 201(g)(1)(B) “drug” claims. 21 C.F.R. § 101.14(a)(6). The proposal would have broadened the definition of “disease” to include:

“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.”

63 Fed. Reg. at 23632 (Proposed 21 C.F.R. §§ 101.14(a)(5), 101.93(g)(1)). “Signs and symptoms” were intended to include references to such laboratory or clinical measurements as “elevated cholesterol fraction,” “uric acid,” “blood sugar,” “glycosylated hemoglobin,” “elevated blood pressure,” or “intraocular pressure.” 63 Fed. Reg. at 23625.

Despite FDA’s stated concern that the inclusion of the word “damage” in the existing disease definition could be interpreted as limiting the definition to serious or long-term illness or imply the need for physiological damage, and in light of the opposition to the proposed definition by a number of commentators, the final rule does not include a new definition of disease, but utilizes the existing definition of “disease or health-related condition” in Section 101.14(a)(5). Accordingly, the definition of disease in 21 C.F.R. § 101.93(f) of the final rule, repeating the language of Section 101.14(a) (which was not changed) is:

“damage to an organ, part, structure, or system of the body such that it does not function properly (*e.g.*, cardiovascular disease), or a state of health leading to such dysfunctioning (*e.g.*, hypertension); except that diseases resulting from essential nutrient deficiencies (*e.g.*, scurvy, pellagra) are not included in this definition.”

65 Fed. Reg. at 1010. FDA explained that if experience were to show a public health need for a different or broader definition, the agency will consider initiating a rulemaking to amend that definition. *Id.*

2. Categories of Prohibited “Disease Claims”

Under the new regulation, FDA will find that a statement about a product claims to “diagnose, mitigate, treat, cure, or prevent disease” (and the product thus is regulable as a Section 201(g)(1)(B) “drug”), if “disease claims” are made. The regulation effectively prohibits “disease claims” for dietary supplements, which are defined to include both explicit and implicit claims in the categories discussed below. Industry had strenuously argued that Section 403(r)(6), in stating that a dietary supplement “may not claim to diagnose, mitigate, treat, cure, or prevent a

specific disease or class of diseases,” prohibited only *express*, and not *implied*, disease claims. FDA vigorously rejected the position, advanced in a number of different ways, that implied disease claims were not barred. Rather, FDA concluded that “a construction of DSHEA that permitted such claims would be fundamentally incompatible with important provisions of the act that were squarely before Congress when it passed DSHEA, including the definitions of ‘drug’ and ‘new drug’ and the health claims provisions of the NLEA.” 65 Fed. Reg. at 1013. FDA also asserted that such an interpretation “would be irreconcilable with FDA’s longstanding interpretation of Section 201(g)(1)(B) of the act, which treats such claims as drug claims.” 65 Fed. Reg. at 1014.

Despite the expansion of the number of recognized structure/function claims contained in the final regulation, and discussed below, the FDA’s adamant position with respect to implied drug claims continues to pose serious risks to industry, particularly in light of the required submission of claims to FDA that gives the agency the opportunity to second guess the manufacturer’s conclusion. The decisions reached by FDA in the final regulation, finding implied drug claims in the previously-accepted platelet aggregation claims and “maintaining healthy cholesterol levels,” suggest the problem that industry faces in trying to gauge whether a particular claim is, or will remain, a structure/function claim. Thus, even with the changes that FDA has made, the final regulation continues to grant FDA significant leeway and discretion in determining when a particular claim may be an impermissible “implied drug claim.”

FDA listed many examples of both disease claims and permissible structure/function claims in the preambles to the proposed and final rules. In some cases, FDA expressly reclassified in the final rule certain claims that had been listed in the proposal. Both sets of claims will be listed in this memorandum. Those cited as appearing in 63 Fed. Reg. were in the proposal and those cited as 65 Fed. Reg. are in the final rule. If a claim was treated consistently in both the proposal and the final rule, the memorandum lists the claim as appearing in the final rule. If FDA discussed the claim or changed its classification as in the final rule, that treatment is discussed in the memorandum.

a. Prohibits claims suggesting the product has an effect on a specific disease or class of diseases. (21 C.F.R. § 101.93(g)(2)(i)).

