CHAPTER 10

Regulatory Considerations for Dietary Supplements and Functional cGMPs

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INTRODUCTION

Current and proposed regulations to the dietary supplements industry are changing the way that companies approach manufacturing and labeling of products. Understanding the regulations and avoiding pitfalls will be a major focus of companies of all sizes. The size of the company determines how fast the proposed GMPs are implemented within a company. No matter what size the company may be, all manufactures need to be compliant as of June 2010.

The cGMP regulations proposed by the FDA are designed to bring the minimum manufacturing and labeling standards from the pharmaceutical industry into the dietary supplements industry. These standards establish basic standards of operation at the manufacturing level to ensure that finished dietary supplement products meet established specifications for identity, purity, strength, and composition and that they limit possible contamination. Manufacturers must adhere to standards regarding production and process controls, manufacturing and testing equipment, quality-control approvals, detailed specifications, master manufacturing records, and batch production records. Procedures must be written and followed to investigate and document product complaints and returns. Manufacturers must include company information on the label to allow consumers to report problems or adverse reactions. All of these regulations move the dietary supplement manufacturers in line with the consumers’ expectations of quality and reliability associated with and expected of pharmaceutical manufacturers.

DEFINITION OF A DIETARY SUPPLEMENT

Dietary supplements are defined, in part, as products (other than tobacco) intended to supplement the diet that bear or contain one or more of the following dietary ingredients: (1) a vitamin, (2) a mineral, (3) an herb or other botanical, (4) an amino acid, (5) a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or (6) a concentrate, metabolite, constituent, extract, or a combination of any ingredient mentioned above.

Furthermore, dietary supplements are products intended for ingestion, are not represented for use as a conventional food or as a sole item of a meal or the diet, and are labeled as dietary supplements. The complete statutory definition is found in § 201(ff) of the Federal Food, Drug, and Cosmetic Act (The Act) (21 U.S.C. 321).

A dietary supplement must be identified by use of the term “dietary supplement” as part of the statement of identity, except that the word “dietary” may be deleted and replaced with the name of the dietary ingredient(s) in the product (e.g., calcium supplement) or an appropriately descriptive term indicating the type of dietary ingredient(s) in the dietary supplement product (e.g., herbal supplement with vitamins) (21 CFR 101.3(g)).

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LABELING REQUIREMENTS FOR DIETARY SUPPLEMENTS

The following five statements are required for dietary supplements:

1. Statement of identity (name of the dietary supplement)
2. Net quantity of contents statement (amount of the dietary supplement)
3. Nutrition labeling
4. Ingredient list
5. Name and place of business of the manufacturer, packer, or distributor. (21 CFR 101.3(a), 21 CFR 101.105(a), 21 CFR 101.36, 21 CFR 101.4(a)(1), and 21 CFR 101.5)

All required label statements must be placed on either the front label panel (the principal display panel) or the information panel (usually the label panel immediately to the right of the principal display panel, as seen by the consumer when facing the product), unless otherwise specified by regulation (i.e., exemptions) (21 CFR 101.2(b) and (d), 21 CFR 101.9(j)(13) and (j)(17), 21 CFR 101.36(g), (i)(2) and (i)(5)).

The statement of identity and the net quantity of contents statement must be placed on the principal display panel. When packages bear alternate principal display panels, this information must be placed on each alternate principal display panel (21 CFR 101.1, 21 CFR 101.3(a) and 21 CFR 101.105(a)).

The principal display panel of the label is the portion of the package that is most likely to be seen by the consumer at the time of display for retail purchase. Many containers are designed with two or more different surfaces that are suitable for use as the principal display panel. These are alternate principal display panels (21 CFR 101.1).

The “Supplement Facts” panel, the ingredient list, and the name and place of business of the manufacturer, packer, or distributor must be included on the information panel; if such information does not appear on the principal display panel, except that if space is insufficient, then the special provisions on the Supplement Facts panel in 21 CFR 101.36(i)(2)(iii) and (i)(5) may be used (21 CFR 101.2(b) and (d), 101.36(i)(2)(iii) and (i)(5), 101.5, 101.9(j)(13)(i)(A) and (j)(17)).

The information panel is located immediately to the right of the principal display panel as the product is displayed to the consumer. If this panel is not usable, because of package design and construction (e.g., folded flaps), then the panel immediately contiguous and to the right of this part may be used for the information panel. The information panel may be any adjacent panel when the top of a container is the principal display panel (21 CFR 101.2(a)).

The street address must be listed if it is not listed in a current city directory or telephone book, including the city or town, the state, and zip code. The address of the principal place of business may be used in lieu of the actual address (21 CFR 101.5).

Intervening material, which is defined as label information that is not required (e.g., universal product bar code), may not be placed between label information that is required on the information panel (21 CFR 101.2(e)).
Unless excepted by law, the Tariff Act requires that every article of foreign origin (or its container) imported into the United States conspicuously indicate the English name of the country of origin of the article (§ 304, Tariff Act of 1930, as amended (19 U.S.C. 304)).

