
Healthcare Nutrition Council

529 14th Street, NW • Suite 750 • Washington, DC 20045

December 3, 2018

Division of Dockets Management
HFA-305
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA-2014-N-1721 for “Agency Information Collection Activities; Proposed Collection; Comment Request; Investigational New Drug Applications.”

Dear Dockets Management Staff,

The Healthcare Nutrition Council (HNC)* submits these comments in response to the U.S. Food and Drug Administration’s (FDA) Notice “Agency Information Collection Activities; Proposed Collection; Comment Request; Investigational New Drug Applications” (Docket No. FDA-2014-N-1721).

Enclosed with this comment submission are previously submitted HNC comments, which were sent to the Center for Food Safety and Applied Nutrition and the Center for Drug Evaluation and Research on February 5, 2018 through FDA’s open docket. The detailed comments attached (point B specifically) outline HNC’s recommendations for repealing portions of the “Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs)”, in particular all portions related to foods including the section that indicates an investigation intended to evaluate the effects of a Medical Food on a disease would require an IND. HNC would like to highlight a few specific aspects of our comments below.

As the Agency solicits comments on information collection activities related to the clinical investigation of unapproved new drugs and biological products, HNC believes it is imperative to also address the significant regulatory burden that would be introduced for both industry and academia, as well as the overt conflict in statutory intent of the IND process, should nutrition research be required to follow the IND process. Moreover, An IND is by its very name intended only for an investigational new drug. Requiring an IND for conducting a study that involves nutritional research using food is unprecedented and unsupported by the Federal Food, Drug and Cosmetic Act. This is particularly true for research on the effect of Medical Foods on diseases, as Medical Foods are required by statute to be intended for the dietary management of a disease or condition. Investigation of a Medical Food’s effects on a disease does not inherently make that Medical Food a drug; rather, it comports with the intended use of Medical Foods set forth by statute.

Furthermore, it fails to address a legitimate public health need, significantly discourages both research and innovation, and incrementally and unnecessarily increases regulatory burden on industry, academic researchers and FDA. Requiring an IND significantly delays nutrition research timelines by requiring the upfront completion of an IND application from nutrition researchers who likely have no experience with the investigational drug process. The current IND guidance has created unnecessary obstacles for nutrition research in the area of Medical Foods and we feel it is important to note this concern as FDA collects information related to IND applications.

HNC previously recommended FDA repeal portions of the IND Guidance, specifically all portions related to foods including section VI(D) which indicates an investigation intended to evaluate the effects of a Medical Food on a disease (including the dietary management of a disease) would require an IND. We still strongly support that recommendation and encourage FDA to consider these aspects when collecting IND-related information for this open docket notice.

Thank you for the opportunity to provide comments on FDA’s Agency Information Collection. Please do not hesitate to contact me with any questions you may have.

Sincerely,



Nadia Cayce, PhD
Executive Director
Healthcare Nutrition Council

***About HNC:** *The Healthcare Nutrition Council (HNC) is an organization representing the manufacturers of enteral nutrition formulas, parenteral nutrition solutions, supplies and equipment. HNC member companies are Abbott Nutrition, B. Braun Medical, Nestlé Health Science and Nutricia North America. We are committed to improving health by advancing policies that address and raise awareness of nutrition and its impact on patient outcomes and healthcare costs. This includes promoting nutritional screenings, diagnoses, assessments and appropriate and timely nutrition clinical interventions while protecting patients' access to specialized nutrition support products and services throughout the continuum of care. For more information on HNC, please visit <https://healthcarenutrition.org>.*

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529 14th Street, NW • Suite 750 • Washington, DC 20045

February 5, 2018

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA-2017-N-5094 titled “Review of Existing Center for Food Safety and Applied Nutrition Regulatory and Information Collection Requirements”

To Whom It May Concern:

The Healthcare Nutrition Council (HNC)* appreciates the opportunity to submit comments to the Food and Drug Administration (FDA) regarding to its open docket titled “Review of Existing Center for Food Safety and Applied Nutrition Regulatory and Information Collection Requirements” (Docket No. FDA-2017-N-5094).