Both the proposal and the final rule prohibit claims suggesting that a product effects a specific disease entity or class of diseases. 63 Fed. Reg. at 23632; 65 Fed. Reg. 1013.

Examples of disease claims:

“Protective against the development of cancer.”

“Reduces the pain and stiffness associated with arthritis.”

“Decreases the effects of alcohol intoxication.”

“Alleviates constipation.”

63 Fed. Reg. at 23626.

Examples of implied disease claims:

“Relieves crushing chest pain” (angina or heart attack).

“Prevents bone fragility in post-menopausal women” (osteoporosis).

“Improves joint mobility and reduces joint inflammation and pain” (rheumatoid arthritis).

“Heals stomach or duodenal lesions and bleeding” (ulcers).

“Anticonvulsant” (epilepsy).

“Relief of bronchospasm” (asthma).

“Prevents wasting in persons with weakened immune systems” (AIDS) (acquired immune deficiency syndrome).

“Prevents irregular heartbeat” (arrhythmias).

“Controls blood sugar in persons with insufficient insulin” (diabetes).

“Prevents the spread of neoplastic cells” (prevention of cancer metastases).

“Antibiotic” (infections).

“Herbal Prozac” (depression).

“According to the National Cancer Institute, ingredient X protects smokers’ lungs.”

“Deters bacteria from adhering to the wall of the bladder and urinary tract.” (implies prevention of bacterial infections of the bladder and urinary tract).

65 Fed. Reg. at 1013, 1015, 1030.

Permitted S/F claims:

“Helps promote urinary tract health.”*

“Helps maintain cardiovascular function and a healthy circulatory system.”

“Helps maintain intestinal flora.”

“Promotes relaxation.”

63 Fed. Reg. at 23626.

“For relief of occasional constipation” (provided that the labeling makes clear that the product is not intended to be used to treat chronic constipation).

65 Fed. Reg. at 1015.

* In the preamble to the proposed rule, FDA listed the claim, “Helps promote urinary tract health” as a permissible structure/function claim. 63 Fed. Reg. at 23626. In the final rule, the agency referred to its inclusion in the preamble to the proposed regulation, “the following examples of claims that do not refer explicitly or implicitly to an effect on a specific disease state: ‘Helps promote urinary tract health.’” 65 Fed. Reg. at 1012. FDA did not indicate in the final rule that it had changed its view with respect to the appropriateness of this claim as a structure/function claim.

b. Prohibits claims suggesting that the product has an effect, using scientific or lay terminology, on the characteristic signs or symptoms of a specific disease or class of diseases. (21 C.F.R. § 101.93(g)(2)(ii)).

The agency takes the position that a reference to a characteristic set of signs and symptoms of disease, even when a disease is not specifically named, can be understood as a reference to the disease itself, and thus may constitute an implied “disease claim.” 63 Fed. Reg. at 23632. A disease claim is made when, in the particular context, the symptoms described are sufficient to characterize one or more specific diseases. *Id.* at 23626. In the proposal, the rule contained a requirement that the one or more signs or symptoms be recognizable to health care professionals or consumers as being characteristic of a specific disease or of a number of diseases. In response to comments received on the proposed rule, the agency substituted a more objective criterion. The final rule eliminates the reference to recognition, and focuses simply on whether the labeling suggests that the product will produce a change in the characteristic signs or symptoms of a specific disease or class of diseases. FDA also explained that it had added a sentence to Section 101.93(g)(2) clarifying that the criteria in that paragraph are not intended to preclude structure/function claims that refer to the maintenance of healthy structure or function, unless they imply disease treatment or prevention. 65 Fed. Reg. at 1018.

Examples of disease claims:

“Improves urine flow in men over 50 years old” (characteristic symptom of, *e.g.*, benign prostatic hypertrophy).

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“Lowers cholesterol” (characteristic sign of, *e.g.*, hypercholesterolemia).

“Reduces joint pain” (characteristic symptom of arthritis).

“Relieves headache” (characteristic symptom of, *e.g.*, migraine or tension headache).

63 Fed. Reg. at 23626.

“Prevents bone fragility in post-menopausal women” (characteristic symptom of osteoporosis).