Expiration dating does not need to be included on the label of a dietary supplement. However, a firm may include this information if it is supported by valid data demonstrating that it is not false or misleading.

NUTRITIONAL LABELING FOR A DIETARY SUPPLEMENT

The nutrition label for a dietary supplement is called a Supplement Facts panel (see example labels below) (21 CFR 101.36(b)(1)(i)).

The major differences between Supplement Facts panel and “Nutrition Facts” panel are as follows:

1. A company must list dietary ingredients without reference daily intakes (RDIs) or daily reference value (DRVs) in the Supplement Facts panel for dietary supplements. A company is not permitted to list these ingredients in the Nutrition Facts panel for foods.
2. A company may list the source of a dietary ingredient in the Supplement Facts panel for dietary supplements. A company cannot list the source of a dietary ingredient in the Nutrition Facts panel for foods.
3. A company is not required to list the source of a dietary ingredient in the ingredient statement for dietary supplements if it is listed in the Supplement Facts panel.
4. A company must include the part of the plant from which a dietary ingredient is derived in the Supplement Facts panel for dietary supplements. A company is not permitted to list the part of a plant in the Nutrition Facts panel for foods.
5. A company is not permitted to list “zero” amounts of nutrients in the Supplement Facts panel for dietary supplements. A company is required to list zero amounts of nutrients in the Nutrition Facts panel for food (21 CFR 101.36(b)(3) and (b)(2)(i), 21 CFR 101.4(b), 21 CFR 101.36(d) and (d)(1), and 21 CFR 101.9).

The names and quantities of dietary ingredients present in the product, the “Serving Size,” and the “Servings Per Container” must be listed. However, the listing of Servings Per Container is not required when it is the same information as in the net quantity of contents statement. For example, when the net quantity of contents statement is 100 tablets and the Serving Size is one tablet, the Serving Per Container also would be 100 tablets and would not need to be listed (21 CFR 101.36(b)).

Definition of Serving Size

One serving of a dietary supplement equals the maximum amount recommended, as appropriate, on the label for consumption per eating occasion or, in the absence of recommendations, one unit (e.g., tablet, capsule, packet, teaspoonful, etc). For example, if the directions on the label say to take one to three tablets with breakfast, the serving size would be three tablets (21 CFR 101.12(b)). The term Serving Size must be used on the label (21 CFR 101.36(b)(1)).
Required Nutrient Declaration Required in the Supplement Facts Panel

Total calories, calories from fat, total fat, saturated fat, cholesterol, sodium, total carbohydrate, dietary fiber, sugars, protein, vitamin A, vitamin C, calcium, and iron must be listed when they are present in measurable amounts. A measurable amount is an amount that exceeds the amount that can be declared as zero in the nutrition label of conventional foods, as specified in 21 CFR 101.9(c). If present in a measurable amount, trans fat must be listed on a separate line underneath the listing of saturated fat, as of January 1, 2006. Calories from saturated fat and the amount of polyunsaturated fat, monounsaturated fat, soluble fiber, insoluble fiber, sugar alcohol, and other carbohydrate may be declared, but they must be declared when a claim is made about them (21 CFR 101.36(b)(2)(i)) (see 68 FR 41434 at 41505, July 11, 2003).

Declaring vitamins and minerals (other than vitamin A, vitamin C, calcium, and iron) is only required when they are added to the product for purposes of supplementation or if making a claim about them (21 CFR 101.36(b)(2)(i)). When vitamin E occurs naturally, it does not need to be declared. This is because vitamin E is not one of the 14 mandatory dietary ingredients (21 CFR 101.36(b)(2)(i)).

It is required to list any other nutrients used in manufacturing when making a claim about calories from saturated fat, insoluble fiber, polyunsaturated fat, sugar alcohol, monounsaturated fat, other carbohydrate, and soluble fiber (21 CFR 101.36(b)(2)(i)).

Dietary ingredients for which no “Daily Values” (DVs) have been established must be listed by their common or usual names when they are present in a dietary supplement. They must be identified as having no DVs by use of a symbol in the column for “% Daily Value” (% DV) that refers to the footnote “Daily Value Not Established” (21 CFR 101.36(b)(2)(iii)(F) and (b)(3)).

Ingredients in dietary supplements that are not dietary ingredients, such as binders, excipients, and fillers, must be included in the ingredient statement (21 CFR 101.4(g)). Products that contain only amino acids may not declare protein for the product (21 CFR 101.36(b)(2)(i)).

Dietary ingredients that have DVs must be listed in the same order as for the labels of conventional foods, except that vitamins, minerals and electrolytes are grouped together. This results in the following order for vitamins and minerals: vitamin A, vitamin C, vitamin D, vitamin E, vitamin K, thiamin, riboflavin, niacin, vitamin B_6, folate, vitamin B_12, biotin, pantothenic acid, calcium, iron, phosphorus, iodine, magnesium, zinc, selenium, copper, manganese, chromium, molybdenum, chloride, sodium, and potassium (21 CFR 101.36(b)(2)(i)(B)).

