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October 31, 2013

VIA ELECTRONIC SUBMISSION

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

Re: Docket No. FDA-2013-D-0880
Draft Guidance for Industry, Frequently Asked Questions About Medical Foods; Second Edition

The Council for Responsible Nutrition (CRN) is the leading trade association for the dietary supplement and nutritional products industry, representing manufacturers of dietary ingredients and of national brand name and private label dietary supplements as well as manufacturers of medical foods.[1]

CRN submits these comments on the Food and Drug Administration's (FDA's) *Draft Guidance for Industry, Frequently Asked Questions About Medical Foods; Second Edition* (Draft Guidance).[2] CRN appreciates FDA's attention to the medical foods category and believes that FDA's regulation of medical foods should simultaneously foster development of these important products while also maintaining the integrity of the medical foods category and its distinction from conventional foods and dietary supplements.

As noted in the Draft Guidance, FDA has many tools that allow the agency to ensure the proper marketing of medical foods. CRN supports FDA's use of these enforcement

[1] Members of CRN, founded in 1973, produce a large portion of the dietary supplements marketed in the United States and globally. Our member companies manufacture popular national brands, as well as the store brands marketed by major supermarket, drug store, and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies. In addition to complying with a host of federal and state regulations governing dietary supplements in the areas of manufacturing, marketing, quality control, and safety, our 75 plus manufacturer and supplier members also agree to adhere to additional voluntary guidelines, as well as CRN's Code of Ethics. Learn more about us at www.crnusa.org.

[2] *See* 78 Fed. Reg. 49,271, 49,271 (Aug. 13, 2013).

tools to ensure that medical foods are marketed in compliance with the statutory criteria for the product category, including requirements related to ingredients, labeling, and claims.

CRN is concerned, however, that FDA's interpretation of the medical foods category is overly narrow and inconsistent with the statutory definition of medical foods. Medical foods play an increasingly important role in the dietary management of many diseases and conditions. In the Draft Guidance, FDA concludes that medical foods may be marketed only for diseases or conditions the "dietary management of which cannot be achieved by modification of the normal diet alone."[3] This criterion circumscribes the category of medical foods in ways not contemplated by the statutory definition of "medical food" and is not in the best interest of the public health, and thus unduly narrows the product category. CRN therefore urges FDA to revise its Draft Guidance to conform to the statutory definition of "medical food" and to eliminate the "modification of the normal diet alone" criterion.

I. Statutory and Regulatory Background on Medical Foods

A. Statutory Definition of Medical Foods

Congress defined the term "medical food" when it enacted the Orphan Drug Act Amendments of 1988. In doing so, Congress defined a "medical food" as:

> a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is 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.[4]

In other words, to qualify as a medical food, a product must: (1) be formulated to be consumed or administered enterally, (2) be consumed or administered under the supervision of a physician, (3) be intended for the specific dietary management of a disease or condition for which there are distinctive nutritional requirements, and (4) these nutritional requirements must be based on recognized scientific principles as established by medical evaluation.

FDA has stated that the agency considers the statutory definition of medical food to narrowly constrain this product category.[5] CRN agrees with FDA that the statutory definition of medical foods is narrow; only products meeting all four statutory criteria may be lawfully marketed as medical foods.

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[3] Draft Guidance at 5.

[4] 21 U.S.C. § 360ee(b)(3).

[5] *See* Draft Guidance at 4; Food Labeling; Reference Daily Intakes and Daily Reference Values; Mandatory Status of Nutrition Labeling and Nutrition Content Revision, 56 Fed. Reg. 60,366, 60,377 (Nov. 27, 1991) (Proposed Rule).