“Prevents shortness of breath, an enlarged heart, inability to exercise, generalized weakness, and edema” (characteristic symptoms of congestive heart failure).

“Maintains healthy lungs in smokers” (implies prevention of tobacco-related lung cancer and chronic lung disease).

“Promotes cholesterol clearance” (implies a cholesterol lowering effect).

65 Fed. Reg. at 1017-19.

Permitted S/F claims:

“Reduces stress and frustration.”

“Improves absentmindedness.”

“Helps maintain regularity.”

63 Fed. Reg. at 23626.

“Helps support cartilage and joint function.”

“Maintains healthy lung function.”

65 Fed. Reg. at 1016-18.

FDA had listed the claim, “Inhibits platelet aggregation” as an example of a permitted structure/function claim in the proposed regulation. 63 Fed. Reg. at 23626. In the preamble to the final rule, however, FDA reversed its position and concluded that the claim was an implied disease prevention or treatment claim based on the fact that the inhibition of platelet aggregation is a well-recognized therapy for the prevention of stroke and recurrent heart attack. 65 Fed. Reg. at 1016. *See*, however, the example of a permitted reference to platelet aggregation under section “m” below.

FDA had also listed the claim, “Helps maintain a healthy cholesterol level,” as an example of a permitted structure/function claim in the proposed regulation. 63 Fed. Reg. at 23626. The agency concluded, however, that the term, “healthy cholesterol” may be misleading to consumers because it is used to refer to high density lipoproteins (HDLs). To avoid this confusion, FDA has decided that an appropriate structure/function claim for maintenance of cholesterol levels would be “helps to maintain cholesterol levels that are already within the normal range.” 65 Fed. Reg. at 1019.

- c. **Prohibits claims suggesting that a 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. (21 C.F.R. § 101.93(g)(2)(iii)).**

The final rule reflects a significant change in FDA’s position over the proposal with respect to claims suggesting that a product “has an effect on a consequence of a natural state, such as aging, pregnancy or the menstrual cycle.” In the proposal, FDA took the position that such natural processes were associated with “abnormalities” that meet the definition of “disease” that was set forth in the proposal. Accordingly, the proposal classified as prohibited “disease claims” statements suggesting that a product effects such an “abnormality” of the body. 63 Fed. Reg. at 23627, 23632. Some of the “abnormalities” identified by FDA are part of natural body functions (*e.g.*, “premenstrual syndrome”) and the proposal thus arguably extended beyond the legitimate bounds of “disease” claims. For example, the proposal seemed to prohibit such a claim as “dietary supplement for the discomforts of the premenstrual woman,” a claim that included no express or implied reference to disease. 63 Fed. Reg. at 23627. By contrast, the final rule has been amended to state 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.” 65 Fed. Reg. at 1050. Accordingly, mild conditions commonly associated with particular stages of life or normal physiological processes will not be considered diseases. FDA normally will consider conditions associated with a stage of life or a normal physiological process to be common if they occur in more than one-half of those experiencing that stage or process. 65 Fed. Reg. at 1020. Based on these criteria, FDA reclassified the claim, “For hot flashes,” which had been designated as a disease claim in the proposal as a permissible structure/function claim in the final rule. 65 Fed. Reg. at 1019-20.

Examples of disease claims:

“For decreased sexual function.”

63 Fed. Reg. at 23627.

“Toxemia of pregnancy.”

“Hyperemesis gravidarum.”

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“Acute psychosis of pregnancy.”

“Osteoporosis.”

“Alzheimer’s disease, and other senile dementias.”

“Glaucoma.”

“Arteriosclerotic diseases of coronary, cerebral or peripheral blood vessels.”

“Cystic acne.”

“Severe depression associated with the menstrual cycle.”

65 Fed. Reg. at 1020.

Permitted S/F claims:

“For men over 50 years old.”

“To meet nutritional needs during pregnancy.”

63 Fed. Reg. at 23627.

“Morning sickness associated with pregnancy.”

“Leg edema associated with pregnancy.”

“Mild mood changes, cramps, and edema associated with the menstrual cycle.”

“Hot flashes.”

“Wrinkles.”