HNC applauds the FDA for being open to identifying existing regulations that could be modified, repealed, or replaced, aiming at achieving meaningful burden reduction while allowing the Agency to achieve its public health mission and fulfill its statutory obligations. One important FDA regulatory area HNC will address is Medical Foods. Medical Foods play an important role in the dietary management of patients with numerous diseases and conditions. Since the Medical Foods category was defined in 1988 (21 U.S.C. §360ee (b)(3)), several attempts to develop a clearer framework were initiated without necessarily leading to the needed result. HNC strongly believes there is a need for a broad and open dialogue with all concerned stakeholders (i.e., government, patients, manufacturers, academia and health care professionals) followed by firm and decisive actions to enact a comprehensive, efficient and science-based framework for Medical Foods. Additionally, we think that such reform would help resolve current ambiguities within the Medical Food category, modernize the category in accordance with advances in nutrition science, incentivize research and innovation in disease and nutrition, better address the evolving patient needs and reduce regulatory burden in areas where such burdens have not served a public health interest.

To achieve the ultimate goal of improving patient health outcomes, and echoing FDA Commissioner Scott Gottlieb on the FDA’s new policy steps related to stem cell therapies and regenerative medicine, “the FDA must advance an efficient and least burdensome framework as a way to help new products remain compliant with the law through a regulatory structure that does not become a barrier to beneficial new innovation”. FDA’s efforts on the Medical Foods framework should also maintain high ethical, quality and scientific standards and prevent unscrupulous actors from being able to deceive patients, caregivers and healthcare providers.

While HNC believes that a longer term modernization of the Medical Foods category is necessary, we would like to call FDA’s attention on the need to initially review and modify specific, unduly, and burdensome regulatory requirements forming the current framework of Medical Foods, resulting in an ambiguous environment that stifles research and innovation. Focusing on the following interim revisions

and recommendations could alleviate confusion and lead to a more efficient and less burdensome regulatory system:

- A. Repeal portion of 21 CFR 101.9(j)(8)(ii) and revise portion of 21 CFR 101.9(j)(8)(iii), the criteria for exempting Medical Foods from labeling and claims provisions established under the Nutrition Labeling and Education Act (NLEA) specifically, in subpart (ii), the portions which added "...the dietary management of which cannot be achieved by the modification of the diet alone" and in subpart (iii), "...provides nutritional support specifically modified for the management of unique nutrient needs that result from the specific disease or condition, as determined by medical evaluation."
- B. Repeal portions of "Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND", specifically all portions related to foods including section VI(D) which indicates an investigation intended to evaluate the effects of a Medical Food on a disease (including the dietary management of a disease) would require an IND.
- C. Revise "Frequently Asked Questions About Medical Foods; Second Edition, Guidance for Industry" as specified herein.

Detailed comments to follow:

- A. Repeal portion of 21 CFR 101.9(j)(8)(ii) and revise portion of 21 CFR 101.9(j)(8)(iii), the criteria for exempting Medical Foods from labeling and claims provisions established under the Nutrition Labeling and Education Act (NLEA) specifically, in subpart (ii), the portions which added "...the dietary management of which cannot be achieved by the modification of the diet alone" and in subpart (iii), "...provides nutritional support specifically modified for the management of unique nutrient needs that result from the specific disease or condition, as determined by medical evaluation."**

The suggestions are framed below in the format requested by the agency:

Food For Human Consumption: Food Labeling – Nutrition Labeling of Food, Exemptions for Medical Foods	
FDA Center	CFSAN
Citation	(1) 21 CFR 101.9(j)(8)(ii) (2) 21 CFR 101.9(j)(8)(iii)
Approved information collection and OMB Control Number (as applicable)	N/A
Brief description of concern	The criteria set forth for the exemptions of Medical Foods from the labeling and claims provisions established under the NLEA creates ambiguity and restricts innovation and at worst excessively constrains the types of products that FDA considers to be Medical Foods, even if they meet statutory

	definition. FDA constrains the types of products than can be considered Medical Foods by following a narrow interpretation.
Available data on cost or economic impact	Available Upon Request
Proposed solution	<p>(1) We recommend repealing a portion of 21 CFR 101.9(j)(8)(ii) that reads “...the dietary management of which cannot be achieved by the modification of the diet alone”, known as “MODA”, as it is not supported by the statutory definition of Medical Foods. This clause was codified in a labeling regulation, further elucidating the fact that it is often taken out of context in its use to narrowly constrain the Medical Food category.</p> <p>(2) HNC recommends revising a portion of 21 CFR 101.9(j)(8)(iii) to remove the words “unique nutrient needs that result from” from the phrase. The revised statement would read: “...provides nutritional support specifically modified for the management of the specific disease or condition as determined by medical evaluation”. This would address this inherent incoherence in 21 CFR 101.9(j)(8) in terms of different interpretations of “distinctive nutritional requirements” (DNR).</p>

