Functional foods: the Food and Drug Administration perspective

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ABSTRACT Because the Federal Food, Drug, and Cosmetic Act (FFDCA) does not provide a statutory definition of functional foods, the Food and Drug Administration has no authority to establish a formal regulatory category for such foods. The primary determinant of the regulatory status of a food is its intended use, which is determined largely by the label and labeling information accompanying the product. This information includes nutrient information, nutrient content claims, and various types of health claims. In marketing these foods, manufacturers may come under one of several existing regulatory options. The first decision manufacturers will make that will help determine their product’s regulatory status is whether the product is a food or a drug. Thus, manufacturers and retailers have a range of legal and regulatory categories in which their products may be classified. This article describes the definitions provided in the FFDCA for a drug and a food, the safety and labeling requirements of various food categories, and types of possible claims for dietary supplements. Am J Clin Nutr 2000;71(suppl):1735S–8S.

KEY WORDS Functional food, Food and Drug Administration, FDA, dietary supplement, medical food, product labeling

INTRODUCTION

The Federal Food, Drug, and Cosmetic Act (FFDCA; 1), as amended, does not provide a statutory definition of functional foods; thus, the Food and Drug Administration (FDA) has no authority to establish a formal regulatory category for such foods. In marketing such products, manufacturers may come under one of several existing regulatory options. The first decision manufacturers will make that will help determine their product’s regulatory status is whether the product is a food or a drug. This article discusses the definitions of a drug and a food set forth by the FFDCA, which provides the regulatory authority and milieu for these products. The primary determinant, however, of the regulatory status of a food or a drug is its intended use, which is determined in large part by the label and the labeling information accompanying the product. If a product is determined to be a food, it can be regulated as a food in conventional form (includes foods for special dietary use), as a dietary supplement, as a medical food, or as an infant formula. With the absence of specific regulatory categories for functional foods, their regulation is accomplished through existing food and drug regulations.

DEFINITIONS OF DRUG AND FOOD

A drug is defined in part as “…an article intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease…” (§ 201(g)(1)(B) of the FFDCA [Title 21 United States Code (21 USC) § 321(g)(1)(B)]). Additionally, a product may be subject to regulation as a drug if it makes a claim that it is an article (other than food) intended to affect the structure or any function of the body (§ 201(g)(1)(C) of the FFDCA [21 USC § 321(g)(1)(C)]). This subparagraph provides an exception for foods regarding claims about structure or function. Foods are defined in the FFDCA as articles used for food or drink or components of any such article (§ 201(f) of the FFDCA [21 USC § 321(f)]).

Through case law, foods have also been defined as substances that provide taste, aroma, or nutritive value (2). As discussed in the preamble of a recent final rule, foods can bear structure or function claims if the claim derives from their nutritive value (3). However, if a claim describes a structure or function effect that is not related to nutritive value, the claim can be made only if the product meets requirements for marketing as a dietary supplement or as a drug.

The exception for foods in the drug definition of the FFDCA [section 201(g)(1)(C) of the FFDCA] is illustrated in a discussion that was part of a final rule on food labeling published in the Federal Register in 1997: “The claim that cranberry juice cocktail prevents the recurrence of urinary tract infections is a claim that brings the product within the ‘drug’ definition whether it appears on a conventional food or on a dietary supplement because it is a claim that the product will prevent disease (section 201(g)(1)(B) of the FFDCA). However, a claim that cranberry products help to maintain urinary tract health may be permissible on both cranberry products in conventional food form and dietary supplement form if it is truthful, not misleading, and derives from the nutritional value of cranberries. If the effect derives from the nutritive value of cranberries, the claim would describe an effect of a food on the structure or function of the body and thus fall under one exception to the definition for the term ‘drug’ found in 201(g)(1)(C) of the FFDCA. The claim is

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not a health claim because no disease is mentioned explicitly or implicitly (see section 403(r)(1)(B) of the FFDCA). Only if the claimed benefit did not derive from the nutritional value of cranberries would it be true that the claim could appear on a dietary supplement but not a conventional food. This result is dictated by section 403(r)(6) of the DSHEA [sic] (3.