“Other signs of aging on the skin, *e.g.*, liver spots, spider veins.”

“Presbyopia (inability to change focus from near to far and vice versa) associated with aging.”

“Mild memory problems associated with aging.”

“Hair loss associated with aging.”

“Noncystic acne.”

“Supports a normal, healthy attitude during PMS.”

“Supportive for menopausal women.”

65 Fed. Reg. at 1020-21.

d. Prohibits claims suggesting that a product has an effect on disease through the name of the product. (21 C.F.R. § 101.93(g)(2)(iv)(A)).

The proposal and the final rule both would prohibit product names suggesting that a dietary supplement has an effect on disease. 63 Fed. Reg. at 23632, 65 Fed. Reg. at 1021. FDA’s recognition of “Cardiohealth” and “Heart Tabs” as permissible structure/function claims appears to conflict with its established policy on health claims. 63 Fed. Reg. at 23627. Section 101.14(a) defines “health claim,” including for dietary supplements, to include “express and implied claims” suggesting that “a relationship exists between . . . a substance in the food and a disease or health-related condition.” The rule specifically identifies the word “heart” and even “heart symbols” as potential disease references. 21 C.F.R. § 101.14(a). The current health claim regulation appears to constitute an overbroad reading of the statute (21 U.S.C. § 343(r)(1)(B)). “Heart” claims (including symbols), relating to the maintenance of normal cardiovascular function would appropriately be recognized as structure/function claims.

Examples of disease claims:

“Carpaltum” (Carpal Tunnel Syndrome).

“Raynaudin” (Raynaud’s Phenomenon).

“Hepatacure” (liver problems).

63 Fed. Reg. at 23627.

“CarpalHealth.”

“CircuCure.”

“Soothing Sleep” (insomnia treatment unless the labeling makes clear the product is intended only for occasional sleeplessness).

“HepataCare” and “HepataHealth” (Hepatitis treatment unless the labeling makes clear the product is intended only for general liver health).

65 Fed. Reg. 1022.

Permitted S/F claims:

“Cardiohealth.”

“Heart Tabs” (if the dietary supplement’s 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).

63 Fed. Reg. at 23627. FDA explained its belief that if a dietary supplement were to be called “HeartTabs” and the product name was not qualified by any further claim in the labeling, the product could be considered, under Section 101.14(a)(1), to be intended for treatment or prevention of cardiovascular disease. FDA also stated its belief 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, but allowed that there may be unusual cases in which, in context, the use of a heart symbol does not imply heart disease prevention, consistent with the examples provided in the January 6, 1993, Federal Register document on health claims (58 FR 2486). 65 Fed. Reg. at 1022.

FDA also advised 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. 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 use of the terms “prescription” or “Rx” will be deemed to be 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. *Id.*

- e. **Prohibits claims suggesting that a product has an effect on disease through 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 or claimed use in preventing or treating disease. (21 C.F.R. § 101.93(g)(2)(iv)(B)).**

The proposal would prohibit claims suggesting that a dietary supplement includes an ingredient that has been “regulated primarily” by FDA as a drug, but would exclude ingredients recognized to have established nondrug (*e.g.*, food, dietary supplement) uses. 63 Fed. Reg. at 23627, 23632. For example, psyllium is recognized for both OTC drug and food use. Reference to a psyllium ingredient would not be prohibited.

The agency states that this provision is not intended to interpret the Section 201(ff)(3)(A) definition of “dietary supplement,” which authorizes the use of certain drug ingredients in dietary supplements. 63 Fed. Reg. at 23627.

Examples of disease claims:

“Aspirin.”

“Digoxin.”

“Laetrile.”

63 Fed. Reg. at 23627.

To avoid a conflict between this provision and Section 201(ff)(3) of the FD&C Act in a situation where the ingredient was marketed as a food first, FDA has revised Section 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. 65 Fed. Reg. at 1023.

- f. **Prohibits claims suggesting that a product has an effect on disease through a citation of a publication or reference, if the citation refers to a disease use, and 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. (21 C.F.R. § 101.93(g)(iv)(C)).**

Possible example of disease claim:

(For Vitamin E Product) “Serial Coronary Angiographic Evidence that Antioxidant Vitamin Intake Reduces Progression of Coronary Artery Atherosclerosis.”

