Guidance for Industry

Frequently Asked Questions About Medical Foods; Second Edition

Draft Guidance

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For questions regarding this draft document contact the Center for Food Safety and Applied Nutrition (CFSAN) at 240-402-1450.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Food Safety and Applied Nutrition
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Frequently Asked Questions About Medical Foods

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I. Introduction

This guidance is intended to provide industry with a convenient place to find answers to frequently asked questions (FAQs) about medical foods. The responses to these FAQs address common questions about the definition of and regulations for medical foods. This guidance is a second edition of the May 2007 guidance titled "Guidance for Industry: Frequently Asked Questions About Medical Foods." This guidance provides responses to additional questions regarding the definition, labeling, and availability of medical foods and updates to some of the existing responses; new questions and answers and amended responses are identified by the date they were added to the guidance.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Questions and Answers

1. What is a medical food?

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[1] This guidance has been prepared by the Office of Nutrition, Labeling, and Dietary Supplements in the Center for Food Safety and Applied Nutrition at the U.S. Food and Drug Administration.

A medical food, as defined in section 5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)), is "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."

FDA considers the statutory definition of medical foods to narrowly constrain the types of products that fit within this category of food.[2] Medical foods are distinguished from the broader category of foods for special dietary use and from foods that make health claims by the requirement that medical foods be intended to meet distinctive nutritional requirements of a disease or condition, used under medical supervision, and intended for the specific dietary management of a disease or condition. Medical foods are not those simply recommended by a physician as part of an overall diet to manage the symptoms or reduce the risk of a disease or condition, and all foods fed to sick patients are not medical foods.[3] Instead, medical foods are foods that are specially formulated and processed (as opposed to a naturally occurring foodstuff used in a natural state) for a patient who is seriously ill or who requires use of the product as a major component of a disease or condition's specific dietary management.

2. Has FDA established by regulation any criteria that clarify the statutory definition of a medical food?

   Yes. The following criteria that clarify the statutory definition of a medical food can be found in FDA's regulations at 21 CFR 101.9(j)(8). A food is a medical food and is exempt from the nutrition labeling requirements of 21 CFR 101.9 only if:

   a. It is a specially formulated and processed product (as opposed to a naturally occurring foodstuff used in its natural state) for the partial or exclusive feeding of a patient by means of oral intake or enteral feeding by tube.[4]

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[2] See Food Labeling; Reference Daily Intakes and Daily Reference Values; Mandatory Status of Nutrition Labeling and Nutrition Content Revision proposed rule (56 FR 60366 at 60377, Nov. 27, 1991)).

[3] See 56 FR 60366 at 60377.

[4] Enteral feeding by tube refers to a tube or catheter that delivers nutrients beyond the oral cavity directly into the stomach or small intestine. It should not be confused with parenteral (or intravenous) nutrient formulations which are regulated by FDA as drugs.

b. It is 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 or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone;
c. It provides 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;
d. It is intended to be used under medical supervision; and
e. It is 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.

We discuss nutrition labeling requirements and medical foods in question 4 below.

3. Does FDA regulate medical foods as drugs?

No. Medical foods are not drugs and, therefore, are not subject to any regulatory requirements that specifically apply to drugs. For example, medical foods do not have to undergo premarket review or approval.

4. Do the labeling requirements for nutrient content claims and health claims apply to medical foods?

No. Medical foods are exempt from the labeling requirements for health claims and nutrient content claims under the Nutrition Labeling and Education Act of 1990 (see 21 U.S.C. 343(q)(5)(A)(iv)).

5. What labeling requirements apply to medical foods?

Medical foods are foods and, therefore, their labeling must comply with all food labeling requirements except for those specific requirements from which medical foods are exempt. Specifically, the labeling of medical foods must contain a statement of identity (the 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 business of the manufacturer, packer, or distributor (21 CFR 101.5), and a complete list of ingredients, listed by their common or usual name and in descending order of predominance (21 CFR 101.4). In addition, all words, statements, and other information required by or under authority of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) to appear on a label or labeling of a medical food must appear with prominence and conspicuousness (21 CFR 101.15) and be in English except that,

for medical foods distributed solely in the Commonwealth of Puerto Rico or in a Territory where the predominant language is one other than English, the predominant language may be substituted for English (21 CFR 101.15(c)(1)). If a label bears any representation in a foreign language, then all mandatory label information must be repeated in each foreign language used on the label (21 CFR 101.15(c)(2)). Medical foods also must be labeled in conformance with the principal display panel requirements (21 CFR 101.1), the information panel requirements (21 CFR 101.2), and the misbranding of food requirements (21 CFR 101.18).

