Frequently Asked Questions About Medical Foods; Third Edition

Guidance for Industry

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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
Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or we) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

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 third edition of the May 2007 guidance titled "Guidance for Industry: Frequently Asked Questions About Medical Foods."

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe our 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?

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 (21 CFR 101.9(j)(8)). Medical foods are distinguished from the broader category of foods for special dietary use 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

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

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. Not all foods fed to patients with a disease, including diseases that require dietary management, are medical foods. 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 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 medical food 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, meaning a tube or catheter that delivers nutrients beyond the oral cavity directly into the stomach or small intestine;[2]
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 questions 4 to 6 below.

[2] Enteral feeding can be achieved by oral intake or by tube. Enteral feeding by tube refers to a tube or catheter that delivers nutrients beyond the oral cavity directly into the stomach or small intestine. These enteral feedings should not be confused with parenteral (or intravenous) nutrient formulations.

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.

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

Medical foods are exempt from the labeling requirements for nutrient content claims under the Nutrition Labeling and Education Act of 1990 (see 21 U.S.C. 343(r)(5)(A)). As with any food, a medical food that bears a false or misleading claim would be considered misbranded under section 403(a)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

5. Do the labeling requirements for health claims apply to medical foods?

Medical foods are exempt from the labeling requirements for health claims under the Nutrition Labeling and Education Act of 1990 (see 21 U.S.C. 343(r)(5)(A)). As with any food, a medical food that bears a false or misleading claim would be considered misbranded under section 403(a)(1) of the FD&C Act.

6. What labeling requirements apply to medical foods?

The labeling for medical foods must comply with all applicable 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 (21 CFR 101.3);
- An accurate statement of the net quantity of contents (21 CFR 101.7);
- The name and place of business of the manufacturer, packer, or distributor (21 CFR 101.5);
- A complete list of ingredients, listed by their common or usual name and in descending order of predominance (21 CFR 101.4); and
- Allergen information, if necessary (section 403(w) of the FD&C Act)

In addition, all words, statements, and other information required by or under authority of 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)). Further, 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 food labels must also conform with the principal display panel requirements under 21 CFR 101.1 and the applicable information panel requirements under 21 CFR101.2. Further, the requirements concerning the misbranding of food (21 CFR 101.18) apply to medical foods.

7. What other FDA requirements apply to medical foods?

Manufacturers of medical foods must comply with all applicable FDA requirements for foods, including the following regulations:

- Current good manufacturing practice (21 CFR part 110);
- Registration of food facilities (21 CFR part 1 subpart H);
- Thermally processed low-acid foods packaged in hermetically sealed containers (21 CFR part 113);
- Acidified foods (21 CFR part 114); and
- Emergency permit control (21 CFR part 108).

8. Do the allergen labeling requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) apply to medical foods?

Yes. The allergen labeling requirements of the FD&C Act apply to all foods other than raw agricultural commodities, including medical foods.

9. Where can I find more information on the allergen labeling requirements of the FD&C Act?

You can find more information on FDA's Web site and the following links:

https://www.fda.gov/food/food-labeling-nutrition/food-allergies

https://www.fda.gov/food/guidance-documents-regulatory-information-topic-food-and-dietary-supplements/food-allergensgluten-free-guidance-documents-regulatory-information

10. What are the registration requirements for medical food facilities?

Any facility engaged in manufacturing, processing, packing, or holding medical foods for consumption in the United States must register with FDA.[3] You can find additional information regarding the registration of food facilities on FDA's Web site.

11. Does FDA maintain a list of medical foods?

FDA does not maintain a comprehensive list of medical food products.

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

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

Yes. FDA has a compliance program guidance manual entitled "Medical Foods Program - Import and Domestic" that is available on FDA's Web site.

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

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

14. 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, but there is no requirement for a prescription.

15. How does FDA interpret "under the supervision of a physician"?

FDA considers the requirement that a medical food be formulated to be consumed or administered enterally under the supervision of a physician 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) by 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 as part of the dietary management of a given disease or condition.

16. 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" to indicate that the product may not lawfully be dispensed without a prescription. Unlike prescription drugs, medical foods are not required by federal law to be dispensed by 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 and misleading statement about that product. However, because medical foods are required by statute to be formulated to be consumed or administered

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 not false or misleading (e.g., "must be used under the supervision of a physician").