63 Fed. Reg. at 23627, 23632.

FDA has modified Section 101.93(g)(2)(iv)(C) to narrow the circumstances under which citation to a scientific reference will be considered a disease claim. Specifically, Section 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, only 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. Thus, using the 1997 example, if the reference was part of a list contained in supplementary literature, and was used to support Vitamin E’s recognized antioxidant capability, it might well not be a “disease claim.” 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. 65 Fed. Reg. at 1024, 1025.

- g. Prohibits claims suggesting that a product has an effect on disease through the use of the term “disease” or “diseased,” except in general statements about disease prevention that do not refer explicitly or implicitly to a specific disease or class of diseases or to a specific product or ingredient. (21 C.F.R. § 101.93(g)(2)(iv)(D)).**

In the proposal, FDA provided neither discussion about nor examples of this provision. 63 Fed. Reg. at 23632. In the preamble to the final rule, however, FDA advised that general statements about health promotion and disease prevention may be acceptable, as long as they do not imply that a specific product can diagnose, mitigate, cure, treat or prevent disease. FDA revised Section 101.93(g)(2)(iv)(D) in the final rule 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.

Example of disease claim:

“Promotes good health and prevents the onset of disease” (refers implicitly to the product).

Permitted S/F claims:

“A good diet promotes good health and prevents the onset of disease.”

“Better dietary and exercise patterns can contribute to disease prevention and better health.”

65 Fed. Reg. at 1025.

- h. Prohibits claims suggesting that a product has an effect on disease through the use of pictures, vignettes, symbols, or other means. (21 C.F.R. § 101.93(g)(2)(iv)(E)).**

Examples of disease claims:

Electrocardiogram tracings.

Pictures of organs that suggest prevention or treatment of a disease state.

63 Fed. Reg. at 23627.

Symbol of the heart (widely recognized as a symbol for disease treatment or prevention).

65 Fed. Reg. at 1026.

Permissible S/F claims:

A picture of a human body.

63 Fed. Reg. at 23627.

A picture of a healthy organ (if in the context of the labeling as a whole, the picture did not imply treatment or prevention of a disease).

65 Fed. Reg. at 1026; some potential leeway is suggested at 1022.

- i. Prohibits claims suggesting that a product belongs to a class of products that is intended to diagnose, mitigate, treat, cure, or prevent a disease. (21 C.F.R. § 101.93(g)(2)(v)).**

The preamble to the proposed rule states that certain product class names are “so strongly associated with the diagnosis, cure, mitigation, treatment or prevention of disease or diseases” that a claim linking the dietary supplement with that class is sufficient to constitute a prohibited disease claim. 63 Fed. Reg. at 23627.

Examples of disease claims:

“antibiotic,” “analgesic,” “antiviral,” “diuretic,” “antimicrobial,” “antiseptic,” “antidepressant,” or “vaccine.”

63 Fed. Reg. at 23627.

Anti-inflammatory.

65 Fed. Reg. at 1026.

Permissible S/F claims:

“energizer,” “rejuvenative,” “revitalizer,” “adaptogen.”

63 Fed. Reg. at 23627.

“appetite suppressant” (unless in the context used, the claim use for obesity as opposed to simple overweight).

“tonic.”

“antispasmodic.”

65 Fed. Reg. at 1026.

In the final rule, FDA also reviewed pain-related claims, smoking claims and OTC drug claims, finding many instances in which claims in these areas were permissible structure/function claims.

Claims regarding pain relief

FDA explained that some minor pain relief claims may be appropriate structure/function claims for dietary supplements. “A claim that a product is intended to treat minor pain, without reference of any other conditions, symptoms, or parts of the body that would imply disease treatment or prevention, would be an appropriate structure/function claims, because minor pain, by itself, can be caused by a variety of conditions, not all of them disease-related.”

Examples of disease claims:

A product with “pain-free” or “pain product” in its name and whose labeling includes claims related to maintenance or support of joints (characteristic symptom of arthritis).

Permissible S/F claim:

A claim regarding pain associated muscle pain following exercise.