6. What other FDA requirements apply to medical foods?

   Medical foods must comply with all applicable FDA requirements for foods, including the Current Good Manufacturing Practice regulations (21 CFR part 110), Registration of Food Facilities regulations (21 CFR part 1 Subpart H) and, if applicable, regulations specific to the product formulation and processing, such as the Thermally Processed Low-Acid Foods Packaged in Hermetically Sealed Containers regulations (21 CFR part 113), Acidified Foods regulations (21 CFR part 114) and Emergency Permit Control regulations (21 CFR part 108).

7. Does the Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA) apply to medical foods?

   Yes. FALCPA's labeling requirements apply to all packaged foods, including medical foods.

8. Where can I find more information on FALCPA's labeling requirements?

   You can find more information on FALCPA's labeling requirements on FDA's Web site.

9. Do medical foods have to be registered or does FDA maintain a list of medical foods?

   Any facility engaged in manufacturing, processing, packing, or holding medical foods for consumption in the United States must register with FDA. Facilities do not have to identify their specific medical food products to FDA when they register.[5] You can find additional information regarding the registration of food facilities on FDA's Web site at

[5] See section 415 of the FD&C Act (21 U.S.C. 350d).

http://www.fda.gov/food/guidancecomplianceregulatoryinformation/registrationoffoodfacilities/default.htm. FDA does not maintain a list of medical food products.

10. Is there a compliance program guidance manual for medical foods?

    Yes. You can find a copy of FDA's compliance program guidance manual entitled "Medical Foods Program - Import and Domestic" on FDA's Web site.

11. What is the purpose of FDA's compliance program for medical foods?

    FDA's compliance program provides direction for FDA inspectors to: (1) obtain information regarding the manufacturing/control processes and quality assurance programs employed by domestic manufacturers of medical foods through establishment inspections; (2) collect domestic and import surveillance samples of medical foods for nutrient and microbiological analyses; and (3) recommend action when significant violations of the FD&C Act (or related regulations) are found.

12. Does FDA require that medical foods be made available by written or oral prescription?

    No. The requirement for a written or oral prescription in section 503(b) of the FD&C Act and its implementing regulations at 21 CFR 201.100 only applies to the dispensing of prescription drug products. The Orphan Drug Act provides that medical foods must be formulated to be consumed or administered enterally under the supervision of a physician. In addition, FDA's regulations clarifying the statutory definition of a medical food provide that a medical food is a food that is intended to be used under medical supervision and is 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 (21 CFR 101.9(j)(8)(iv) and (v)). However, FDA does not interpret either the Orphan Drug Act or FDA's implementing regulations at 21 CFR 101.9(j)(8) to require that medical foods be made available by prescription. Instead, the statute requires that a medical food be consumed or administered enterally *under the supervision of a physician*. FDA considers this requirement to mean that the intended use of a medical food is for the dietary management of a patient receiving active and ongoing medical supervision (e.g., in a health care facility or as an outpatient) of a physician who has determined that the medical food is necessary to the patient's overall medical care. The patient should generally see the physician on a recurring basis for, among other things, instructions on the use of the medical food. FDA does not consider foods that are simply recommended by a physician or other health care professional

as part of an overall diet designed to reduce the risk of a disease or medical condition or as weight loss products to be medical foods.[6]

13. May the labeling of a medical food bear the symbol "Rx only?"

The labeling of medical foods may not bear the symbol "Rx only." Section 503(b)(4)(A) of the FD&C Act (21 U.S.C. 353(b)(4)(A)) provides that a prescription drug is misbranded if the label of the drug fails to bear, at a minimum, the symbol "Rx only." Section 503(b)(4)(B) of the FD&C Act further provides that a drug that is not a prescription drug is misbranded if the label of the drug bears the symbol "Rx only." The requirements about the symbol "Rx only" were added to the FD&C Act by section 126 of the Food and Drug Administration Modernization Act of 1997 (FDAMA). Prior to the enactment of FDAMA, section 503(b)(4) of the FD&C Act provided that a prescription drug was misbranded unless its label bore the statement "Caution: Federal law prohibits dispensing without prescription." FDAMA amended section 503(b)(4) of the FD&C Act to remove the requirement for this caution statement and instead to require the "Rx only" symbol.

The requirement that the labeling of prescription drugs bear the symbol "Rx only" replaced the requirement that the labeling of prescription drugs bear the statement "Caution: Federal law prohibits dispensing without prescription."[7] Section 126 of FDAMA made no substantive changes to section 503(b)(4) of the FD&C Act other than to replace the longer caution statement with the symbol "Rx only." FDA concludes that, in making this amendment to section 503(b)(4) of the FD&C Act, Congress intended for the symbol "Rx only" to communicate the same message to consumers that the longer caution statement communicated -- specifically, that federal law prohibited a prescription drug product from being dispensed without a prescription. Therefore, the symbol "Rx only" is not to be used in the labeling of products that are not prohibited by federal law from being dispensed without a prescription.