The label may use the following synonyms in parentheses after dietary ingredients: vitamin C (ascorbic acid), thiamin (vitamin B_1), riboflavin (vitamin B_2), folate (folacin or folic acid), and calories (energy). Alternatively, “folic acid” or “folacin” may be listed without parentheses in place of “folate.” Energy content may also be expressed parenthetically in kilojoules immediately after the caloric content (21 CFR 101.36(b)(2)(i)(B)(2)).
Reporting Amounts

When using materials such as calcium carbonate as the source of calcium in the product, the list must include the weight of the calcium rather than the weight of the calcium carbonate in the Supplement Facts panel (21 CFR 101.36(b)(2)(ii)). Also, the amount of the dietary ingredient may be placed in a separate column or immediately after the name of the dietary ingredient (21 CFR 101.36(b)(2)(ii)). When using a separate column for amounts of dietary ingredients, the heading “Amount per Serving” may be placed over the column of amounts (21 CFR 101.36(b)(2)(i)(A)).

Language consistent with the declaration of the serving size, such as “Each Tablet Contains” or “Amount per 2 Tablets,” may be used in place of the heading “Amount per Serving.” Other terms may be used as well, such as capsule, packet, or teaspoonful (21 CFR 101.36(b)(2)(i)(A)). It is also acceptable to declare information on a “per unit” basis in addition to the required “per serving” basis (21 CFR 101.36(b)(2)(iv)).

If the product has different servings, such as one tablet in the morning and two at night, additional columns may be used. The columns must be labeled appropriately, e.g., “Amount per 1 Tablet” and “Amount per 2 Tablets” (21 CFR 101.36(b)(2)(i)(A)).

It is required to use the units of measurement specified for use in the Nutrition Facts panel. For example, the amount of fat would be listed in terms of grams in both the Nutrition Facts and Supplement Facts panels. However, units of measurement for amounts of vitamins and minerals are not specified for use in the Nutrition Facts panel because they must be listed by % DV and not by weight. The units of measurement given should be used in 21 CFR 101.9(c)(8) for the DVs of vitamins and minerals when listing these nutrients in Supplement Facts (e.g., the amount of vitamin C must be listed in terms of milligrams because its DV is stated in milligrams) (21 CFR 101.36(b)(2)(ii)(B) and 101.9(c)).

Percent of Daily Value

The % DV is the percentage of the DV (i.e., RDIs or DRVs) of a dietary ingredient that is in a serving of the product (21 CFR 101.36(b)(2)(ii)(B) and 21 CFR 101.9(c)(8) and (9)). The % DV must be declared for all dietary ingredients for which the FDA has established DVs, except that (1) the percentage for protein may be omitted, and (2) labels of dietary supplements to be used by infants, children less than four years of age, or pregnant or lactating women must not list any percent for total fat, saturated fat, cholesterol, total carbohydrate, dietary fiber, vitamin K, selenium, manganese, chromium, molybdenum, chloride, sodium, or potassium. See FDA’s proposed labeling guides for the DVs to be used for adults and children four or more years of age and the DVs to be used for infants, children less than four years of age, or pregnant or lactating women (21 CFR 101.36(b)(2)(iii)).

The % DV is calculated by dividing the quantitative amount weight by the established DV for the specified dietary ingredient and multiplying by 100 (except that the % DV for protein must be calculated in accordance with 21 CFR 101.9(c)(7)(iii)). In this calculation, the unrounded amount must be used as the quantitative amount, except that for total fat, saturated fat, cholesterol, sodium, potassium, total carbohydrate, and
dietary fiber, the quantitative amount by weight declared on the label may be used (i.e., the rounded amount). For example, the % DV for 60 mg of vitamin C is 100 (60 mg divided by the DV for vitamin C, multiplied by 100) (21 CFR 101.36(b)(2)(iii)(B) and 21 CFR 101.9(c)(7)(iii)). The % DV must be expressed to the nearest whole percent, except that “Less than 1%” or “<1 %” must be used when the amount present is big enough to be listed but so small that the % DV when rounded to the nearest percent is zero. For example, a product containing 1 g of total carbohydrate would list the % DV as Less than 1% or <1 % (21 CFR 101.36(b)(2)(iii)(C)).

If the amount of a dietary ingredient in the product in high enough to declare but so low that the % DV rounds to zero, Less than 1% or <1% must be declared because the label might confuse consumers if 5 mg is declared and the listed DV is 0%. For example, if a product contains 5 mg of potassium, the % DV calculates to 0.14% (5 mg divided by 3,500 mg), which would round to zero. In this case, Less than 1% or <1% would be declared for the % DV. Note that this does not pertain to dietary ingredients having RDIs because they may not be listed when present at less than 2% of the RDI (21 CFR 101.36(b)(2)(iii)(C) and 101.36(b)(2)(i)).

Other Dietary Ingredients

“Other Dietary Ingredients” are those dietary ingredients that do not have DVs (i.e., RDIs or DRVs), such as phosphatidylserine (21 CFR 101.36(b)(3)(i)). The statement Other Dietary Ingredients can be listed in the Supplement Facts panel after the listing of dietary ingredients having DVs (21 CFR 101.36(b)(3)(i)).

