BEFORE THE
UNITED STATES FOOD AND DRUG ADMINISTRATION

In re Comments in Response to Draft Guidance for Industry on Frequently Asked Questions About Medical Foods; Second Edition	**FDA Docket No. FDA-2013-D-0880-0001**

COMMENTS OF THE ALLIANCE FOR NATURAL HEALTH-USA

The Alliance for Natural Health-USA (ANH) hereby submits its comments in response to the FDA's request in the above-referenced docket. The docket references the availability of a draft guidance for industry entitled "Frequently Asked Questions About Medical Foods; Second Edition" ("Draft Guidance"). According to the FDA, that Draft Guidance provides "responses to additional questions regarding the definition, labeling, and availability of medical foods…" *See* 78 Fed. Reg. 49271 (Aug. 13, 2013).

ANH is a Virginia nonprofit corporation founded in 1992. Formerly the American Association for Health Freedom, and, before that, the American Preventative Medical Association, ANH is a membership-based organization consisting of consumers, healthcare practitioners, food, medical food, and dietary supplement company members, and over 240,000 consumer advocate members. ANH focuses on the protection and promotion of access to information and products in the market concerning the actual and potential benefits of healthy foods, dietary nutrition, and a healthy lifestyle. By educating the general public and ANH members about the actual and potential benefits of a healthy diet and lifestyle, as well as natural ingredients and clinical nutrition, ANH strives to arm consumers with the information necessary to make informed market selections and take personal responsibility for their health. ANH aims to prevent disease, use nutrition to help manage chronic diseases, reduce the incidence of medical intervention, and reduce the public cost of healthcare in the United States. Among ANH's members are companies that sell medical foods, including medical foods for the dietary management of Diabetes Mellitus types 1 and 2, and other illnesses or disease states caused, associated with, or begat by nutrient deficiencies and metabolic etiologies.

Background

FDA lacked a statutory definition for the term "medical food" until Congress amended the Orphan Drug Act in 1988. Prior to 1972, FDA regulated such products, including the infant formula Lofenalac® (a product intended for the dietary management of phenylketonuria ("PKU")), as prescription drugs. 61 Fed. Reg. 60661, 60662 (Nov. 29, 1996). FDA regulated medical foods as drugs, in part, because the products addressed the adverse effects of underlying diseases. *Id.* FDA wanted medical foods administered with physician supervision. *Id.*; Rani H. Singh, *The Enigma of Medical Foods*, 92 Molecular Genetics and Metabolism 3 (2007).[1] As a result, FDA required manufacturers of medical foods to proceed through the costly drug approval process before marketing their nutritional products. *See* Sing, *supra*, at 3. Medical foods were thus, unsurprisingly, "very limited in number and were being produced by a small number of … manufacturers[.]" 61 Fed. Reg. at 60662.

In 1972, FDA relaxed standards for medical foods by reclassifying them as foods for "special dietary use."[2] *See id.*; John M. Talbot, *Guidelines for the Scientific Review of Enteral Food Products for Special Medical Uses*, 15 J. of Parenteral and Enteral Nutrition i (1991). FDA revised its regulatory approach because health care professionals had widely accepted the usefulness of foods in patient populations, such products were safe when used under physician supervision, and nutritional formulation requirements became better understood and established in the medical community. *See* 61 Fed. Reg. at 60662. FDA also sought to encourage innovation and product development so that medical foods would be more readily available and reasonably priced. *See id.*

FDA distinguished medical from conventional foods because healthy individuals would receive inadequate nutrition if they consumed medical foods as a substitute for the daily diet. *See id.* Because medical foods were distinct from conventional foods, FDA exempted medical foods from mandatory nutrition labeling requirements. *See* 38 Fed. Reg. 2124, 2126 (Jan. 19, 1973) (noting that nutrition labeling developed for foods intended for consumption by the general population was not well-suited for all food products, including foods represented for use solely under medical supervision in the dietary management of specific diseases and disorders).