65 Fed. Reg. at 1030.

Smoking-related claims

Examples of disease claim:

“To be used as a dietary adjunct in conjunction with your smoking cessation plan.”

Permissible S/F claims:

“Smoking alternative,” “Temporarily reduces your desire to smoke” and “Mimics the oral sensations of cigarette smoke” (if the context does not imply treatment of nicotine addiction, *e.g.*, by suggesting that the product can be used in smoking cessation, or prevention or mitigation of tobacco-related diseases. Such claims would not be disease claims if the context made clear that they were for short-term use in situations where smoke is prohibited or socially unacceptable).

65 Fed. Reg. at 1030.

OTC Monograph claims

Examples of disease claims:

Nighttime sleep-aids: “Helps you fall asleep if you have difficulty falling asleep,” and “Helps to reduce difficulty falling asleep” (unless the context makes clear that the product is only for occasional sleeplessness).

Daytime sedatives: “Nervous tension headache.”

Aphrodisiacs: “Helps restore sexual vigor, potency, and performance,” “Improves performance, staying power, and sexual potency,” and “Builds virility and sexual potency” (unless these claims made clear that they were intended solely for decreased sexual function associated with aging).

Products for relief of symptoms of benign prostatic hypertrophy: “To relieve the symptoms of benign prostatic hypertrophy, *e.g.*, urinary urgency and frequency, excessive urinating at night, and delayed urination.”

Anticholinergics: “Relieve excessive secretions of the nose and eyes” (characteristic symptoms of hay fever).

Products for certain uses: “Nasal decongestant,” (treatment for a characteristic symptom of colds), “expectorant,” (treatment for a characteristic symptom of colds, flu, and bronchitis), and “bronchodilator,” (treatment for bronchospasm, a characteristic symptom of asthma).

Permissible S/F claims:

Antacids: “Relief of heartburn” and “Relief of acid indigestion” (if the labeling makes clear that the claim refers to “occasional” heartburn or acid indigestion).

Antiflatulents: All claims are structure/function claims, including, “Alleviates the symptoms referred to as gas,” “alleviates bloating,” “alleviates pressure,” “alleviates fullness,” and “alleviates stuffed feeling.”

Antiemetics: “For the prevention and treatment of the nausea, vomiting, or dizziness associated with motion.”

Nighttime sleep-aids: “For the relief of occasional sleeplessness.”

“Stimulants” (alertness aids): “Helps restore mental alertness or wakefulness when experiencing fatigue or drowsiness” (should not imply treatment of chronic fatigue syndrome or narcolepsy).

Daytime sedatives: “Occasional simple nervous tension,” “nervousness due to common every day overwork and fatigue,” “a relaxed feeling,” “calming down and relaxing,” “gently soothe away the tension,” “calmative,” “resolving that irritability that ruins your day,” “helps you relax,” “restlessness,” “nervous irritability,” and “when you’re under occasional stress, helps you work relaxed.”

Aphrodisiacs: “Arouses or increases sexual desire and improves sexual performance.”

Products for certain uses: “digestive aid,” “stool softener,” “weight control,” and “menstrual” (if the labeling does not otherwise imply treatment or prevention of a disease).

Products for the treatment and/or prevention of nocturnal leg muscle cramps: “Treatment and/or prevention of nocturnal leg muscle cramps, *i.e.*, a condition of localized pain in the lower extremities usually occurring in middle life and beyond with no regular pattern concerning time or severity,” (Nocturnal leg cramps do not meet the definition of disease).

65 Fed. Reg. at 1031.

The proposed rule had also included the term, “laxative” in the list of class names that would be considered disease claims. FDA decided, however, that claims for relief of “occasional constipation” will not be considered disease claims. The term “laxative” will not be considered a disease claim under the final rule as long as the labeling makes clear that the product is not intended to treat chronic constipation. 65 Fed. Reg. at 1026.