17. Should National Drug Code (NDC) numbers be used in the labeling of medical foods?

The labeling of medical foods should **not** include 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.[4] NDC numbers are intended for uniquely identifying drugs and should not be used in the labeling of medical foods since they are not drugs. The presence of an NDC number on a food product that is not a drug misbrands the product under section 403(a)(1) of the FD&C Act. In addition, any representation that creates an impression of official FDA approval through the use of an NDC number in labeling constitutes misbranding.[5]

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

An ingredient that is added to a medical food should be safe and in compliance with all applicable provisions of the FD&C Act and FDA 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 part 172); (2) a color additive used in accordance with the color additive regulations (see 21 CFR parts 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 (see 21 CFR 170.3(l), 21 U.S.C. 321(s)(4)).

19. Where can I find additional information on food additives and GRAS ingredients?

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

20. Does FDA generally consider inborn errors of metabolism (IEMs) to be diseases or conditions that a medical food could be used to manage?

Yes. FDA generally considers IEMs to be diseases or conditions that a medical food could be used to manage. IEMs 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 other compounds that the body normally makes may become deficient (Ref. 1). Without

[4] See section 510(e) of the FD&C Act (21 U.S.C. 360(e)); 21 CFR 207.35.
[5] See 21 CFR 207.39.

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.[6]

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 in order to obtain adequate levels of essential nutrients (e.g., essential amino acids, essential fatty acids) that 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 question 21).

21. 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, 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).

22. Does FDA consider pregnancy to be a disease?

FDA does not consider pregnancy to be a disease.[7]

23. Are there distinctive nutritional requirements associated with pregnancy?

No. There are no distinctive nutritional requirements associated with pregnancy. Essential nutrient requirements to support pregnancy can be met by diet modification. The Institute of Medicine (IOM) established nutrient recommendations to meet essential nutrient requirements associated with 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

[6] Medical foods may also include infant formulas used for IEM which are regulated as exempt infant formulas under section 412(h)(1) of the FD&C Act; 21 CFR 107.50.
[7] See, e.g., 65 FR 999 at 1000 (Jan. 6, 2000); 63 FR 23623 at 23627 (Apr. 29, 1998).

to be applied to those with acute or chronic disease or for the repletion of nutrient levels in previously deficient individuals (Ref. 2).

24. 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 some diets *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 to meet the regulatory criteria for a medical food.

25. Are there distinctive nutritional requirements associated with the management of diabetes mellitus (DM)?

No. There are no distinctive nutritional requirements associated with the management of DM. Essential nutrient requirements for individuals affected by DM are no different than those for unaffected (generally healthy) persons. Following an individualized healthy, well-balanced diet is crucial to managing conditions such as DM. There are nutritional recommendations established for persons to manage DM (Refs. 3, 4, and 5).

26. Does FDA consider DM to be a condition 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 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.

27. 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. Diseases (e.g., scurvy, pellagra) that result from essential nutrient deficiencies (e.g., deficiencies of vitamin C, niacin) are primarily 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/or consumed. Because such diseases can typically be managed through consumption of a healthy, well-balanced diet, FDA generally would not consider a product labeled and marketed for these diseases to meet the statutory and regulatory criteria for a medical food (see 21 CFR 101.9(j)(8)(ii)).

28. Does FDA consider conventional foods that, in their natural state, do not contain protein or are 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 be significantly low in protein or to contain no 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 statutory and regulatory criteria for medical foods.

III. References

We have placed the following references on display in the Dockets Management Staff, 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. As of April 12, 2016, FDA had verified the Web site address for the references it makes available as hyperlinks from the Internet copy of this guidance, but FDA is not responsible for any subsequent changes to Non-FDA Web site references after April 12, 2016.

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, 107:3-9, 2012. Available: http://www.ncbi.nlm.nih.gov/pubmed/22854513.

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3. American Diabetes Association. Nutrition Therapy Recommendations for the Management of Adults With Diabetes. A Position Statement of the American Diabetes Association. Diabetes Care, 37(1):S120-S143, January 2014. Available: http://care.diabetesjournals.org/content/37/Supplement_1/S120.full.pdf+html.

4. Standards of Medical Care in Diabetes 2016, American Diabetes Association, Diabetes Care. 39 (Supplement 1): S1-S112, January 2016. Available: http://professional.diabetes.org/content/clinical-practice-recommendations.

5. Centers for Disease Control and Prevention. Eat Right! www.cdc.gov/diabetes/consumer/eatright.htm (accessed April 12, 2016).

Document History

May 2007 – First edition of guidance was issued.
May 2016 – Second edition of guidance was issued.
March 2023 – Third edition. The guidance was updated to include updates on allergens.