Furthermore, Other Dietary Ingredients must be listed by common or usual name in a column or linear display. The FDA has not specified an order that must be followed. The quantitative amount needs to be listed by weight per serving immediately after the name of the dietary ingredient or in a separate column. Furthermore, a symbol in the column for % DV that refers to the footnote Daily Value Not Established must be included, except that the symbol must follow the weight when not using the column format (21 CFR 101.36(b)(3)).

All liquid extracts are to be listed using the volume or weight of the total extract and the condition of the starting material before extraction when it was fresh. Also included may be information on the concentration of the dietary ingredient and the solvent used, e.g., “fresh dandelion root extract, x (y:z) in 70% ethanol,” where x is the number of milliliters or milligrams of the entire extract, y is the weight of the starting material, and z is the volume (milliliters) of solvent. The solvent must be identified in either the nutrition label or ingredient list. (21 CFR 101.36(b)(3)(i)(B)).

For dietary ingredients that are extracts from which the solvent has been removed, the weights of the dried extracts must also be included (21 CFR 101.36(b)(3)(ii)(C)).

The list of constituents of a dietary ingredient indented under the dietary ingredient and followed by their quantitative amounts by weight per serving are to be listed as well. The constituents in a column or in a linear display may be declared as well (21 CFR 101.36(b)(3)(iii)).

Proprietary blends are to be identified by use of the term “Proprietary Blend” or an appropriately descriptive term or fanciful name. On the same line, the total
weight of all Other Dietary Ingredients contained in the blend must be included. Indented underneath the name of the blend, list the Other Dietary Ingredients in the blend must be recorded, in either a column or linear manner, in descending order of predominance by weight. These ingredients should be followed by a symbol referring to the footnote Daily Value Not Established. Dietary ingredients having RDIs or DRVs must be listed separately and the individual weights declared (21 CFR 101.36(b)(2) and (c)).

If the product contains two or more packets of supplements (e.g., a packet of capsules for the morning and a different packet for the evening), the information for each packet may be presented in an individual nutrition label or may include an aggregate nutrition label. For two packets, this would consist of five columns. All of the dietary ingredients should be listed in the first column. The amounts and percentages of the morning packet should be listed in the second and third columns and similar information for the evening packet in the fourth and fifth columns (see the illustration of aggregate nutrition labeling in 21 CFR 101.36(e)(10)(iii); see also 21 CFR 101.36(e)(8)).

**LABELING COMPLIANCE**

The FDA will collect a composite of 12 subsamples (consumer packages) or 10% of the number of packages in the same inspection lot, whichever is smaller. The FDA will randomly select these packages (21 CFR 101.36(f)(1)). The FDA may permit use of an alternative means of compliance or additional exemptions in accordance with 21 CFR 101.9(g)(9). If a firm needs such special allowances, the request must be made in writing (to Office of Nutritional Products, Labeling, and Dietary Supplements (HFS-800), The Food and Drug Administration, 5100 Paint Branch Parkway, College Park, Maryland 20740-3835) (21 CFR 101.36(f)(2)). For dietary ingredients that are specifically added, the product must contain 100% of the volume or weight that has been declared on the label, with the exception of a deviation that is attributable to the analytical method. Products that contain less than this amount of such a dietary ingredient would be misbranded and in violation of the law. Dietary ingredients that are naturally occurring must be present at 80% of the declared value. For example, if vitamin C is added that was isolated from a natural source or made synthetically to the dietary supplement product, it would be subject to the 100% rule. However, if rose hips were added to a product, the vitamin C in the rose hips is naturally occurring and must be present at least 80% of the declared value (21 CFR 101.9(g)(3) and (g)(4)).

The dietary supplement product is not required to have a Supplement Facts panel if any of the following apply:

1. The company is a small business that has not more than $50,000 gross sales made or business done in sales of food to consumers or not more than $500,000 per year from total sales in accordance with 21 CFR 101.36(h)(1).
2. The company sells less than 100,000 units of the product annually, the firm has fewer than 100 full-time equivalent employees in accordance with 21 CFR 101.36(h)
(2) and the company files an annual notification with the FDA as specified in 21 CFR 101.9(j)(18)(iv).

3. The company ships the product in bulk form, does not distribute it to consumers in such form, and supplies it for use in the manufacture of other dietary supplements in accordance with 21 CFR 101.36(h)(3).

The two exemptions for small businesses and low-volume products (items 1 and 2 above) apply only if the products’ labels bear no claims or other nutrition information (21 CFR 101.36(h)(1)-(3)).

Special Labeling Provisions

On products for children less than two years of age, other than infant formula, the following are not be included on the label: calories from fat, calories from saturated fat, saturated fat, polyunsaturated fat, monounsaturated fat, and cholesterol. Also, on products for children less than four years of age, % DVs for total fat, saturated fat, cholesterol, total carbohydrate, dietary fiber, vitamin K, selenium, manganese, chromium, molybdenum, chloride, sodium, or potassium may not be included (21 CFR 101.36(b)(2)(iii) and (i)(1)).