21 CFR 101.9(j)(8) sets forth criteria for the exemptions of Medical Foods from the labeling and claims provisions established under NLEA. FDA often cites the criteria enumerated in this regulation as the requirements for a product to be classified as a Medical Food. This includes two specific requirements establishing that the product:

- “...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**” (emphasis added).
- “...provides nutritional support specifically modified for the management of the **unique nutrient needs** (emphasis added) that result from the specific disease or condition as determined by medical evaluation.”

FDA at best creates ambiguity and restricts innovation, and at worst, excessively constrains the types of products that FDA considers to be Medical Foods, on the basis of this clause, even though such products meet the statutory definition. FDA has acknowledged very few specific examples of diseases or conditions that would justify the use of a Medical Food include Phenylketonuria, food protein allergies and Very Long-Chain Acyl-CoA dehydrogenase deficiency. FDA’s interpretation is unduly restrictive, limiting advancements in Medical Foods which provide clinically meaningful improvements to patient health outcomes and reduce the overall cost of care for patients.

HNC requests FDA modify this regulation as noted in below:

- Repeal portion of 21 CFR 101.9(j)(8)(ii), specifically “**...the dietary management of which cannot be achieved by the modification of the normal diet alone**”.

- Revise portion of 21 CFR 101.9(j)(8)(iii) to “...provides nutritional support specifically modified for the management of **unique nutrient needs that result from** the (emphasis added) specific disease or condition, as determined by medical evaluation”

HNC requests these modifications out of consideration that:

- a) The term “modification of the normal diet alone” (MODA) itself does not have statutory basis. Specifically, this portion of the regulation (“...the dietary management of which cannot be achieved by the modification of the normal diet alone”) is not supported by the statutory definition of Medical Food and thus should not be tied to a determination of a product’s ability to meet the statutory definition of Medical Food. This clause was codified in a labeling regulation, further elucidating the fact that it is often taken out of context in its use to narrowly constrain the Medical Food category. The term Medical Food, as defined in section 5(b) 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”. Although Medical Food was first defined within the Orphan Drug Act, the definition does not limit the category only to rare diseases, nor is there evidence that this was the intent of Congress in carving out Medical Foods. However, FDA’s later addition of the overly restrictive “MODA” requirement has significantly limited the categories of diseases for Medical Foods beyond legislative intent.
- b) While in certain cases it could be theoretically possible to find alternative ways of satisfying the nutritional needs of patients for which the Medical Food is intended without consumption of the Medical Food, those alternatives might be unrealistic or not practical. FDA should consider whether it is difficult, impractical, cost-prohibitive, unsafe or nutritionally/clinically disadvantageous for the patients suffering from the specific diseases or medical conditions to satisfy their nutritional needs through the exclusive consumption of foods other than Medical Foods. Therefore, the phrase “the dietary management of which cannot be achieved by the modification of the normal diet alone”, a phrase referred to as “MODA”, needs to be pragmatically assessed on whether and to what extent it is possible to satisfy the nutritional needs of the patients suffering from a specific disease or medical condition without the Medical Food.ⁱ In addition, it is unclear what constitutes the “normal diet” under the regulation and FDA’s broad interpretation of the normal diet to include all foods and dietary supplements effectively prohibits manufacturers from communicating the health benefits of Medical Foods with the same or similar active ingredients of other foods or dietary supplements despite the fact that the Medical Foods are clinically proven to help manage certain diseases or conditions. Further, it is unclear how or whether FDA has considered the practicality, feasibility and sustainability of successfully modifying the “normal diet”, especially for those patients on the more severe end of the spectrum of a given disease, which could include multiple comorbidities that also result in necessary nutritional modifications. Repealing “MODA” is one step towards ensuring the Medical Food category is not unjustifiably limited and will spur further innovation of Medical Foods and improve public health.