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[1] *Available at* http://www.georgiapku.org/PDFfiles/singh%20mgm%202007%20enigmaMFs.pdf (last accessed Oct. 14, 3013).

[2] Under FDA's current regulations, "special dietary uses" include, *inter alia*, "[u]ses for supplying particular dietary needs which exist by reason of a physical, physiological, pathological or other condition, including but not limited to the conditions of diseases, convalescence, pregnancy, lactation, allergic hypersensitivity to food, underweight, and overweight." 21 C.F.R. § 105.3(a)(1).

The Orphan Drug Amendments of 1988 provided the first statutory definition of "medical food":

> The term "medical food" means 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.

21 U.S.C. § 360ee(b)(3). That definition appeared in the Orphan Drug Amendments because certain medical foods were considered "orphans" in the sense that they generally treat rare disorders affecting less than 200,000 individuals in the United States. *See* Sing, 92 Molecular Genetics and Metabolism at 3. Nonetheless, in the Orphan Drug Act, Congress intended to enlarge the manufacturing market and encourage development of medical foods.

Congress subsequently incorporated the "medical food" definition originally contained in the Orphan Drug Amendments into the Nutrition Labeling Education Act of 1990 ("NLEA"). The NLEA exempted medical foods from nutrition labeling, health claim prior approval requirements, and nutrient content claim requirements applicable to conventional foods. *See* 21 U.S.C. § 343(q)(5)(A)(iv). FDA proposed regulations to implement the NLEA in 1991. *See* 56 Fed. Reg. 60366 (Nov. 27, 1991).

Because Congress did not clarify the definition of a medical food in the legislative history of the Orphan Drug Amendments, FDA explained in the preamble to the proposed NLEA regulations that it "considers the statutory definition of medical foods to narrowly constrain the types of products that can be considered to fall within [the nutrition labeling] exemption." *Id*. at 60377. FDA intended to use its expertise on medical foods and a survey of literature to clarify the definition and provide criteria for identifying medical foods. *Id*. In the proposed regulations, FDA paraphrased the basic requirements for a medical food under the Orphan Drug Amendments. Specifically, FDA stated:

> In general, to be considered a medical food, a product must, at a minimum, meet the following criteria: The product must be a food for oral or tube feeding; the product must be labeled for the dietary management of a specific medical disorder, disease, or condition for which there are distinctive nutritional requirements; and the product must be intended to be used under medical supervision[.]

Id. FDA then clarified the terms in the statutory definition. *See id*. (clarifying FDA's interpretation of "formulated,"[3] "enteral,"[4] "under the supervision of a physician,"[5] "distinctive nutritional requirements,"[6] "and "dietary management"[7]). Third, FDA added new criteria to identify medical foods. *See id*. For example, FDA stated that medical foods are not intended for medical disorders, diseases, or conditions that can be managed by the "modification of the normal diet alone," which severely limited the broad definition contained in the Orphan Drug Amendments. *Id*. That latter requirement was not tethered to any specific empirical market analysis, and did not necessarily reflect the full use of medical foods underlying Congressional impetus for adoption of the Orphan Drug Act. For instance, FDA offered no defined delineation of when "modifications" to the normal diet would be sufficient to give rise to a "medical food." FDA's proposed "criteria" were similar to those contained in the definition of "foods for special medical purposes" the Codex Alimentarius Commission adopted in 1991. *See* Codex Stan. 180-1991 (Codex Standard for the Labelling of and Claims for Foods for Special Medical Purposes).[8]

In 1993, FDA published a final rule implementing the NLEA's exemption of medical foods from nutritional labeling requirements. *See* 58 Fed. Reg. 2079 (Jan. 6, 1993). That final rule reiterated the statutory definition of "medical food" appearing in the Orphan Drug Act, and offered criteria to clarify when a medical food qualifies for the nutrition labeling exemption. *See*

[3] "Medical foods are foods that are specially formulated and processed (as opposed to a naturally occurring foodstuff used in its natural state) . . ." 56 Fed. 60366, 60377 (Nov. 27, 1991).