Required in the footnote is the statement “Percent Daily Values Are Based on a 2,000 Calorie Diet” when total fat, saturated fat, total carbohydrate, dietary fiber, or protein are declared (21 CFR 101.36(b)(2)(iii)(D)).

If there is insufficient space for the Supplement Facts panel on the information panel or the principal display panel, it may be located on other panels that can readily be seen by consumers in accordance with 21 CFR 101.9(j)(17) (see 21 CFR 101.36(i)(2)(iii) and (i)(5) and 21 CFR 101.9(j)(17)).

The Supplement Facts panel may be omitted on individual units if nutrition information is fully provided on the outer package of the multiunit pack and the unit containers are securely enclosed and are not intended to be separated for retail sale. Each individual unit must be labeled with the statement “This Unit Not Labeled For Retail Sale” in accordance with 21 CFR 101.9(j)(15) (see 21 CFR 101.36(i)(3) and 21 CFR 101.9(j)(15)).

If dietary supplements are sold from bulk containers, the retailer must display a Supplement Facts panel clearly at the point of purchase (e.g., on a counter card, sign, tag affixed to the product, or some other appropriate device). Alternatively, the required information may be placed in a booklet, loose-leaf binder, or some other appropriate format that is available at the point of purchase (21 CFR 101.36(i)(4), 21 CFR 101.9(a)(2) and (j)(16)).

SAMPLE LABELS

See Label 10.1 for dietary supplement containing multiple vitamins (see 21 CFR 101.36(e)(10)(i)). See Label 10.2 for dietary supplement containing multiple vitamins for children and adults (see 21 CFR 101.36(e)(10)(ii)). See Label 10.3 for multiple
virations in packets (see 21 CFR 101.36(e)(10)(iii)). See Label 10.4 for dietary supplement containing dietary ingredients with and without RDIs and DRVs (see 21 CFR 101.36(e)(10)(iv)).

INGREDIENT LABELING

The Dietary Supplement Health and Education Act uses the term “ingredient” to refer to the compounds used in the manufacture of a dietary supplement. For instance, when calcium carbonate is used to provide calcium, calcium carbonate is an “ingredient” and calcium is a “dietary ingredient.” The term ingredient also refers to substances such as binders, colors, excipients, fillers, flavors, and sweeteners (Public Law 103-417, 60 Federal Register 67194 at 67199 (December 28, 1995)).

Ingredients that are sources of dietary ingredients may be listed within the Supplement Facts panel, for example, “Calcium (as calcium carbonate).” When ingredients are listed in this way, they do not have to be listed again in the ingredient statement (also called an ingredient list) (21 CFR 101.36(d)). If all source ingredients are placed in the Supplement Facts panel and there are no other ingredients, such as excipients or fillers, an ingredient statement is not necessary (21 CFR 101.4(a)(1)).

How to Identify the Ingredient List

To identify the ingredient list, the ingredient list must be preceded by the word “Ingredients,” except that words “Other Ingredients” must be used when some ingredients have been identified (i.e., as sources) within the nutrition label (21 CFR 101.4(g)).

When present, the ingredient list must be placed on dietary supplements immediately below the nutrition label or, if there is insufficient space below the nutrition label, immediately contiguous and to the right of the nutrition label (21 CFR 101.4(g)).

The ingredients are to be listed in descending order of predominance by weight. This means that the ingredient that weighs the most is first and the ingredient that weighs the least is last (21 CFR 101.4(a)). Also, spices, natural flavors, or artificial flavors must be declared in the ingredient lists by using either specific common or usual names or by using the declarations “spice,” “natural flavor,” or “artificial flavor,” or any combination thereof (21 CFR 101.22(h)(1) and 21 CFR 101.4(a)(1)).

Paprika, turmeric, saffron, and other spices that are also colorings may be declared by either name or the term “spice and coloring.” For example, paprika may be listed as “paprika” or as “spice and coloring” (21 CFR 101.22(a)(2)).

Declaration of an artificial color depends on whether or not the artificial color is certified. List a certified color by its specific or abbreviated name, e.g., “FD&C Red No. 40” or “Red 40.” A color that is not certified may be listed as an “Artificial Color,” “Artificial Color Added,” “Color Added,” or by its specific common or usual name (21 CFR 101.22(k)(1) and (k)(2)).

When a blend of fats and/or oils is not the predominant ingredient of the product and the makeup of the blend varies, the following “and/or” labeling or language must be used, such as the following: “INGREDIENTS: … vegetable oil shortening
(contains one or more of the following: cottonseed oil, palm oil, soybean oil)” (21 CFR 101.4(b)(14)).

Any added water must be identified in the list of ingredients in descending order of predominance by weight, for example: “Ingredients: Cod liver oil, gelatin, water, and glycerin” (21 CFR 101.4(a) and (c) and 21 CFR 101.36(c)(10)(iv)).

When using a chemical preservative, the common or usual name of the preservative must be listed, followed by a description that explains its function e.g., “preservative,” “to retard spoilage,” “a mold inhibitor,” “to help protect flavor,” or “to promote color retention” (21 CFR 101.22(j)).