- c) The unduly narrow interpretation of MODA conflicts with FDA’s goal of improving public health and ignores healthcare realities. The current interpretation results in a Medical Food category limited to only those products medically necessary to sustain life, rather than a category which includes (and allows for the development of) articles demonstrated to provide clinically meaningful improvements to disease dietary management. Patients are not successfully modifying their normal diet to manage many acute or chronic diseases or conditions, indicating that this regulation and FDA’s literal interpretation is not practical for the sustainability of disease dietary management. Most diseases include a spectrum of patients, ranging from those who live in the community and disease dietary management is monitored through outpatient care to those patients who fall on the severe end of the spectrum and must also account for nutritional implications of associated conditions and comorbidities, acute trauma or injury, are malnourished or at risk for malnutrition, and/or require tube feeding. FDA should encourage well-substantiated, safe nutritional therapies, as restricting options for alternative means of dietary management of acute or chronic diseases or conditions may contribute to health disparities, worsened outcomes, and increased healthcare costs.

This interpretation also deters research and innovation in the field of nutritional management of chronic diseases. Nutrition science and patient needs have evolved considerably since the enactment of the Orphan Drug Act and the codification of the Medical Food definition, and it has become increasingly clear that nutrition is a cornerstone to disease management.

- d) FDA recognizes in 21 CFR 101.9(j)(8) that a product intended for the dietary management of a patient who, because of therapeutic or chronic medical needs, has limited or impaired capacity to ingest, digest or absorb ordinary foodstuffs or certain nutrients can be classified as a Medical Food. However, it subsequently imposed a requirement for the product to meet “unique nutrient needs” which inherently creates a conundrum. This incompatibility as already mentioned, is being narrowly interpreted by FDA and unduly limiting advancements in Medical Foods.
- e) By removing “unique nutrient needs”, as proposed, FDA would address this inherent incoherence in 21 CFR 101.9(j)(8) and address the different interpretations of “distinctive nutritional requirements” (DNR). This would encompass those products intended for the dietary management of diseases or conditions associated with distinctive physiological nutrient requirements, as currently interpreted by FDA, and those intended for diseases and conditions affecting one’s ability to ingest, digest or absorb conventional foods. The examples below (non-exhaustive list) illustrate the different cases that could be covered by this proposed interpretation:
- An inability to take sufficient quantities of ordinary food: this may result from mechanical impairment or swallowing difficulties associated with a disease, condition or injury (e.g. head and neck cancer or surgery), or from neurological impairment associated with a stroke;
 - An inability to digest or absorb sufficient foods/nutrients: this may result from impairments of the gastrointestinal tract linked to a disease (e.g. short bowel syndrome) or a treatment (e.g. gastrectomy);
 - An inability to metabolize specific nutrients: this may result from inherited metabolic disorders such as phenylketonuria or Maple Syrup Urine Disease, where whole protein cannot be metabolized and its intake must be severely limited;

- An inability to excrete certain nutrients or their metabolites: this may result from diseases of the renal, liver or respiratory systems where it is important to control intakes of the offending nutrient to prevent build-up of toxic levels of the nutrients or their metabolites (e.g. phosphate and potassium for patients suffering from kidney failure)
- And other medically-determined nutrient requirements: these are specific nutrient requirements that are, based on medical evidence, linked to the particular disease/disorder/medical condition, such as increased requirements for protein or other specific nutrients (e.g. glutamine) in patients pre or post-surgery, with severe wounds, burns or pressure sores or in patients suffering from specific diseases (e.g. vitamin A for patients suffering from cystic fibrosis)ⁱⁱ

While HNC believes a longer term modernization of the Medical Foods category is necessary, focusing on the above revisions and recommendations is one step towards a more efficient and less burdensome regulatory system. Revising specific portions of the criteria for exempting Medical Foods from labeling and claims provisions established under NLEA will ensure the Medical Food category is not unduly restrictive but rather fosters the innovation of foods which not only help patients live, but help them live better, a philosophy that would align to FDA’s goals of improving public health. As we look to additional opportunities to expand upon these proposed changes to the Medical Foods category with FDA and other stakeholders, we encourage FDA to consider the above initial changes as steps toward a regulatory system that allows for product innovation while ensuring products remain compliant with the law.