Dietary supplement products provide the other exception for which a product would not be considered a drug if it made a structure or function claim on the label or in labeling. The Dietary Supplement Health and Education Act (DSHEA) of 1994 (4) provides for claims on supplement labels that describe the effect of a product on the structure or function of the body if they are not also disease claims (see later discussion on statements permitted by the DSHEA, which amended the FFDCA). If the claim is to diagnose, cure, mitigate, treat, or prevent a disease, the product would be considered a drug.

CONVENTIONAL FOODS

The FDA recognizes different categories of foods, one of which is foods in conventional food form, the most prevalent foods in the general food supply. Within the conventional food category is a category called foods for special dietary use (FSDU). The term special dietary use as applied to food means particular (as distinguished from general) uses of food that supply a dietary need that exists by reason of a physical, physiologic, pathologic, or other condition including, but not limited to, diseases, convalescence, pregnancy, lactation, allergen hypersensitivity, underweight, or overweight [Title 21 Code of Federal Regulations (21 CFR) § 105.3]. Both conventional foods and FSDU are subject to the labeling requirements of the Nutrition Labeling and Education Act of 1990 (NLEA; 5). The safety requirements for these products are the general food safety requirements. The only substances that may be used in foods are food ingredients whose use is safe and suitable under the applicable food safety provisions of the FFDCA; that is, the substance is generally recognized as safe (GRAS) for such use, is used in accordance with the FDA's food additive regulations, or is authorized by a prior sanction [sections 201, 401, 402, 408, and 409 of the FFDCA (21 USC §§321, 341, 342, 346a, and 348)]. In addition, the FFDCA requires that the food be a safe, clean, and wholesome product and that its labeling be truthful and not misleading [§ 402 and 403 of the FFDCA (21 USC § 342 and 343)].

MEDICAL FOODS

Another category of foods, defined in the Orphan Drug Amendments of 1988 (6), are medical foods (section 5(b)(3) of the Orphan Drug Act [21 USC 360ee(b)(3)]), which are foods formulated to be consumed or administered enterally under the supervision of a physician and are intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements based on recognized scientific principles are established by medical evaluation. Medical foods are distinguished from FSDU by being targeted for distinctive nutritional requirements of disease conditions and by the intention for use under a physician’s supervision (the definition of an FSDU does not include a requirement for such supervision). Medical foods are exempted from the labeling requirements of the NLEA (403(q)(5)(A)(iv) of the FFDCA (21 USC 343(q)(5)(A)(iv))). In an advance notice of proposed rulemaking in the Federal Register of November 29, 1996 (7), the FDA announced its intent to propose rulemaking in this still-evolving area.

DIETARY SUPPLEMENTS

In the DSHEA, dietary supplements are defined as vitamins, minerals, herbs or other botanicals, amino acids, and other dietary substances intended to supplement the diet by increasing the total dietary intake, or as any concentrate, metabolite, constituent, extract, or combination of these ingredients (§ 201(ff) of the FFDCA [21 USC § 321 (ff)]). Section 201(ff) of the FFDCA further specifies the term dietary supplement to mean products intended for ingestion in a form described in section 411(c)(1)(B)(i) of the FFDCA [21 USC § 350(c)(1)(B)(i)] (ie, tablet, capsule, powder, softgel, gelcap, and liquid) that are not represented as a conventional food or as the sole item of a meal or of the diet and that are labeled as dietary supplements. In addition, according to the law, dietary supplements can include an article previously approved as a drug, antibiotic, or biologic, provided the article was first marketed as a dietary supplement (§ 201(ff)(3)(A) of the FFDCA [21 USC § 321 (ff)(3)(A)]). Under section 413 of the FFDCA [21 USC § 350b], a manufacturer of a dietary supplement that is or that contains a new dietary ingredient (ie, not marketed in the United States before October 15, 1994) must submit information to the FDA 75 d before marketing that includes any citation to published articles substantiating the manufacturer’s conclusions that use of the dietary supplement will reasonably be expected to be safe. This submission is a notification (8), not a premarket authorization as would be the case for a food additive (21 CFR § 190.6).

