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Part IV

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 101

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. 98N-0044]

RIN 0910-AB97

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing final
regulations defining the types of statements that can be made
concerning the effect of a dietary supplement on the structure or
function of the body. The regulations also establish criteria for

determining when a statement about a dietary supplement is a claim to diagnose, cure, mitigate, treat, or prevent disease. This action is intended to clarify the types of claims that may be made for dietary supplements without prior review by FDA and the types of claims that require prior authorization as health claims or prior approval as drug claims.

DATES: The final rule will become effective February 7, 2000.

FOR FURTHER INFORMATION CONTACT: Ann Marlin Witt, Office of Policy, Planning, and Legislation (HF-11), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-0084.

SUPPLEMENTARY INFORMATION:

I. Introduction

In the Federal Register of April 29, 1998 (63 FR 23624), FDA proposed regulations to identify the types of statements that may be made without prior FDA review about the effects of dietary supplements on the structure or function of the body ('`structure/function claims''), and to distinguish these claims from claims that a product diagnoses, treats, prevents, cures, or mitigates disease (disease claims). FDA received over 235,000 submissions in response to the proposed rule. Many of these were form letters, but over 22,000 were individual letters from the dietary supplement industry, trade associations, health professional groups, and consumers. Almost all the comments from the dietary supplement industry and from individuals, which made up the vast majority of the comments, objected to all or part of the proposed rule, arguing that it inappropriately restricted the structure/function claims that could be made for dietary supplements. Most of the comments from health professional groups and groups devoted to particular diseases supported the proposed rule, or believed it did not go far enough in limiting structure/function claims for dietary supplements.

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

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

A. Highlights of the Final Rule

Like the proposed rule, the final rule contains criteria to determine when a labeling statement made about a dietary supplement

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

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

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

Third, FDA has revised the criterion that relates to the use in labeling of the titles of publications that refer to diseases. In response to comments objecting that, as proposed, this criterion would hamper manufacturers from providing consumers with information substantiating their claims, FDA has revised this criterion. Under the revised criterion, the use in labeling of a publication title that refers to a disease will be considered a disease claim only if, in context, it implies that the product may be used to diagnose, treat, mitigate, cure, or prevent disease. Highlighting, bolding, using large type size, or prominent placement of a citation that refers to a disease use in the title could suggest that the product has an effect on disease. Placing a citation to a scientific reference that refers to a disease in the title on the

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immediate product label or packaging will be considered a disease claim for that product. The agency will also consider whether the cited article provides legitimate support for the express structure/function statement made for that dietary supplement. Enhancing the bibliography with citations to scientific references that refer to a disease in the title and that have no reasonable relation to the statement made will be considered a disease claim. Similarly, the agency will consider whether citations are to bona fide research.

B. Background

DSHEA created a new regime for the regulation of dietary supplements. These products were previously regulated either as foods

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

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

Although a dietary supplement manufacturer who wishes to make a statement permitted under section 403(r)(6) of the act need not obtain prior review of the statement, the manufacturer must possess substantiation that the statement is truthful and not misleading, and must include in the statement the following disclaimer: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." DSHEA also requires the manufacturer of a dietary supplement bearing a statement under section 403(r)(6) of the act to notify FDA, no later than 30 days after the first marketing of the dietary supplement with the statement, that such a statement is being made for the product. Regulations implementing these requirements were published in the Federal Register of September 23, 1997, and are codified at Sec. 101.93 (21 CFR 101.93) (62 FR 49883 at 49886, September 23, 1997).

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

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

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

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disease may increase the risk of adverse reactions due to the interaction of the dietary supplement with other compounds a consumer is taking for that disease or for other conditions, e.g., prescription medications.

This final rule is intended to apply only to structure/function claims and disease claims within the meaning of section 403(r)(6) of the act. DSHEA, generally, and section 403(r)(6) of the act, specifically, apply only to dietary supplements for human consumption and were enacted to provide a unique regulatory regime for these products. Thus, this rule is neither intended to apply to products other than dietary supplements for human consumption nor to interpret other provisions of the act.

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

product to be misbranded under section 403(a)(1) of the act.

C. The Proposed Rule

The proposed rule defined criteria for determining when a statement about a dietary supplement is a claim to diagnose, cure, mitigate, treat, or prevent disease ("disease claim"), and thus requires prior approval as a drug or prior authorization as a health claim. The proposed rule included a definition of "disease," which was to replace a definition of "disease or health-related condition" issued for implementation of the health claims regulations, and 10 criteria for identifying express or implied disease claims. FDA proposed to treat a statement about a dietary supplement as a disease claim if the statement claimed, explicitly or implicitly, that the product: (1) Has an effect on a specific disease or class of diseases; (2) has an effect, using scientific or lay terminology, on one or more signs or symptoms that are recognizable to health care professionals or consumers as being characteristic of a specific disease or of a number of different specific diseases; (3) has an effect on a consequence of a natural state that presents a characteristic set of signs or symptoms recognizable to health care professionals or consumers as constituting an abnormality of the body; (4) has an effect on disease through one or more of the following factors: (a) The name of the product; (b) a statement about the formulation of the product, including a claim that the product contains an ingredient that has been regulated by FDA as a drug and is well known to consumers for its use in preventing or treating a disease; (c) citation of a publication or reference, if the citation refers to a disease use; (d) use of the term "disease" or "diseased;" or (e) use of pictures, vignettes, symbols, or other means; (5) belongs to a class of products that is intended to diagnose, mitigate, treat, cure, or prevent a disease; (6) is a substitute for a product that is a therapy for a disease; (7) augments a particular therapy or drug action; (8) has a role in the body's response to a disease or to a vector of disease; (9) treats, prevents, or mitigates adverse events associated with a therapy for a disease and manifested by a characteristic set of signs or symptoms; or (10) otherwise suggests an effect on a disease or diseases.

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

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