A few years after the Orphan Drug Act Amendments were enacted, Congress incorporated the statutory definition of "medical food" into the Nutrition Labeling and Education Act (NLEA) of 1990, codified at section 403(q)(5)(A)(iv) of the Federal Food, Drug, and Cosmetic Act (FDCA), thereby exempting medical foods from the nutrition labeling, health claim, and nutrient content claim requirements applicable to most other foods. Congress did not alter the definition of medical food when it exempted such products from the requirements of the NLEA.[6]

B. Regulatory Status of Medical Foods

FDA has never defined the category of "medical food" in its regulations and the agency has never promulgated any regulations governing medical foods specifically. The agency has, however, promulgated 21 C.F.R. § 101.9(j)(8) to implement the statutory exemption of medical foods from the requirements of the NLEA. To qualify for the section 101.9(j)(8) exemption as a medical food, a food must:

> (1) be "a specially formulated and processed product . . . for the partial or exclusive feeding of a patient by means of oral intake or enteral feeding by tube";
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> (2) be "intended for the dietary management of a patient who, because of therapeutic or chronic medical needs, has limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs of certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by modification of the normal diet alone";
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> (3) "provide[] nutritional support specifically modified for the management of the unique nutrient needs that result from the specific disease or condition, as determined by medical evaluation";
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> (4) be "intended to be used under medical supervision"; and
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> (5) be "intended only for a patient receiving active and ongoing medical supervision wherein the patient requires medical care on a recurring basis for, among other things, instructions on the use of the medical food."[7]

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[6] *See* 21 U.S.C. § 343(q)(5)(A)(iv) (incorporating by reference the definition of medical food as defined by the Orphan Drug Act).

[7] 21 C.F.R. § 101.9(j)(8).

II. FDA Should Enforce the Statutory Criteria for Medical Foods, Without Unduly Narrowing the Product Category

CRN supports FDA's articulation of the statutory criteria for medical foods in the Draft Guidance, and encourages the agency's continued efforts to make clear the distinction between medical foods, conventional foods, dietary supplements, and drugs. Such agency actions should not, however, narrow the category of medical foods beyond the parameters established by Congress.

A. Medical Foods Must Be Food

To be a medical food, a product must be a "food." This means that medical foods may contain only ingredients that are generally recognized as safe (GRAS), approved food additives used in accordance with FDA's food additive regulations, color additives used in accordance with FDA's color additive regulations, or substances that are authorized by a prior sanction.[8] Medical foods may not contain "dietary ingredients," as defined in section 201(ff) of the Federal Food, Drug, and Cosmetic Act, that are not otherwise lawful food ingredients. In addition, all medical food ingredients must "be safe and suitable and comply with all applicable provisions of the FD&C Act and FDA's regulations."[9] As FDA states in the Draft Guidance, medical foods "must comply with all applicable FDA requirements for foods," including the agency's cGMP regulations for foods, the requirement for food facilities registration, and where applicable, regulations specific to the product formulation and processing and Emergency Permit Control regulations.[10]

In addition, medical food manufacturers may make only truthful and nonmisleading statements in their product labeling, and must comply with all labeling requirements other than the NLEA requirements from which medical foods are specifically exempted. Medical foods may bear claims about helping to meet the distinctive nutritional requirements of patients suffering from diseases or health-related conditions for which distinctive nutritional requirements have been established, or about providing nutritional support for such patients. A medical food may not, however, bear claims that it can be used in the diagnosis, cure, treatment, or prevention of disease. Products that bear such claims are drugs regardless of whether they are in food form. CRN appreciates FDA's emphasis of this core distinction between medical foods and drugs.

B. Medical Foods Must Meet Distinctive Nutritional Requirements

As noted above, a medical food must be intended for use in diseases or conditions for which "distinctive nutritional requirements, based on recognized scientific principles, are

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[8] Draft Guidance at 9 (setting forth the applicable regulations for each type of ingredient).

[9] Draft Guidance at 9.