Medical foods are not prohibited by federal law from being dispensed without a prescription. Therefore, the use of the symbol "Rx only" in the labeling of a medical food would misbrand a medical food under section 403(a)(1) of the FD&C Act because it would be a false statement about that product. However, because medical foods are required by statute to be formulated to be consumed or administered

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[6] See, e.g., 56 FR 60366 at 60377.

[7] See, e.g., 65 FR 81081 at 81100 (Dec. 22, 2000).

enterally *under the supervision of a physician*, FDA would not object to the use of language to communicate this requirement in the labeling of a medical food product that is otherwise not false or misleading (e.g., "must be used under the supervision of a physician").

14. Should National Drug Code numbers be used in the labeling of medical foods?

    The labeling of medical foods should not include National Drug Code (NDC) numbers. Drug products are identified and reported using a unique, three-segment number, called the NDC, which is a universal product identifier for human drugs.[8] NDC numbers are intended for uniquely identifying drugs and should not be used in the labeling of medical foods. The presence of an NDC number on a product that is not a drug may be a false or misleading representation that misbrands the product under section 403(a)(1) of the FD&C Act. In addition, FDA considers any representation that creates an impression of official FDA approval through the use of an NDC number in labeling to be misleading.[9]

15. What requirements apply to ingredients added to medical foods?

    An ingredient that is added to a medical food must be safe and suitable and comply with all applicable provisions of the FD&C Act and FDA's regulations. Any ingredient added to a medical food should be (1) a food additive used in accordance with FDA's food additive regulations (see 21 CFR 172); (2) a color additive used in accordance with the color additive regulations (see 21 CFR 73 and 74); (3) a substance that is generally recognized, by qualified experts, to be safe under the conditions of its intended use (Generally Recognized As Safe, GRAS) (see 21 CFR 170.30 and 21 U.S.C. 321(s)); or (4) a substance that is authorized by a prior sanction issued by FDA (see 21 CFR 170.3(l)).

16. Where can I find additional information on food additives and generally recognized as safe (GRAS) ingredients?

    Additional information on food additives and GRAS ingredients can be found under the food topic "Ingredients, Packaging & Labeling" on FDA's Web site..

17. Does FDA generally consider inborn errors of

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[8] See section 510(e) of the FD&C Act (21 U.S.C. 360(e)); 21 CFR 207.35.

[9] See 21 CFR 207.39.

metabolism (IEMs) to be diseases or conditions that a medical food could be used to manage?

Yes. FDA generally considers inborn errors of metabolism (IEMs) to be diseases or conditions that a medical food could be used to manage. Inborn errors of metabolism include inherited biochemical disorders in which a specific enzyme defect interferes with the normal metabolism of protein, fat, or carbohydrate. As a result of diminished or absent enzyme activity in these disorders, certain compounds accumulate in the body to toxic levels and levels of others that the body normally makes may become deficient (Ref. 1). Without appropriate and accessible management, these metabolic disturbances can lead to a host of medical and developmental consequences ranging from intellectual disability to severe cognitive impairment and even death (Ref. 1). Management may include one or a combination of the following: drug therapy, modification of the normal diet, or use of a medical food.[10]

Some of these disorders can be managed with modification of the normal diet alone (e.g., reduction of galactose and lactose for galactosemia). However, others cannot be managed solely with diet modification. For these IEMs, a medical food is required in addition to a specific dietary modification (e.g., reduced total protein/phenylalanine for phenylketonuria) in order to obtain adequate levels of essential nutrients which are restricted by modifying the normal diet. Medical foods become indispensable for individuals with these IEMs in order to meet the daily requirements of essential nutrients and to limit the metabolic disturbances associated with the particular IEM (e.g., see Q. 18). Therefore, if a product meets the definition of a medical food, it could be used in the management of some IEMs.

18. Are there any examples of specific IEMs that medical foods could be used to manage?

Yes. Some examples of specific IEMs that medical foods could be used to manage involve amino acid/protein, organic acid, or fatty acid metabolism. These IEMs primarily require significant restriction of particular amino acids and/or total protein such as in phenylketonuria (phenylalanine restriction), ornithine transcarbamylase deficiency (nonessential amino acid restriction), methylmalonic acidemia (isoleucine,

[10] Medical foods may also include infant formulas used for inborn errors of metabolism which are regulated as exempt infant formulas under section 412(h)(1) of the FD&C Act; 21 CFR 107.50)

methionine, threonine, and valine restriction), or significant modification of fatty acids/total fat such as in very long-chain acyl-CoA dehydrogenase deficiency (long chain fatty acid restriction with an increase in medium chain fatty acid levels).