[4] "Enteral nutrition is defined as nutrition provided through the gastrointestinal tract, taken by mouth, or provided through a tube or catheter that delivers nutrients beyond the oral cavity (i.e., directly to the stomach)[.]" 56 Fed. at 60377.

[5] "Under the supervision of a physician means 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). The physician determines that the medical food is necessary to the patient's overall medical care. The patient sees the physician on a recurring basis for, among other things, instructions on the use of the medical food." 56 Fed. at 60377.

[6] "Medical foods are intended for the partial or exclusive dietary management of patients under medical supervision who, because of specific therapeutic or chronic medical needs, have limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients, or who have other special medically determined nutrient requirements . . ." 56 Fed. at 60377.

[7] "Medical foods are intended for the dietary management of such patients by providing nutrition specifically modified to include as many nutrients as necessary while minimizing adverse signs and symptoms that might result from the provision of other nutrients that are not ingested, digested, absorbed, or metabolized normally by the patient[.]" 56 Fed. at 60377.

[8] The Codex standard defines "foods for special medical purposes" as:

> [A] category of foods for special dietary uses which are specially processed or formulated and presented for the dietary management of patients and may be used only under medical supervision. They are intended for the exclusive or partial feeding of patients with limited or impaired capacity to take, digest, absorb or metabolize ordinary foodstuffs or certain nutrients contained therein, or who have other special medically-determined nutrient requirements, whose dietary management cannot be achieved only by modification of the normal diet, by other foods for special dietary uses, or by a combination of the two.

21 C.F.R. § 101.9(j)(8). Specifically, the final rule stated that a medical food, as defined in the Orphan Drug Act, is exempt from nutrition labeling requirements contained in section 101.9 only if:

> (i) 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;
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> (ii) 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;
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> (iii) 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;
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> (iv) It is intended to be used under medical supervision; and
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> (v) 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.

21 C.F.R. § 101.9(j)(8).

On August 13, 2013, FDA revised its Draft Guidance, which, *inter alia*, answers the following question: "What is a medical food?" FDA answered that question consistent with its prior description of medical foods in the NLEA implementing regulations in 1991. Specifically, FDA states in the Draft Guidance:

> 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. 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. 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.

The Draft Guidance also addressed five criteria contained in 21 C.F.R. § 101.9(j)(8). According to FDA, those criteria not only clarify the statutory definition of a medical food, but also must be satisfied before a product can be marketed as a medical food. The agency's interpretation conflicts with the literal meaning of section 101.9(j)(8). *Compare* 21 C.F.R. § 101.9(j)(8) (stating that a food is a medical food if it meets the definition in 21 U.S.C. § 360ee(b)(3) and that such food is exempt from nutrition labeling requirements if it satisfies the five criteria contained in section 101.9(j)(8)(i)-(v)), *with* Draft Guidance (stating that a food *is* a medical food and is exempt from the nutrition labeling requirements only if it satisfies the five criteria contained in section 101.9(j)(8)(i)-(v)). The former defines a medical food using the definition in 21 U.S.C. § 360ee(b)(3), whereas the latter defines a medical food using the criteria in 21 C.F.R. § 101.9(j)(8)(i)-(v).

FDA's position in the Draft Guidance also differs from its past interpretation of section 101.9(j)(8) and its explanation of the minimum requirements for a medical food. *See, e.g.*, 56 Fed. Reg. at 60377 ("In general, to be considered a medical food, a product must, *at a minimum*, meet the following criteria: The product must be a food for oral or tube feeding; the product must be labeled for the dietary management of a specific medical disorder, disease, or condition for which there are distinctive nutritional requirements; and the product must be intended to be used under medical supervision[.]") (emphasis added); 61 Fed. Reg. at 60663 ("The regulation provides that a food may claim the exemption from nutrition labeling requirements only if it meets the following criteria in §101.9(j)(8) . . .").