- j. Prohibits claims suggesting that a product is a substitute for a product that is a therapy for a disease, or augments a particular therapy or drug action that is intended to diagnose, mitigate, treat, cure, or prevent a disease or class of diseases. (21 C.F.R. § 101.93(g)(2)(vi), (vii)).**

Claims implying that a dietary supplement has the same effect as a recognized drug or disease therapy, or should be used as an adjunct to such a therapy in the treatment of disease would constitute an impermissible disease claim. 63 Fed. Reg. at 23627, 23632. On its own initiative, FDA modified Section 101.93(g)(2)(vii) in the final rule to limit its applicability to claims for augmentation of drugs or therapies that are intended to diagnose, mitigate, treat, cure, or prevent disease. 65 Fed. Reg. at 1028.

Examples of disease claims:

“Herbal Prozac.”

“Use as part of your diet when taking insulin to help maintain a healthy blood sugar level.”

63 Fed. Reg. at 23627.

Permissible S/F claims:

“Use as part of your weight loss plan.”

“Use as part of your diet to help maintain a healthy blood sugar level.”

65 Fed. Reg. at 1027, 1028.

FDA also opined that the use of synonyms for “augment,” such as “strengthen,” “reduce,” “improve,” “modify,” “inhibit,” “protect,” or “defend,” may be appropriate when the statements do not suggest disease prevention or treatment use, but they will be considered disease claims when their use implies that the dietary supplement augments a particular therapy or drug action or otherwise suggests an effect on disease. 65 Fed. Reg. at 1028.

- k. Prohibits claims suggesting that a product has a role in the body’s response to a disease or to a vector of disease. (21 C.F.R. § 101.93(g)(2)(viii)).**

Claims suggesting that a dietary supplement “augment[s] the body’s own disease-fighting capabilities” such as by playing a role in the body’s specific response to a disease or vector (*e.g.*, kill/neutralize a virus or bacterium) would be prohibited under the proposal. In contrast, general references to an effect on a body system that has several functions, only one of which is resistance to diseases, would not be a disease claim. 63 Fed. Reg. at 23627, 23632. These conclusions were reiterated in the preamble to final rule. 65 Fed. Reg. at 1028-29.

Examples of disease claims:

“Supports the body’s antiviral capabilities.”

“Supports the body’s ability to resist infection.”

Permissible S/F claim:

“Supports the immune system.”

I. Prohibits claims suggesting that a product treats, prevents, or mitigates adverse events associated with a therapy for a disease, if the adverse events constitute diseases. (21 C.F.R. § 101.93(g)(2)(ix)).

Claims indicating that a dietary supplement is “intended to counter adverse events resulting from medical intervention” would be prohibited as disease claims under the proposal. 63 Fed. Reg. 23628, 23632. Claims making no reference to a course of therapy would not constitute a disease claim in this context.

Example of disease claims:

“Reduces nausea associated with chemotherapy.”

“Helps avoid diarrhea associated with antibiotic use.”

“To aid patients with reduced or compromised immune function, such as patients undergoing chemotherapy.”

63 Fed. Reg. 23628.

“Helps individuals using antibiotics to maintain normal intestinal flora.”

65 Fed. Reg. at 1029.

Permissible S/F claim:

“Helps maintain healthy intestinal flora.”

65 Fed. Reg. at 1029.

Because FDA revised the definition of disease in the final rule, the agency revised Section 101.93(g)(2)(ix) to state that claims about adverse events are disease claims only “if the adverse events constitute diseases.” 65 Fed. Reg. at 1029. FDA explained that a claim that a product is useful because it counterbalances the effects of a drug in depleting a nutrient or interfering with the metabolism of a nutrient would be acceptable as a structure/function statement. If, however, the claim expressly or impliedly suggests that the supplement is intended to augment a specific drug, drug action, or therapy for a disease, or serve the same purpose as a specific drug or therapy for a disease, then FDA may consider the statement to be a disease claim. *Id.* This suggests that a claim to “restore normal intestinal flora following antibiotic treatment” arguably would be a permissible claim.

m. Prohibits claims otherwise suggesting that a product has an effect on a disease or diseases. (21 C.F.R. § 101.93(g)(2)(x)).

This catch-all provision was included in the proposed regulation without discussion. 63 Fed. Reg. at 23628, 23632. In the preamble to the final rule, FDA explained its belief that this provision is necessary to allow for implied disease claims that may not fit into the nine enumerated criteria, and that Section 101.93(g)(2)(x) recognizes the possibility that other types of statements may also imply disease treatment or prevention. FDA further stated that it did not believe that the provision will cause the agency to classify any structure/function statement as a disease claim, and that the agency would have to show that the statement implied an effect on disease in order to regulate a statement as a disease claim under this provision.