19. Does FDA consider pregnancy to be a disease?

    FDA does not consider pregnancy to be a disease.[11]

20. Are there nutrient requirements associated with pregnancy?

    Yes. The Institute of Medicine (IOM) established nutrient recommendations for pregnancy. Pregnancy is one of the twelve life stage groups identified by the IOM. For each life stage group, where data were available, IOM established dietary reference intakes (DRIs) to apply to the healthy general population. DRIs are standards for apparently healthy people and are not meant to be applied to those with acute or chronic disease or for the repletion of nutrient levels in previously deficient individuals (Ref. 2).

21. Does FDA consider pregnancy to be a condition for which a medical food could be labeled and marketed?

    Under 21 CFR 101.9(j)(8)(ii), a medical food must be intended for a patient who has a limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone. While a specific individual diet alone *may* not supply the full amount of nutrients necessary for women who are pregnant or planning to become pregnant, generally the levels of micronutrients necessary for pregnancy *can* be achieved by the modification of the normal diet alone. It is generally practicable for women who are pregnant or planning to become pregnant to follow the IOM and FDA recommendations for nutrient intake within a normal diet. Therefore, FDA generally would not consider a product labeled and marketed for pregnancy (rather than a specific disease or condition associated with pregnancy) to meet the regulatory criteria for a medical food.

22. Are there nutrient requirements associated with the management of type 1 and type 2 Diabetes Mellitus (DM)?

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[11] See, e.g., 65 FR 999 at 1000 (Jan. 6, 2000); 63 FR 23623 at 23627 (Apr. 29, 1998).

Yes. Patients with type 1 DM should use carbohydrate counting or the carbohydrate exchange system to match insulin dose to carbohydrate intake and facilitate physiologic insulin replacement. Patients with type 2 DM should restrict calories, eat regularly, increase fiber intake, and limit intake of refined carbohydrates and saturated fats (Ref. 3).

23. Does FDA consider type 1 or type 2 DM to be conditions for which a medical food could be labeled and marketed?

    No. Diet therapy is the mainstay of diabetes management. A regular diet can be modified to meet the needs of an individual affected by either type of DM (along with appropriate drug therapy if necessary). Under 21 CFR 101.9(j)(8)(ii), a medical food must be intended for a patient who has a limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone. Therefore, FDA generally would not consider a product labeled and marketed for DM to meet the regulatory criteria for a medical food.

24. Does FDA consider diseases resulting from essential nutrient deficiencies (e.g., scurvy, pellagra) to be diseases for which a medical food could be labeled and marketed?

    No. Classical nutrient deficiency diseases (e.g., scurvy, pellagra) that result from essential nutrient deficiencies (e.g., deficiencies of vitamin C, niacin) are typically caused by inadequate intake (e.g., famine, significant calorie restriction, eating disorders, alcoholism, diet practices/fad diets). The deficiencies, excluding any permanent physical damage, can typically be corrected once foods with these essential nutrients (or dietary supplements, if necessary) are made available and consumed.

    Because such diseases can typically be managed through dietary modification alone, FDA generally would not consider a product labeled and marketed for these diseases to meet the regulatory criteria for a medical food (see 21 CFR 101.9(j)(8)(iii)).

25. Does FDA consider conventional foods that do not ordinarily contain protein or are ordinarily low in protein to meet the definition of a medical food?

    No. Conventional foods such as fruits, certain vegetables, fats, and sugars generally are not specially formulated to not contain protein or to be significantly low in protein -- instead, they are low in protein in their natural state. Under 21 CFR 101.9(j)(8)(i), a medical food must be a specially formulated and processed product (as opposed to a

naturally occurring foodstuff used in its natural state) for the partial or exclusive feeding of a patient by means of oral intake or enteral feeding by tube. Therefore, conventional foods that do not ordinarily contain protein or are ordinarily low in protein would not meet the regulatory criteria for medical foods.

III. References

We have placed the following references on display in the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You may see them at that location between 9 a.m. and 4 p.m., Monday through Friday.

1. Camp, K., Lloyd-Puryear, M., Huntington, K. Nutritional treatment for inborn errors of metabolism: Indications, regulations, and availability of medical foods and dietary supplements using phenylketonuria as an example. Molecular Genetics and Metabolism, 107 (2012) 3-9.

2. Otten, J., Hellwig, J., Meyers, L. eds. Institute of Medicine. Dietary Reference Intakes. The Essential Guide to Nutrient Requirements, Parts 1: Development and Application, Introduction to the Dietary Reference Intakes and Applying the Dietary Reference Intakes, p. 13, 2006.

3. Porter, Robert S., ed. The Merck Manual of Diagnosis and Therapy, 19th ed. New Jersey: Merck, 2011, p. 872.