**DIETARY SUPPLEMENT LABELING CLAIMS**

A nutrient content claim is a claim that expressly or by implication characterizes the level of a nutrient in a dietary supplement (21 CFR 101.13(b)).

The nutrient levels needed to use nutrient content claims are shown in Appendix D of the FDA’s proposed labeling guide. Only those nutrient content claims, or their synonyms, that are specifically defined in regulations may be used (21 CFR 101.13(b)).

The regulations for specific nutrient content claims may be found in 21 CFR 101, Subpart D (Specific Requirements of Nutrient Content Claims) as follows:

- § 101.54(b), “high” claims
- § 101.54(c), “good source” claims
- § 101.54(e), “more” claims
- § 101.54(f), “high potency” claims
- § 101.54(g), “antioxidant” claims
- § 101.56, “light” or “lite” claims
- § 101.60, “calorie” or “sugar” claims
- § 101.61, “sodium” or “salt” claims
- § 101.62, “fat, fatty acids, and cholesterol” claims
- § 101.65, implied nutrient content claims
- § 101.65(d), “healthy” claims
- § 101.67, use of nutrient content claims for butter

A nutrient content claim may be no larger than twice the type size of the statement of identity (the name of the food) and may not be unduly prominent in style compared with the statement of identity (21 CFR 101.13(f)).

A Supplement Facts panel is required if a nutrient content claim is made (21 CFR 101.13(n)).

A disclosure statement is a statement that calls the consumer’s attention to one or more nutrients (other than the nutrient that is the subject of the claim) in a dietary supplement (e.g., “See nutrition information for fat content”) (21 CFR 101.13(h)(1)).

A disclosure statement must be used when making a nutrient content claim and the food (including dietary supplements) contains one or more of the nutrients listed in Table 10.1 in excess of the levels listed below per reference amount customarily

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consumed, per labeled serving, or, for a product with a reference amount of 30 g or less or 2 tablespoons or less, per 50 g (21 CFR 101.13(h)(1)).

The disclosure statement must be presented in easily legible boldface print or type, in distinct contrast to other printed or graphic matter (21 CFR 101.13(h)(4)(i)).

The disclosure statement is to be placed immediately adjacent to (i.e., right next to) the claim with no intervening material (such as vignettes or other art work) other than information in the statement of identity or any other information that is required to be presented with the claim (21 CFR 101.13(h)(4)(ii)).

Omission of the disclosure statement is permitted from the panel bearing the nutrition information when the nutrient content claim appears on more than one panel of a label (21 CFR 101.13(h)(4)(ii)).

Only one disclosure statement is required per panel when making multiple claims on a panel. The statement is required to be adjacent to the claim printed in the largest type on that panel (21 CFR 101.13(h)(4)(iii)).

A “high” claim may be made when the dietary supplement contains at least 20% of the DV (i.e., the RDIs or DRVs) of the nutrient that is the subject of the claim per reference amount customarily consumed. A “good source” claim may be made when the dietary supplement contains 10–19% of the Daily Value (21 CFR 101.54(b)(1) and (c)(1)).

A statement a nutrient for which there is no established DV is also allowed as long as the claim specifies only the amount of the nutrient per serving and does not imply that there is a lot or a little of that nutrient in the product (e.g., “x grams of phosphatidylserine”). The dietary ingredient for which there is no DV and the quantitative amount of that dietary ingredient in the Supplement Facts panel must be listed in the section below the nutrients with DVs. These dietary ingredients must be identified as having no DVs by the use of the footnote Daily Value Not Established (21 CFR 101.13(i)(3) and 21 CFR 101.36(b)(3)).

Statements using the words “contain” and “provides” may be used for nutrients without DVs if, and only if, the specific amount of the nutrient is included (e.g., “Contains X grams of phosphatidylserine per serving” or “Provides X g of phosphatidylserine”) (21 CFR 101.13(i)(3) and 101.54(c)(1)).

A statement outside of the Supplements Facts panel that describes the percentage of the RDI of a vitamin or mineral in a dietary supplement product are considered nutrient content claims and are not exempt from bearing a disclosure statement when required (21 CFR 101.13(b)(1), (c) and (i)).

If a similar dietary supplement is normally expected to contain a nutrient and the dietary supplement is specially processed, altered, formulated, or reformulated as to lower the amount of the nutrient in the food, remove the nutrient in the food,
or not include the nutrient, then it is permitted to make a “low” or “free” claim as applicable (21 CFR 101.13(e)(1)).

However, a “low” or “free” claim may not be allowed for the dietary supplement product if it is normally low in or free of a nutrient. However, a claim may be used if it is indicated to refer to all products of that type and not merely to that particular brand (21 CFR 101.13(e)(2)).

**Are Claims Such as “100 Percent Milk Free” and “Contains No Preservatives” Subject to the Nutrient Content Claim Requirements?**

Claims such as “100 percent milk free” and “contains no preservatives” are not nutrient content claims as long as they are not used in a nutrient context that would make them an implied claim under 21 CFR 101.13(b)(2). The statement “100 percent milk free” is generally a claim to facilitate avoidance of milk products. “Contains no preservatives” is a claim about a substance that does not have a nutritive function (21 CFR 101.65(b)(1) and (b)(2)).