Under the DSHEA, a dietary supplement is adulterated in several ways (§ 402(f)(1) of the FFDCA [21 USC § 342(f)(1)]). First, it is considered adulterated if it presents a significant or unreasonable risk of illness or injury under the labeled conditions of use or, if conditions of use are not indicated, under usual conditions of use. Second, it is adulterated if it poses an imminent hazard to public safety or health. The Secretary of the Department of Health and Human Services (through the FDA) can make this determination and take appropriate action. Third, it is adulterated if it contains a poisonous or deleterious substance that may render the product injurious. A dietary supplement that contains a new dietary ingredient may also be adulterated unless the ingredient has a history of use as a food in a form that is not chemically altered or the manufacturer submits evidence of safety to the FDA 75 d before marketing the product.

LABELING OF FOODS

Foods may be classified into a range of legal and regulatory categories, which provides a great deal of flexibility for manufacturers and retailers who wish to develop functional foods. As stated above, the primary determinants of the regulatory status of a food is its intended use, which is largely determined by the label and by labeling information accompanying the product. The labeling provisions covered under the NLEA, implemented by FDA regulations that are codified in the Code of Federal Regulations, specify the labeling of the nutrient composition or nutrient facts of a food product (21 CFR § 101.9). Several nutrients (eg, vitamins A and C) must be declared when they are in the product. Declaration of the remaining nutrients
on the label is optional. Declarations are amount per serving and as a percentage of the daily value. In the September 23, 1997, Federal Register (9), the FDA published final rules governing the nutrition labeling of dietary supplements; these regulations became effective March 23, 1999.

Other mandatory information for food labels includes a statement of identity (common or usual name of the product) (21 CFR § 101.3); an accurate statement of the net quantity of contents (21 CFR § 101.105); the name and place of the business, manufacturer, packer, or distributor (21 CFR § 101.5); and, if the food was fabricated from ≥2 ingredients, a complete list of those ingredients, in descending order of predominance, by their common or usual names (21 CFR § 101.4). All labeling information that the FFDCA requires on a food label must appear in English. In addition, if a label bears any representation in a foreign language, all mandatory label information must be repeated in that language (21 CFR § 101.15). These regulations also apply to dietary supplements.

Under the NLEA, nutrient content claims are also permitted, provided they are covered by and consistent with an authorizing regulation (see 21 CFR § 101.13 for general principles). Such claims expressly or implicitly characterize the amount of a nutrient of the type required in nutrition labeling under § 101.9 (21 CFR 101.9). For example, a high-potency nutrient content claim was finalized in the September 23, 1997, Federal Register (10). This regulation authorizes the use of the term high potency on the label or in the labeling of foods to describe individual vitamins or minerals that are present at ≥100% of the recommended daily intake.

Health claims can also be made on food labels. Under the NLEA, these claims, once authorized by regulation, may be used on any food and dietary supplement that meets the qualifying criteria for amount of nutrient per serving and other requirements (21 CFR § 101.14). A petition process is available for seeking FDA authorization for new claims (21 CFR § 101.70). New provisions for making both health and nutrient content claims were included in the Food and Drug Administration Modernization Act of 1997 (11; FDAMA) (specifically, sections 303 and 304, which amend, respectively, sections 403(r)(3) and 403(r)(2) [21 USC 343(r)(3) and 21 USC 343(r)(2)]) of the Food, Drug, and Cosmetic Act. The FDAMA amended the FFDCA to permit distributors and manufacturers to use health claims in food labeling if such claims are based on current, published, authoritative statements from certain federal scientific bodies or from the National Academy of Sciences. In this regard, the FDA recently announced the availability of a document entitled Guidance for Industry: Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body (12), obtainable by written request to the FDA or from the Center for Food Safety and Applied Nutrition World Wide Web site (13). The FDAMA does not include a provision that dietary supplements may bear health claims in their labeling that are based on authoritative statements, but the FDA intends to propose that health claims based on such statements be permitted for dietary supplements.