[10] *See, e.g.*, Draft Guidance at 6.

established by medical evaluation."[11] The distinctive nutritional requirements criterion may be interpreted to refer to the body's "physiological" need for specific amounts of nutrients associated with a disease or condition. Under this interpretation, the distinctive nutritional requirements of a disease or condition "reflect the total amount needed by a healthy person to support life or maintain homeostasis, adjusted for the distinctive changes in the nutritional needs of the patient as a result of the effects of disease process on absorption, metabolism, and excretion."[12]

The distinctive nutritional requirements criterion may also be interpreted "to encompass physical or physiological limitations in a person's ability to ingest or digest conventional foods."[13] Under this alternative interpretation, "distinctive nutritional requirements" would include those requirements that result from a disease or condition that causes a physical or physiological limitation in the ability of a person to ingest or digest conventional nutrient sources and result in that person needing specially formulated foods to meet part or all of their daily nutrient needs.[14]

If distinctive nutritional requirements have not been established for a particular disease or condition under either of these interpretations, then a medical food may not be marketed for that disease or condition. The failure to meet the distinctive nutritional requirements criterion has been a key violation cited by FDA in its enforcement letters to manufacturers of purported medical foods. For example, FDA has issued several enforcement letters to manufacturers of products purporting to be medical foods for the management of irritable bowel syndrome (IBS). In those letters, one of the chief reasons that FDA highlighted regarding why the cited products were not medical foods was that there are no medically accepted nutritional requirements established for the management of IBS.[15]

CRN supports FDA's emphasis on the "distinctive nutritional requirements" element of the statutory definition of "medical food," as it is a key feature distinguishing medical foods from conventional foods and dietary supplements. As FDA has stated, medical foods "are not foods simply recommended by a physician as part of an overall diet designed to reduce the risk of a disease or medical condition, to lose or maintain weight, or to ensure the consumption of a healthy diet."[16] Products so recommended would be conventional foods or dietary supplements (or potentially drugs, if they bear claims to prevent or treat disease). Similarly, CRN agrees that classical nutrient deficiency diseases, such as scurvy and pellagra, that result

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[11] 21 U.S.C. § 360ee(b)(3).

[12] 61 Fed. Reg. 60,661, 60,667 (Nov. 29, 1996).

[13] *Id.*

[14] *Id*., at 60,667-68.

[15] *See, e.g.*, Letter to Andrew R. Lefkowitz, President and Chief Executive Officer, Ganeden Biotech, Inc., from Carol A. Heppe, District Director, Cincinnati District, FDA (Dec. 8, 2006).

[16] 61 Fed. Reg., at 60,668.

from inadequate intake of essential nutrients likewise are not diseases or conditions for which medical foods could be labeled and marketed.

C. Medical Foods Must Be Intended for Use By Patients Under Ongoing Physician Supervision

Finally, to be a medical food, a product must be intended for use by a patient subject to continuing physician supervision, either in a healthcare facility or as an outpatient. The physician-supervision requirement does not preclude the retail sale of medical foods, but medical foods must not be marketed in a manner that encourages self-diagnosis or self-treatment. CRN believes that this limitation is linked to the requirement that medical foods be marketed only for diseases or conditions that have distinctive nutritional requirements. Patients suffering from such diseases or conditions are likely already under a physician's care, and the physician's supervision of their condition likely involves discussion of the patients' diet. Products marketed for general conditions such as heart health, digestive health, or joint comfort and flexibility are likely to be dietary supplements or conventional foods, not medical foods.

D. FDA's Narrowing of the Medical Foods Category is Unnecessary and Inconsistent with the Statutory Definition of Medical Foods

As reflected above, the definition of medical foods is narrow and specific, and FDA has a number of enforcement tools at the agency's disposal to ensure the safety of medical foods and the boundaries of the product category. The agency has nonetheless decided to impose an extra-statutory limitation on medical food manufacturers to constrain the products that may be marketed as medical foods. As reflected in the Draft Guidance, FDA has concluded that medical foods may be marketed only for diseases and conditions "the dietary management of which cannot be achieved by modification of the normal diet alone."[17]

This regulatory limitation is not in the statutory text. If Congress had intended to limit the category of medical foods in this way, then it would have included such a limitation in the statutory definition of medical foods. This is particularly so where Congress was otherwise incredibly precise with respect to the criteria for defining medical foods.