B. Repeal portions of “Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND”, specifically all portions related to foods including section VI(D) which indicates an investigation intended to evaluate the effects of a medical food on a disease would require an IND.

The suggestions are framed below in the format requested by the agency:

Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs) – Determine Whether Human Research Studies Can Be Conducted Without an IND” (IND Guidance)	
FDA Center	CFSAN, CDER, CBER
Citation	21 CFR part 312
Approved information collection and OMB Control Number (as applicable)	N/A
Brief description of concern	We are concerned with certain sections of IND Guidance that relate to studies involving foods, specifically the fact that FDA would expect an IND for clinical studies evaluating the effects of a Medical Food on disease, including dietary management of disease. An IND is by its very name intended only for an investigational new <i>drug</i> . Requiring an IND for conducting a study that involves nutritional research and food is unprecedented and unsupported by the Federal Food, Drug and Cosmetic

	Act, particularly for research on the effect of Medical Foods on diseases, as Medical Foods are required by statute to be intended for the dietary management of a disease or condition. Requiring an IND also significantly delays nutrition research timelines by requiring the upfront completion of an IND application from nutrition researchers who likely have no experience with the investigational drug process. This has created unnecessary obstacles for nutrition research in the area of Medical Foods. HNC has several additional concerns that are outlined in detail below.
Available data on cost or economic impact	Available Upon Request
Proposed solution	HNC recommends FDA repeal portions of the IND Guidance, specifically all portions related to foods including section VI(D) which indicates an investigation intended to evaluate the effects of a Medical Food on a disease (including the dietary management of a disease) would require an IND.

We appreciated the Agency re-opening the final guidance as described above (hereafter referred to as IND Guidance) for public review and comment in February 2014, given the previous version of the IND Guidance had never before referenced food investigations. This provided the research community with an opportunity to comment and elaborate on important distinctions between food-related research and drug-related research. Numerous comments submitted to FDA expressed serious concerns about the food-related aspects of the IND Guidance and its implementation. The final version of the IND Guidance represents a fundamental change in FDA’s interpretation and application of food regulations (especially the delineation between food and drug definitions) and the investigation of the role of nutrition in health, both of which are now having broad implications on clinical research in the U.S. Specifically, FDA concluded in the IND Guidance that an investigation intended to evaluate the effects of a Medical Food on a disease would require an IND because such an investigation would be evaluating a drug use. However, this conclusion directly conflicts with the statutory purpose of a Medical Food, which is to assist *in the dietary management of a disease or condition*. Investigation of a Medical Food’s effects on a disease does not inherently make that Medical Food a drug; rather, it comports with the intended use of Medical Foods set forth by statute.

Although FDA eventually stayed portions of the final IND Guidance in October, 2015, HNC still remains concerned about its intent and effect on clinical investigation of Medical Foods consistent with the statutory definition, especially the new, misplaced burden on Institutional Review Boards (IRBs) and academia. Requiring an IND for conducting a study that involves nutritional research and food is unprecedented and unsupported by the Federal Food, Drug and Cosmetic Act (FD&C Act), particularly for research on the effect of Medical Foods on diseases, as Medical Foods are required by statute to be intended for the dietary management of a disease or condition. Furthermore, it fails to address a legitimate public health need, significantly discourages both research and innovation, and incrementally and unnecessarily increases regulatory burden on industry, academic researchers and FDA. IRBs have long served the purpose of certifying that appropriate procedures are in place to ensure the ethical conduct of clinical research and protect the safety and interests of clinical research subjects. Further, nutrition and food research is distinct from research related to the development of new drugs as there is no intent to market foods as drugs or make drug claims, and the authority under which FDA regulates each is likewise distinguishable: IND requirements pertain to drugs and not foods, and evaluating the effects of a Medical Food on a disease does not inherently cause that Medical Food to be a drug.