Health claim messages must contain reference to both a food substance and to outcomes related to disease or health. Claims that reference only the substance—for example, the dietary guidelines to choose a diet with plenty of grain products, vegetables, and fruit—are not covered under the health claims provisions but would be subject to regulation under the truthful and nonmisleading provisions of the FFDCA (21 USC 343). A food is disqualified from bearing a health claim if it is high in fat, saturated fat, cholesterol, or sodium, and health claims are permitted only on foods that contain ≥10% of the reference daily intake or the daily reference value for vitamin A, vitamin C, iron, calcium, protein, or fiber per reference amount customarily consumed before any nutrient addition [21 CFR 101.14(e)(6)]. This rule, sometimes referred to as the “jelly bean” rule, does not apply to health claims on dietary supplements.

The science standard to support a claim between a food substance and disease or health must be based on the totality of publicly available scientific evidence (ie, this evidence cannot be chosen selectively to support a particular viewpoint and there must be significant scientific agreement among qualified experts that the relation is valid). The science standard for health claims was specified by law for foods in conventional food form (§ 403(r)(3)(B) of the FFDCA [21 USC § 343(r)(3)(B)]), and the FDA uses the same standard for health claims for dietary supplements [21 CFR § 101.14 (a)].

On February 18, 1998, the FDA authorized its most recent health claim, which pertains to soluble fiber from psyllium seed husks (14). In this and a previous rule on β-glucan soluble fiber from whole oats (15), the agency concluded that each of these sources of soluble fiber, when included as part of a diet low in saturated fat and cholesterol, may reduce the risk of coronary heart disease by lowering blood cholesterol concentrations. The agency concluded in these documents that there was significant scientific agreement among qualified experts to support the relation between these sources of soluble fiber and reduced risk for coronary heart disease. The consumer studies branch of the FDA’s Center for Food Safety and Applied Nutrition has performed research on the consumer impact of health claims (16).

Under the DSHEA, there is a provision for use of nutritional support statements on dietary supplements (section 403(r)(6) of the FFDCA [21 USC § 343(r)(6) and 21 CFR § 101.93]). Certain of these statements or claims are sometimes referred to as structure or function claims. These claims are of 4 different types:

1) They claim a benefit related to classic nutrient deficiency diseases but must disclose the prevalence of such disease in the United States.
2) They describe the role of a nutrient or dietary ingredient intended to affect structure or function in humans.
3) They characterize the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function.
4) They describe the general well-being from consumption of a nutrient or dietary ingredient.

For a dietary supplement to bear 1 of the 4 statement types on its label or in its labeling, the DSHEA requires that a manufacturer have evidence that the claim is truthful and not misleading. The DSHEA requires manufacturers to provide notification to the FDA within 30 d after marketing a product that it is making such a claim, but it does not require them to provide the FDA with the data that substantiate the claim (17; 21 CFR § 101.93). Use of these claims on dietary supplement products must be accompanied by a disclaimer; the disclaimer that is authorized through the DSHEA is the following: “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent disease.”
SUMMARY

I described the statutory definition for foods and drugs and provided a brief outline of the safety and labeling requirements for various food categories. Foods and drugs are regulated in part by their intended use, which is determined by label claims, the direction of use on the product label, and accompanying label information. The FDA believes that available regulatory categories of foods provide flexibility and opportunity in regulating the so-called functional foods. When deciding the category in which they wish a product to fall, manufacturers should be mindful of the safety requirements, the various labeling requirements, and the appropriate petition or notification procedures for ingredients in their products (e.g., food additive petitions for foods and new dietary ingredient notifications for dietary supplements).

REFERENCES