A “no sugar” content claim is subject to the nutrient content claim requirements (21 CFR 101.60(c)(1)).

To avoid misleading consumers, the term “no added sugar” should be limited to dietary supplements containing no added sugars that are normally expected to contain them (21 CFR 101.60(c)(2)(iv)).

A “sugar free” dietary supplement may not claim “low calorie,” except when an equivalent amount of a dietary supplement that the labeled dietary supplement resembles and for which it substitutes (e.g., another protein supplement) normally exceeds the definition for “low calorie” (21 CFR 101.60(c)(1)(iii)(A)).

**Antioxidant Claims**

An antioxidant claim is a nutrient content claim that characterizes the level of one or more antioxidant nutrients present in a dietary supplement (21 CFR 101.54(g)).

When making an antioxidant nutrient claim, the names of the nutrients that are the subject of the claim must be included as part of the claim (e.g., “high in antioxidant vitamins C and E”). Alternatively, the term “antioxidant” or “antioxidants” may be linked in a nutrient content claim (as in “high in antioxidants”) by a symbol (e.g., an asterisk) that refers to the same symbol that appears elsewhere on the same panel, followed by the name or names of the nutrients with recognized antioxidant activity. This list should be in letters at least $\frac{1}{16}$ of an inch in height or no smaller than half the type size of the largest nutrient content claim, whichever is larger (21 CFR 101.54(g)(4)).

To qualify as an antioxidant, the nutrient or dietary ingredient must have an RDI, except as noted above (21 CFR 101.54(g)(1)).

Nutrients that are the subject of the claim must have recognized antioxidant activity. In addition, the level of each nutrient that is the subject of the claim must be sufficient to qualify for either “high” claims in 21 CFR 101.54(b), “good source” claims in 21 CFR 101.54(c), or “more” claims in 21 CFR 101.54(e). For example, for
a product to qualify for a “high in antioxidant vitamin C” claim, it must contain 20% or more of the RDI for vitamin C. That is, it must meet the level for “high” defined in § 101.54(b). For a product to qualify for a “good source of antioxidant vitamin C” claim, it must contain 10–19% of the RDI for vitamin C (21 CFR 101.54(g)(2) and (g)(3)).

Recognized antioxidant activity means that there is scientific evidence that, after absorption from the GI tract, the substance participates in physiological, biochemical, or cellular processes that inactivate free radicals or prevent free-radical-initiated chemical reactions (21 CFR 101.54(g)(2)).

A claim may be made for beta-carotene, which does not have an RDI, when the level of vitamin A present as beta-carotene is sufficient to qualify for the claim. For example, a company may make the claim “good source of antioxidant beta-carotene” when 10% or more of the RDI for vitamin A is present as beta-carotene (21 CFR 101.54(g)(3)).

When making additional claims that describe the antioxidant properties of the product, a statement, subject to § 403(a) of The Act (the false and misleading provisions), that describes how a dietary ingredient that does not have an RDI participates in antioxidant processes may be made. Likewise, structure/function claims may be made about antioxidants as long as such claims are not false or misleading and, if appropriate, are made in accordance with § 403(r)(6) of The Act (the provisions for statements of nutritional support). For example, a claim that reads “_____ involved in antioxidant processes” would be acceptable as long as it is (1) truthful and not misleading and (2) meets the requirements of § 403(r)(6) of The Act (62 FR 49868 at 49873 (September 23, 1997)).

High Potency Claims

The term “high potency” may be used on the dietary supplement labels to describe individual vitamins or minerals that are present at 100% or more of the RDI per reference amount customarily consumed (21 CFR 101.54(f)(1)(i)).

The term high potency can be used for combination products, such as botanicals with vitamins. However, when using the term high potency to describe individual vitamins or minerals in the product that contains other nutrients or dietary ingredients, the vitamin or mineral that is being described by the term high potency must be clearly identified (e.g., “Botanical X with high potency vitamin E”) (21 CFR 101.54(f)(1)(ii)).

The high potency may be used on the multinutrient product to describe the product if it contains 100% or more of the RDI for at least two-thirds of the vitamins and minerals that are listed in 21 CFR 101.9(c)(8)(iv) and that are present in the product at 2% or more of the RDI (e.g., “High potency multivitamin, multinutrient dietary supplement tablets”) (21 CFR 101.54(f)(2)).

Percentage Claims

A percentage claim is a statement that characterizes the percentage level of a dietary ingredient for which an RDI or DRV has not been established. A percentage
A health claim is an explicit or implied characterization of a relationship between a substance and a disease or a health-related condition. This type of claim requires significant scientific agreement and must be authorized by the FDA. The claim can be a written statement, a “third party” reference, a symbol, or a vignette (21 CFR 101.14(a)(1) and (c)).