Further, FDA's imposition of this extra-statutory criteria is based on its labeling regulation in 21 C.F.R. § 101.9(j)(8). Section 101.9(j)(8), however, does not mandate imposition of this limitation. Rather, Section 101.9(j)(8) simply provides for an exemption from the requirements of the NLEA for certain medical foods.[18] That regulation is not a definitional

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[17] Draft Guidance at 9-13.

[18] Section 101.9(j)(8) was a small piece of a massive new regulation governing nutrition labeling. The sole purpose of section 101.9(j)(8) was to implement the NLEA's exemption from nutrition labeling for medical foods. Industry likely did not perceive section 101.9(j)(8) to be narrowing the entire category of medical foods, and thus it is not surprising that industry did not object to that provision when promulgated. Medical foods intended for conditions that can be managed through modification of the normal diet alone may still be marketed as medical foods, but would not be exempt from nutrition labeling requirements.

regulation intended to limit the entire scope of the medical foods category. To the contrary, the regulation refers explicitly to "[m]edical foods as defined in section 5(b) of the Orphan Drug Act,"[19] and then states that a "food is subject to this exemption [from nutrition labeling] only if" among other things, it "is intended for the dietary management of a patient with specially determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone."[20] FDA's use of the section 101.9(j)(8) exemption from nutrition labeling as a definitional regulation to limit an entire product category is unsupported by the regulation itself and inconsistent with the statutory definition of medical foods.

Additionally troubling is FDA's adoption of the "modification of the normal diet alone" criterion in its nutrition labeling exemption with virtually no explanation for doing so. FDA adopted this criterion relying entirely on a 1990 Life Sciences Research Office of the Federation of American Societies for Experimental Biology (LSRO/FASEB) Report entitled "Guidelines for Scientific Review of Enteral Food Products for Special Medical Purposes."[21] The LSRO consultants, in turn, adopted these criteria from a draft report by the Food and Agriculture Organization/World Health Organization's Codex Alimentarius Commission.[22] The LSRO report, which relied on a draft Codex report, is the only support that FDA offered when adopting the "modification of the normal diet alone" criterion.[23]

The agency's decision to limit the category of medical foods in this way ignores the importance of medical foods in making the dietary management of many diseases and conditions easier, more convenient, and less expensive. For example, individuals with type II diabetes have an impaired capacity to metabolize ordinary dietary carbohydrates. Medical foods for diabetics can be specially formulated to meet these distinctive nutritional requirements, including, for example, by providing slowly digestible carbohydrates. Such dietary management of type II diabetes is based on recognized scientific principles and is managed under the supervision of a physician, as diabetics are typically under a doctor's care, because the disease is not one that can be self-diagnosed or self-treated.

FDA's Draft Guidance, however, states that the agency does not consider a product labeled and marketed for type II diabetes to meet the regulatory criteria for a medical food because a regular diet can be modified to meet the needs of an individual affected by type II diabetes. FDA ignores the fact that compliance with treatment plans for chronic illnesses,

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[19] 21 C.F.R. § 101.9(j)(8).

[20] 21 C.F.R. § 101.9(j)(8)(ii).

[21] John M. Talbot, *Guidelines for the Scientific Review of Enteral Food Products for Special Medical Purposes*, J. of Parenteral and Enteral Nutrition (Dec. 1990).

[22] *See id.* at 101S, *citing* Report of the Sixteenth Session of the Codex Committee on Nutrition and Foods Standards Programme, Codex Alimentarius Commission, Eighteenth Session, Joint Food and Agricultural Organization of the United Nations and World Health Organization (1989).