Despite FDA’s partial stays on certain sections of the IND Guidance that relate to studies involving foods, a key section communicating that FDA would expect an IND for clinical studies evaluating the effects of a Medical Food on disease remains in effect. Because Medical Foods are, by statutory definition, intended for the dietary management of diseases or conditions, this has created unnecessary obstacles for nutrition research in the area of Medical Foods. As IRBs and researchers attempt to comply with the IND Guidance in good faith, the lack of clarity is causing confusion and unnecessarily burdening important clinical research and innovation. Implying or otherwise stating that the IND requirements now apply to food and nutrition research, including research conducted on Medical Foods, results in objectionable consequences. These include but are not limited to:

- **The addition of new regulatory and resource burdens:** The IND process would significantly delay nutrition research timelines by requiring upfront completion of an IND application from nutrition researchers who likely have no experience with the investigational drug process, awaiting FDA approval of an IND application, and ultimately slowing time-to-market for any innovative developments that stem from such nutritional research. FDA’s processing and approval of an IND in these cases is also complicated by the fact that although the Center for Drug Evaluation and Research (CDER) routinely processes INDs for clinical studies on drugs, this Center has yet to establish a standard procedure for processing INDs for foods. Likewise, the Center for Food Safety and Applied Nutrition (CFSAN) is lacking a formal process to receive, review and act upon an IND Application.
- **FDA Overstepping of Statutory Authority:** There is a lack of consistency between the IND Guidance and the FD&C Act’s statutory definition of food, as there is no basis in FDA’s statutory authority for requiring an IND application for food and nutritional research. The definitions in the FD&C Act establish a clear distinction between drugs and foods. Congress did not grant FDA the authority to require an IND for foods in the FD&C Act. A food that is contemplated to be tested in a clinical trial to assess whether it affects the structure or any function of the body of man remains a “food” under the FD&C Act. This remains true for Medical Foods, which are expressly intended for the dietary management of a specific disease or condition; clinical evaluation of a Medical Food’s use in the dietary management of disease or condition is *not* evaluation of a drug use, but rather evaluation of a Medical Food use. The intended use of a Medical Food is not to treat, cure, mitigate, diagnose or prevent a disease and Medical Foods cannot be marketed as such. Further, requiring an IND for the clinical research of Medical Foods directly contradicts Congressional intent of the Orphan Drug Act in removing Medical Foods from the drug category (21 U.S.C. §360ee).
- **Failure to Address a Legitimate Public Health Need:** Force-fitting applicable IND rules onto food and nutrition research, the IND Guidance significantly increases regulatory complexity to multiple stakeholders in this field and, at the same time, does not address any identified public health problem. Identifying such a public health need is ordinarily a prerequisite for a new rule or substantive change in policy. If FDA is concerned with violative disease claims, the Agency can take other more appropriate enforcement actions instead of unnecessarily constraining clinical research. Even after the partial, temporary stays this IND Guidance may continue to negatively impact the quality and quantity of scientific evidence necessary to adequately inform

the development of new and innovative Medical Foods. The impact may not be isolated to food manufacturers and marketers, but could also create hurdles for individual academic research and the conduct of clinical research necessary to develop, update and refine health claims, dietary guidelines and nutrient requirements, which inform public health policy. Furthermore, requiring an IND for new research does nothing to attenuate violative Medical Foods currently in the marketplace.

- **The Conflict With and Violation of the FD&C Act:** The FD&C Act defines drugs, in part, according to the article’s “intended use” and distinguishes such articles from those that are otherwise classified as foods. More specifically:
 - Section 201 of the FD&C Act (21 U.S.C. §321) defines “food” and “drug” in relevant part as follows:
 - (f) The term “food” means (1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.
 - (g)(1) The term “drug” means ... (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (**other than food**) intended to affect the structure or any function of the body of man or other animals.... (**emphasis added**).

The parenthetical phrase “(other than food)” in the definition of drug draws a clear line with respect to a food being studied for its potential to affect the structure or any function of the body of man. Any such food is not a “drug,” but remains a “food” for all relevant purposes under the FD&C Act. The IND Guidance, however, conflates these two different statutory classifications. HNC recognizes that the IND Guidance carved out studies evaluating the intended structure or function effect when such effect is derived from the nutritive value of the food (either taste, aroma, or nutritive value) and also recognizes that FDA later stayed the portion of the IND Guidance which implicated studies evaluating the intended structure or function effect when such effect is *not* derived from taste, aroma, or nutritive value. However, the IND Guidance appears to narrowly interpret structure or function derived from nutritive value to studies which essentially quantify serum nutrient levels (example given is a study of the effect of iron consumed through food on hemoglobin levels) but considers studies evaluating a food or food component’s physiological effect as intended drug research (example given is a study of the effect of soy isoflavones on bone metabolism). This is entirely inconsistent with the historical interpretation industry has come to understand regarding a food’s role on the structure or function of the body. Further, it’s inconsistent with the well-understood connection of food and health and would unduly limit the advancement of nutrition science through research. Although this portion is stayed, it continues to promulgate confusion in the nutrition arena, including research involving Medical Foods when the endpoint is physiological in nature.