Permissible S/F claims:

“Provides nutritional support for women during premenstruation by promoting proper fluid balances and breast health.”

“Ginger supports the cardiovascular system by inhibiting leukotriene and thromboxane synthesis, substances associated with platelet aggregation.”

65 Fed. Reg. at 1030.

n. Other specific claims not mentioned in the proposed rule.

Example of disease claim:

“Dietary support during the cold and flu season” and “Promotes general well-being during the cold and flu season.” (imply that the product will prevent colds and flu or will mitigate the symptoms of those diseases).

Permissible S/F claims:

“Boosts stamina.”

“Helps increase muscle size.” (FDA notes, however, that a claim to increase muscle size implies an effect that may subject the product regulation as an anabolic steroid under the Controlled Substances Act (see 21 U.S.C. 802(41)).

“Helps enhance muscle tone.”

65 Fed. Reg. at 1030.

E. Dietary Supplements That Are Also Foods

At the time of the passage of the Dietary Supplement Health and Education Act of 1994 (DSHEA), the question was raised as to whether traditional structure/function claims for RDI nutrients, such as “calcium helps build strong bones,” were subject to the requirements of Section 403(r)(6) of the Act, requiring notification to FDA of the claim and the use of the statutory disclaimer. It was our analysis, generally adopted by industry, that Section 403(r)(6) compliance was not required, because such supplements were “food” independent of the new definition of “dietary supplement,” and Section 403(r)(6) provided a safe harbor for those dietary supplement products that would not have qualified as “food” prior to the passage of DSHEA. In 1997, in the preamble to the final dietary supplement labeling regulations, FDA acknowledged the correctness of this interpretation.

In the preamble to the final structure/function regulation, FDA reversed itself and now takes the position that dietary supplements are precluded from being “food” for purposes of Section 201(g)(1)(C) of the FD&C Act, so any structure/function claim must comply with Section 403(r)(6) to avoid drug classification. 65 Fed. Reg. at 1033. FDA’s legal analysis fails to take into account the fact that definitions under the Act are generally not mutually exclusive, so an item can be both an “article” under Section 201(f) (the food definition) and a “product” under Section 201(ff) (the dietary supplement definition) and so gain the benefit of the “food” exclusion under Section 201(g)(1)(C) as a “food” even if not as a “dietary supplement.”

This reversal is important because FDA takes the position that all new products must make a 403(r)(6) submission for RDI-nutrient claims and use the statutory disclaimer, and all existing products that do not fall under a “small business” exemption must be relabeled and 403(r)(6) submissions made within 12 months. This action also unlevels the playing field between traditional foods and dietary supplements: “builds strong bones” claims are acceptable for calcium fortified orange juice and cereals, but would require the statutory disclaimer on multivitamin-mineral products.

F. Effective Date

The final rule will become effective on February 7, 2000. The proposal had indicated that a phase-in process would apply to products already “on the market” on the date the final rule is published, and for which a Section 403(r)(6) premarket notification was filed with FDA. The phase-in would not have applied when the agency had objected to claims contained in a premarket notification (*e.g.*, issued a “courtesy” letter). The final rule did not incorporate the phase-in period, however, and provided instead:

All manufacturers will have 11 months after the effective date to bring claims into compliance. “Small businesses,” that is, any business having total annual revenues of less than \$20 million, will have a 17-month period after the effective date to bring claims into compliance. FDA does not intend to take enforcement action against firms who have relied on the agency’s September 1997 preamble statements to make a structure/function claim for a dietary supplement under Section 201(g)(1)(C) of the Act for the same periods set forth above. By those dates, the

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firms either must remove the claim or comply with the requirements of Section 403(r)(6) of the Act and 21 C.F.R. § 101.93, by notifying FDA of the claim and relabeling to add the required disclaimer. Any firm that makes a new structure/function claim in the labeling of a dietary supplement after the effective date of the new rule must comply with Section 403(r)(6) of the Act and 21 C.F.R. § 101.93.

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