HEALTHCARE NUTRITION COUNCIL

Healthcare Nutrition Council (HNC) is an advocate for patient access to enteral and parenteral nutrition products. HNC continues to educate and collaborate with legislative and regulatory policymakers, patient and consumer advocacy groups, academia, industry, and other stakeholders to promote awareness of the impact of nutrition on health for vulnerable populations.

# Medical Foods

### Importance of Medical Foods for Patients

Medical foods play a critical role in supporting the nutritional needs of those with certain conditions and/or rare diseases. **Inborn errors of metabolism** are examples of metabolic conditions which prevent individuals from metabolizing nutrients in a normal way, necessitating the need for medical foods to meet the nutritional needs of the individual in order to prevent clinical complications and to sustain life. For example, **phenylketonuria (PKU)** is a condition, occurring in 1 in 25,000 infants in the U.S.,[1] which prohibits the individual from being able to metabolize phenylalanine causing it to accumulate in the body at harmful levels which could cause permanent cognitive impairment. **Maple syrup urine disease (MSUD)** is another inborn error of metabolism occurring in less than 1 in 185,000 infants worldwide.[2] In this condition, branched amino acids and the corresponding keto acids accumulate in the blood and can cause life-threatening seizures, coma, and brain damage.

In both of these conditions, it is impractical for individuals to modify their diets to carefully control their intake of the offending amino acid(s) while still meeting their nutritional needs, without the use of medical foods. Medical foods provide the nutrition needed to support growth and development while managing the symptoms of their condition. PKU and MSUD are just two of many inborn errors of metabolism which require the use and consumption of medical foods.[3]

Other patients may rely on medical foods related to a "distinctive nutritional requirement" by reason of **physical impairment** associated with a disease or condition such as **stroke, head or neck cancer, or gastrointestinal surgery** interfering with the ability to consume food required to maintain health. For example, patients who cannot consume food orally must rely on adjustments in the delivery of the food to enable nutritional intake (e.g., enteral tube feeding). These patients often rely on the sole source of their nutritional intake from medical foods. These formulas are designed to meet the sole source of nutrition and are processed in such a way to ensure they can be safely fed through a feeding tube.

Enteral nutrition (EN) is a well-established recommended therapy for people with **Crohn's disease** and **inflammatory bowel disease (IBD)**. In Crohn's disease, EN prior to surgery reduces post-operative complications by reducing inflammation, improving nutritional status, and decreasing the antigenic load through bowel rest. The benefits of exclusive EN for the induction of remission of active Crohn's disease have been well described over the last decades and is now recommended in international guidelines as the first line of therapy for children or adolescents with active Crohn's disease. A review of adult patients with stricturing Crohn's disease managed with preoperative exclusive EN found 25% of patients had stricture resolution **eliminating the need for surgery** while those who still required surgery had shorter operations, reduced period of time to recommence oral intact postoperatively, and **fewer surgical complications**. Enteral tube feeding improves total energy intake and prevents malnutrition. EN is recommended by healthcare professionals for Crohn's disease and is optimal for a non-pharmacological approach.[4,5,6,7]

### Distinctive Nutritional Requirements

"Distinctive nutritional requirements" (DNR) is a critical term in the medical food statutory definition. Determining whether a medical food can be developed and marketed is dependent on whether a disease or condition results in a DNR.[8]

## What is a Medical Food?

The term medical food was defined in 1988 as part of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)) amendments, thus creating a category distinct from the broader category of foods for special dietary use (FSDU). The term medical food was defined "...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."

## Examples of Medical Foods

- Sole source tube feeding formulas
- Metabolic formulas intended for patients with inborn errors of metabolism which require dietary management
- Renal-tailored specialized nutrition for patients with kidney disease

## Medical Food Regulatory Timeline[9]

- **In 2016** the FDA published final guidance on medical foods intended to help manufacturers better understand the regulations.
- **In 2004** the FDA withdrew the advance notice of proposed rulemaking (ANPRM) owing to limited resources, and it is no longer under active consideration.
- **In 1996** the FDA recognized the need to re-examine the regulatory framework of medical foods and published an ANPRM announcing its intent to re-evaluate the medical food definition.
- **In 1993**, the final Nutritional Labeling and Education Act (NLEA) rule enumerated regulatory criteria that medical foods should meet for exemption from the nutritional labeling requirements of 21 CFR 101.9.
- **In 1990**, the NLEA exempted medical foods from the nutrition labeling requirements applicable to conventional foods.
- **In 1988**, the Orphan Drug Act was amended and created a statutory definition of medical food (21 USC 360ee(b)(3)).
- **In late 1972**, the phenylketonuria (PKU) product was moved to the category of foods for special dietary use (FSDUs).
- **Before 1972**, medical foods were regulated as drugs by the FDA. This included a nutrition product to help manage PKU, an inborn error of metabolism.