Further, FDA’s attempt to broaden the scope of the IND requirements to cover studies being conducted on foods (including Medical Foods) lacks credibility when these products can legally be commercially distributed. Section 505 of the FD&C Act, 21 U.S.C. §355, “New Drugs,” generally prohibits new drugs from being introduced into interstate commerce without an approval from FDA. In order to put an unapproved drug in interstate commerce for clinical testing purposes, new drugs are subject to Section 505(i) of the FD&C Act. This Section contains the statutory language requiring

FDA to promulgate regulations to establish procedures for filing, and FDA approval of, IND Applications.

(i)(1) The Secretary shall promulgate regulations for exempting from the operation of the [new drug application requirements] drugs intended solely for investigational use by experts qualified by scientific training and expertise to investigate the safety and effectiveness of drugs

The corresponding regulation promulgated by FDA, 21 C.F.R. Part 312, entitled “Investigational New Drug Application” has a “Scope” and “Applicability” section that limits the coverage of the regulations to “drugs”:

312.1 Scope. (a) This part contains procedures and requirements governing the use of investigational new drugs, including procedures and requirements for the submission to, and review by, the Food and Drug Administration of investigational new drug applications (IND’s).

312.2 (a) Applicability. Except as provided in this section, this part applies to all clinical investigations of products that are subject to section 505 of the Federal Food, Drug and Cosmetic Act...

Section 505 of the FD&C Act does not prohibit the shipment of foods (including Medical Foods) in interstate commerce, and, as discussed above, the investigation of a Medical Food as part of the dietary management of a disease or condition does not make that Medical Food a drug. Therefore, an exemption from the New Drug provisions of the FD&C Act pursuant to an Investigational New Drug Application for such articles is not supported within the scope of this regulation.

- **Failure to Comply With Both the Administrative Procedures Act and the Congressional Review Act:** FDA must comply with the Administrative Procedures Act (APA) when it seeks to change its practices and established policies on which products are subject to the IND requirements. The issuance of the IND Guidance marked the first time FDA expressly stated that foods are subject to the IND regulations. FDA may not depart from a precedent without providing reasoned explanation for the change. (*Greyhound Corp. v. ICC*, 551 F.2d 414, 416 (D.C. Cir. 1977)). The APA requires notice-and-comment rulemaking whenever a federal agency wants to act in a way that materially changes established burdens and benefits, “by which rights or obligations have been determined, or from which legal consequences will flow.” (*Bennett v. Spear*, 520 U.S. 154, 178 (1997)). FDA was acting to substantively change the “rights and obligations” of food manufacturers and nutritional researchers by extending the IND requirements to articles of food, including Medical Foods when being investigated for use in the dietary management of a disease (which does not make such products “drugs”). Additionally, FDA must comply with the Congressional Review Act when it issues any statement – even in the form of a Guidance Document – of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency” (5 U.S.C. § 551(4)). Despite FDA’s

classification of the IND Guidance as final, before it can become effective, FDA must submit a report to both Houses of Congress and to the Comptroller General.

Requiring an IND to study the effects of Medical Foods on the dietary management of disease, when these products can legally be commercially distributed as foods makes little sense and does not seem to offer any benefit to the study subjects, IRBs, investigators, FDA, public health, or safety of the food supply. Therefore, HNC recommends FDA repeal portions of the IND Guidance, including section VI(D), which indicates an investigation intended to evaluate the effects of a Medical Food on the dietary management of a disease would require an IND, even though Medical Foods must, by statute, be intended for the dietary management of a disease or condition.