[23] *See* 61 Fed. Reg. at 60,663.

including changes to diet and lifestyle, are adhered to only about fifty percent of the time.[24] As a group, patients with diabetes are particularly prone to regimen adherence problems.[25] Medical foods formulated to meet the distinctive nutritional requirements of diabetics are a much needed tool to improve compliance with dietary changes among individuals with type II diabetes, changes that diabetics cannot necessarily make successfully through modification of the normal diet alone. If FDA continues to enforce this extra-statutory criteria, the agency will stifle medical food innovation and deny patients access to safe and healthful products that can greatly improve their ability to manage the diseases and conditions from which they suffer.

FDA's approach to regulating medical foods in the Draft Guidance also implicates the First Amendment. How and whether FDA regulates a particular product depends on the intended use of the product, as represented by the product's manufacturer.[26] Where FDA concludes that a particular product may not be marketed as a medical food, the agency is inherently limiting the commercial speech about that product, i.e., limiting the claims that may be made about the product. Here, FDA has placed an outright prohibition on the marketing of certain medical foods intended for use in the dietary management of particular diseases and conditions, such as diabetes. FDA may restrict commercial speech in this way only if it can show that doing so is necessary to directly advance a substantial governmental interest, and that the means chosen to restrict the commercial speech are narrowly tailored.[27]

The agency, however, cannot make these required showings with respect to the restrictions expressed in the Draft Guidance for medical foods. Medical foods that meet the statutory criteria established for the product category and that meet the other FDA requirements intended to ensure that medical foods are not adulterated or misbranded, are lawful products. The agency cannot show a substantial governmental interest in restricting truthful and non-misleading commercial speech about how these lawful products can assist in the dietary management of certain diseases and conditions for which distinctive nutritional requirements have been established. Further, FDA's blanket prohibition on all medical foods marketed for use in certain patient populations, such as diabetics, is certainly not narrowly tailored given the other enforcement tools available to the agency to enforce against false or misleading claims, or any other impermissible claims made by medical food manufacturers, such as claims to cure, prevent, or treat disease. FDA should consider these First Amendment principles in reevaluating its approach to the medical foods category expressed in the Draft Guidance.

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[24] Delamater AM. Improving Patient Adherence. *Clin Diab. 2006;24:71-77*; Kirkpatrick SI, Dodd KW, Reedy J, Krebs-Smith SM. Income and race/ethnicity are associated with adherence to food-based dietary guidance among US adults and children. *J Acad Nutr Diet*. 2012;112:624-635.

[25] Kurtz SM. Adherence to diabetes regimens: empirical status and clinical applications. Diabetes Educ. 1990;16:50-9.

[26] *See, e.g.*, 21 C.F.R. § 201.128 (defining intended use).

[27] *See Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557 (1980).

III. Conclusion

FDA originally permitted the marketing of "medical foods" in an effort to "foster[] innovation in the development of these products," recognizing that the usefulness of medical foods was widely accepted by healthcare professionals for patients under their supervision.[28] FDA should further these same goals today by permitting access to any medical foods that meet the statutory criteria that Congress established for the product category. CRN therefore urges FDA to revise its Draft Guidance to eliminate the extra-statutory criteria that medical foods may be marketed only for diseases and conditions "the dietary management of which cannot be achieved by the modification of the normal diet alone."

At the same time, CRN supports and encourages FDA's efforts to articulate and enforce the boundaries of the statutory definition of "medical foods" and to reiterate that Congress intended this to be a narrow category of foods, comprised of food ingredients, for patients suffering from diseases or conditions with distinctive nutritional requirements. Products that provide nutritional support to the general population or help support the structure or function of the body may be marketed as dietary supplements or as conventional foods.

Respectfully submitted,

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[28] *See* 61 Fed. Reg. 60,661, 60,662 (Nov. 29, 1996). In the 1970s, FDA originally regulated "medical foods" such as Lofenalac, which was designed for use in the dietary management of a rare genetic condition known as phenylketonuria (PKU), as "food for special dietary use" because Congress did not codify the definition of medical food until 1988.