## Existing and Proposed Interpretations of Distinctive Nutrient Requirements[10]

| A Physiologic Interpretation of DNR by the FDA[11] | An Alternative Interpretation of DNR by the FDA[12] | A Modernized Interpretation of DNR as proposed by the Healthcare Nutrition Council |
|---|---|---|
| "...the distinctive nutritional needs associated with a disease 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 the disease process on absorption, metabolism, and extraction. These distinctive nutritional requirements may be greater than, less than, or in a narrower range of tolerance than for an otherwise healthy individual." | "...those requirements that result from a disease or condition that cause a physical or physiological limitation in the ability of a person to ingest or digest conventional sources and result in that person needing specially formulated foods to meet part or all of their daily nutrients needs." | The clinical need for a specific nutritional intake (compared with the intake of healthy populations) which may exist by reason of abnormal physiologic manifestation or physical impairment associated with a disease or condition, the dietary management of which results in clinically meaningful improvements, including but not limited to nutritional status, health outcomes, or quality of life.* |

## 3 Pillars to a Patient-Centric Approach to Defining Distinctive Nutritional Requirements[13]

| Focus on patients' complete nutritional requirements beyond just nutrient levels. | Keep positive health outcomes for patients as the core goal. | Recognize that the continuum of disease severity can amplify the need for medical foods. |
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| • Narrows the medical foods category to high-quality products formulated to a high standard of scientific rigor.<br>• Allows for sufficient flexibility to support innovation. | • Places patients' needs and quality of life first.<br>• Gives people living with disease the right to utilize medical foods to improve the quality of their medical care. | • Recognizes that patients with severe disease may have additional comorbidities and increased risk of malnutrition.<br>• Prevents patients on the severe end of the disease spectrum from being precluded access to medical foods. |

## Different FDA Regulatory Categories

| Conventional Food | Dietary Supplement | Foods for Special Dietary Use (FSDU) | Medical Foods |
|---|---|---|---|
| The mainstay of the diet. FDA has clearly defined labeling regulations for foods (NLEA).** | To supplement the diet. FDA has definitions for dietary supplements from the 1994 Dietary Supplement and Health Education Act (DSHEA).*** Defined in Section 201(ff) of the Federal Food, Drug, and Cosmetic Act (21 USC 321(ff)). | Meets a special dietary need. Defined in 21 CFR 105.3(a)(1). Must follow FDA food labeling regulations (NLEA). Additional labeling related to the special dietary usefulness in disease is not explicitly defined. | Dietary management of a disease. Exempt from NLEA labeling to enable labeling tailored to the needs of the medical community. Labeling related to the dietary management of the disease is permitted. |

Food is medicine initiatives should consider the use of FSDU and medical foods.

* This would include maintaining homeostasis and prevention of disease progression.

** NLEA: Nutrition Labeling and Education Act. In 1990, NLEA exempted medical foods from the nutrition labeling health claim, and nutrient content claim requirements applicable to most other foods. In 1993, food labeling regulations implementing NLEA identified 5 criteria for medical foods (21 CFR 101.9(j)(8)).

*** DSHEA provided a statutory definition for dietary supplements, distinguishing them from conventional foods. It removed these products from the category of FSDU. It did **not** bring these products under the definition of medical foods.

## References


1. National Institutes of Health (NIH). U.S. National Library of Medicine. MedlinePlus. "Phenylketonuria." Retrieved from: https://medlineplus.gov/genetics/condition/phenylketonuria/#frequency.
2. National Institutes of Health (NIH). U.S. National Library of Medicine. MedlinePlus. "Maple syrup urine disease." Retrieved from: https://medlineplus.gov/genetics/condition/maple-syrup-urine-disease/#frequency.
3. Susan A. Berry, Christine S. Brown, Carol Greene, Kathryn M. Camp, Stephen McDonough, Joseph A. Bocchini and on behalf of the Follow-up and Treatment (FUTR) Workgroup for the Advisory Committee on Heritable Disorders in Newborns and Children. Medical Foods for Inborn Errors of Metabolism: History, Current Status, and Critical Need. Pediatrics. March 2020, 145 (3) e20192261; DOI: https://doi.org/10.1542/peds.2019-2261.
4. Di Caro S, Fragkos KC, Keetarut K, Koo HF, Sebepos-Rogers G, Saravanapavan H, Barragry J, Rogers J, Mehta SJ, Rahman F. Enteral Nutrition in Adult Crohn's Disease: Toward a Paradigm Shift. Nutrients. 2019 Sep 14;11(9):2222. doi: 10.3390/nu11092222.
5. Heerasing N, Thompson B, Hendy P, et al. Exclusive enteral nutrition provides an effective bridge to safer interval elective surgery for adults with Crohn's disease. Aliment Pharmacol Ther. 2017;45:660–669. doi: 10.1111/apt.13934
6. Wall CL, Day AS, Gearry RB. Use of exclusive enteral nutrition in adults with Crohn's disease: a review. World J Gastroenterol. 2013;19:7652–7660. doi: 10.3748/wjg.v19.i43.7652.
7. Day AS, Lopez RN. Exclusive enteral nutrition in children with Crohn's disease. World J Gastroenterol. 2015;21:6809–6816. doi: 10.3748/wjg.v21.i22.6809.
8. Katie Chmielecki, Berit Dockter, Wendy Johnson, Madeline Jurch, Pamela Pacht, Jena Rostorfer. What is a "Distinctive Nutritional Requirement"? A Position Paper of the Healthcare Nutrition Council. *Current Developments in Nutrition*. Volume 7, Issue 11, 2023, 102013, ISSN 2475-2991, https://doi.org/10.1016/j.cdnut.2023.102013.
9. Jennifer L Holmes, Alexandre Biella, Timothy Morck, Jena Rostorfer, Barbara Schneeman, Medical Foods: Science, Regulation, and Practical Aspects. Summary of a Workshop, *Current Developments in Nutrition*, Volume 5, Issue Supplement_1, January 2021, nzaa172, https://doi.org/10.1093/cdn/nzaa172.
10. *Ibid Chmielecki et al.*
11. Food and Drug Administration. "Regulation of Medical Foods." Federal Register Vol. 61, No. 231 (November 29, 1996): 60661 – 60671.
12. Food and Drug Administration. "Regulation of Medical Foods." Federal Register Vol. 61, No. 231 (November 29, 1996): 60661 – 60671.
13. *Ibid Chmielecki et al.*