C. Revise “Frequently Asked Questions About Medical Foods; Second Edition, Guidance for Industry”

The suggestions are framed below in the format requested by the agency:

Frequently Asked Questions About Medical Foods; Second Edition, Guidance for Industry	
FDA Center	CFSAN
Citation	Medical Food Guidance, 21 CFR 101.9(j)(8)
Approved information collection and OMB Control Number (as applicable)	N/A
Brief description of concern	The FAQ about Medical Foods; Second Edition Guidance for Industry imposes presumptions on specific diseases and conditions that fail to meet the statutory criterion of “distinctive nutritional requirements”; however, FDA has not appropriately defined “distinctive nutritional requirements”. Determinations as to whether particular diseases or conditions fail to meet the definition of “distinctive nutritional requirements” would be premature at this time.
Available data on cost or economic impact	Available Upon Request
Proposed solution	HNC recommends revising the “Frequently Asked Questions About Medical Foods; Second Edition, Guidance for Industry” to reflect the proposals outlined in sections (A) of HNC’s comments. In addition, we suggest removing the sections referring to “distinctive nutritional requirements” until such a time that FDA is able to appropriately define “distinctive nutritional requirements” in partnership with relevant stakeholders.

HNC suggests the “Frequently Asked Questions About Medical Foods; Second Edition, Guidance for Industry” (hereafter referred to as the Medical Foods Guidance) be revised to reflect the proposals outlined in part (A) above.

In addition, HNC respectfully suggests to remove those sections in which FDA imposes a presumption that specific diseases or conditions fail to meet the statutory criterion of “distinctive nutritional requirements” until such time that FDA is able to appropriately define “distinctive nutritional requirements” in partnership with all relevant stakeholders. More specifically, HNC is aware that FDA is sponsoring a workshop planned by the National Academies of Science, Engineering and Medicine in April 2018, titled “Examining Special Nutritional Requirements in Disease States.” The purpose of this workshop is to initiate the scientific exploration of what constitutes a special nutritional requirement for a disease, and what type of scientific evidence is needed to establish the existence of the special nutritional requirement. It is evident that this workshop is intended to help shape the scientific framework for nutrient needs and disease management. HNC applauds FDA’s efforts to initiate and engage in a broader scientific dialogue on this matter and looks forward to participating in this critical effort to advance both the scientific framework but also patient health through modernization of the Medical Food category. However, HNC respectfully suggests that determinations as to whether particular diseases or conditions fail to meet the definition of “distinctive nutritional requirements” would thus be premature at this time. For this reason, the Medical Foods Guidance should be revised to remove these sections.

In summary, HNC believes that the regulatory framework of Medical Foods needs to evolve to reflect the latest advancements and understanding in the science of nutrition, foster innovation and accelerate the access of patients to safe and effective products. The above revisions and recommendations are just the start of a broader dialogue HNC looks forward to having with FDA and all relevant stakeholders. As significant progress is being made on science-based, evidence-driven approaches to develop nutritional products, like Medical Foods, to help patients with the dietary management of certain diseases and conditions, the regulatory framework needs to provide a clear, consistent and scientifically sound path for these products to reach the patients who need them the most. It is critical that the FDA, its inter-agency offices and related Agencies continue focusing on ways to reduce, modify and/or repeal regulations that inhibit innovation while maintaining high ethical, quality, and scientific standards for the Medical Foods category. Implementing the above recommendations is the first step towards an efficient, less burdensome and innovative regulatory system. We respectfully request that the above recommendations be taken into consideration as FDA works to achieve its goals. HNC looks forward to having continued discussions with FDA in the near future. Please do not hesitate to contact me at 202-207-1122 or mjurch@kellencompany.com if you have any questions regarding these comments or if any additional information may be helpful.

Sincerely,

/s/

Madeline Jurch, Government Affairs Manager

***About HNC:** The Healthcare Nutrition Council (HNC) is an organization representing the manufacturers of enteral nutrition formulas, parenteral nutrition solutions, supplies and equipment. HNC member companies are Abbott Nutrition, B. Braun Medical, Nestlé Health Science and Nutricia North America. We are committed to improving health by advancing policies that address and raise awareness of nutrition and its impact on patient outcomes and healthcare costs. This includes promoting nutritional screenings, diagnoses, assessments and appropriate and timely nutrition clinical interventions while protecting patients' access to specialized nutrition support products and services throughout the continuum of care. For more information on HNC, please visit <https://healthcarenutrition.org>.

References

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