A health claim is different from a structure/function claim in that a health claim describes the effect a substance has on reducing the risk of or preventing a disease, for example, “calcium may reduce the risk of osteoporosis.” A health claim requires the FDA evaluation and authorization before its use. A structure/function claim describes the role of a substance intended to maintain the structure or function of the body. Structure/function claims do not require preapproval by the FDA (21 CFR 101.14(a)(1) and (c) and 21 CFR 101.93(f)).

An updated list of FDA authorized health claims is maintained on the FDA website at http://www.cfsan.fda.gov/~dms/flg-6c.html#upd. In addition to these authorized health claims, there are certain “qualified” health claims permitted by the FDA. Qualified health claims are listed on the FDA website at http://www.fda.gov/oc/nutritioninitiative/list.html.

A qualified health claim is a claim supported by less scientific evidence than an authorized health claim. The FDA requires that qualified claims be accompanied by a disclaimer that explains the level of the scientific evidence supporting the relationship.

Unlike authorized health claims, the FDA does not issue regulations for qualified health claims (see the FDA’s Guidance for Industry, Interim Procedures for Qualified Health Claims in the Labeling of Conventional Human Food and Human Dietary Supplements, July 2003).
The FDA will permit the use of a qualified health claim provided that the following apply:

1. The FDA has issued a letter stating the conditions under which it will consider exercising enforcement discretion for the specific health claim.
2. The qualified claim is accompanied by an agency-approved disclaimer.
3. The claim meets all the general requirements for health claims in 21 CFR 101.14, except for the requirement that the evidence for the claim meet the validity standard for authorizing a claim and the requirement that the claim be made in accordance with an authorizing regulation (see the FDA’s Guidance for Industry, Interim Procedures for Qualified Health Claims in the Labeling of Conventional Human Food and Human Dietary Supplements, July 2003).

An agency-approved disclaimer is a statement that discloses the level of scientific evidence used to substantiate the health claim (see FDA Task Force Final Report: Consumer Health Information for Better Nutrition Initiative, Attachment E—Interim Procedures for Qualified Health Claims in the Labeling of Conventional Human Food and Human Dietary Supplements, July 2003).

To use additional health claims, an individual must submit a health claim petition in accordance with 21 CFR 101.70. A new health claim may be used only after the FDA issues either an authorizing regulation or a letter stating enforcement discretion conditions for a qualified health claim (21 CFR 101.14 and 21 CFR 101.70).

**Structure/Function Claims**

A company may make the following types of structure/function claims under § 403(r)(6) of The Act:

1. A statement that claims a benefit related to a classical nutrient deficiency disease and that discloses the prevalence of such disease in the United States;
2. A statement that describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans or characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function; or
3. A statement that describes the general well-being from consumption of a nutrient or dietary ingredient (21 U.S.C. 343(r)(6)).

When making structure/function claims, the claim must (1) have substantiation that such statement is truthful and not misleading, (2) include the disclaimer, and (3) notify the FDA no later than 30 days after the first marketing of the product that the company is making the statement in accordance with 21 CFR 101.93.

The following text must be used for the disclaimer, as appropriate:

1. Singular: “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;” or
2. Plural: “These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”

The wording of these disclaimer may not be modified (21 CFR 101.93(c)). The disclaimer must be placed immediately adjacent to the claim with no intervening
material or elsewhere on the same panel or page that bears the statement. In the latter case, the disclaimer must be placed in a box and linked to the statement by a symbol (e.g., an asterisk) placed at the end of each statement that refers to an identical symbol placed adjacent to the disclaimer (21 CFR 101.93(d)).

The notification procedures require that a manufacturer, packer, or distributor making such a statement must do the following:

1. Notify the FDA within 30 days of first marketing a product whose label or labeling bears a statement made under § 403(r)(6) of The Act.
2. Submit an original and two copies of the notification to the Office of Nutritional Products, Labeling, and Dietary Supplements (HFS-800), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Parkway, College Park, Maryland 20740-3835.
3. The notification must be signed by a person who can certify that the information in the notification is complete and accurate and that the notifying firm has substantiation that the § 403(r)(6) statement is truthful and not misleading (21 CFR 101.93(a)(1) and (a)(3)).

When reporting to the FDA, there is no official form to use. The notification may be made by a letter containing the required information in any format that is convenient.

The following information must be included in the notification:

1. The name and address of the manufacturer, packer, or distributor of the dietary supplement that bears the statement.
2. The text of the statement that the company is making.
3. The name of the dietary ingredient or supplement that is the subject of the statement.
4. The name of the dietary supplement (including its brand name) on whose label, or in whose labeling, the statement appears (21 CFR 101.93(a)(2)).

REGULATION AROUND THE WORLD

The FDA is not the only governing body trying to improve the quality and reliability of dietary supplements. The governing bodies of Canada, Europe, India, Japan, and numerous others are all trying to acknowledge the health benefits of supplements, while protecting the general public. Each governing body has a slightly different approach to controlling manufacturing and labeling, but, ultimately, these governing bodies are moving in the same direction. As the world economy expands, the manufacturers and governing bodies will continue to approach one unified set of standards that will reduce manufacturer confusion and increase consumer confidence.

REFERENCE