Rather than *define* "medical foods," the five criteria contained in section 101.9(j)(8) are *added* requirements that a medical food, as defined under the Orphan Drug Amendments, must satisfy to be exempt from nutrition labeling requirements. Failure to satisfy the criteria in section 101.9(j)(8) only means that a product must bear Nutrition Facts labeling, not that the product cannot be marketed as a medical food. In fact, the plain meaning of the statutes and regulations reveal that a product meeting the statutory definition of a medical food is, in fact, a "medical food." Because the Draft Guidance provides otherwise, FDA violates the statutory definition of a "medical food," and imposes substantive legal obligations on the regulated class beyond those authorized by Congress and beyond those permitted in the exercise of agency discretion under the Administrative Procedure Act. *See, e.g.,* 5 U.S.C. § 553 (b)-(d) (prohibiting arbitrary and capricious agency action and abuses of agency discretion).

The Draft Guidance does not, therefore, offer an "interpretation" of the pre-existing law, or an interpretive policy, but creates a new substantive rule[9] that is both procedurally and substantively defective. The following requirements, which FDA says in the Draft Guidance must be met for a food to be a medical food, are not found in either the statute, 21 U.S.C. § 360ee(b)(3), or in the prior rule adopted through notice and comment rulemaking, 21 C.F.R. § 101.9(j)(8):

- Requiring all medical foods to be processed, as opposed to just formulated;
- Requiring all medical foods to be intended only for diseases or conditions that cannot be managed by "modification of the normal diet alone"; and
- Requiring all medical foods to be "intended only for a patient receiving active and ongoing medical supervision wherein the patient requires medical care on a recurring basis for, among other things, instructions on the use of the medical food."

[9] Although labeled a "guidance," this document, like many other guidances adopted by the FDA, in fact is designed to define new standards for regulation. By not mirroring standards established by statute and promulgated by rulemaking, following notice and comment, the agency makes an end run around the Administrative Procedure Act,thus acting in an arbitrary and capricious fashion open to judicial challenge. *See Sierra Club v. Johnson*, 541 F.3d 1257, 1265 n.3 (11th Cir. 2008); *United States v. Franck's Lab, Inc.*, 816 F. Supp. 2d 1209, 1211 (M.D. Fla. 2011), order vacated, appeal dismissed (Oct. 18, 2012) (vacated as moot).

21 C.F.R. § 101.9(j)(8). Rather, heretofore those requirements have not defined a medical food but only the circumstance when a medical food has been exempt from the nutrition labeling requirements contained in section 101.9.[10]

The unilateral, sua sponte transformation of the labeling criteria into conditions precedent to what constitutes a medical food violates the Administrative Procedure Act, which forbids the agency from promulgating new substantive rules without following the rulemaking notice and comment procedures required by that statute. *See* 21 C.F.R. § 10.115(e).

I. FDA's Present Enforcement of the Draft Guidance Violates the APA's Notice-and-Comment Requirements

The FDA is presently enforcing the new standard articulated in the guidance, a further confirmation that the standard is a substantive rule. *See*, *e.g.*, FDA Ltr. to Metagenics, Inc. (Aug. 13, 2013). The Administrative Procedures Act ("APA") requires that FDA follow notice-and-comment procedures prior to promulgating a legislative rule, also referred to as a substantive rule.[11] *See* 5 U.S.C. § 553 (b)-(d) (notice-and-comment rule making procedures include, *inter alia*, publishing a notice in the *Federal Register* and giving "interested persons" an opportunity "to participate in the rule making through submission of written data, views, or arguments"). The APA, however, exempts from the notice-and-comment procedures "interpretive rules [and] general statements of policy[.]" *Id*. at § 553(b). Legislative rules, interpretive rules, and general statements of policy have varying procedural requirements:

(1) **Legislative Rules:** A "legislative rule" has "the force and effect of law." *Appalachian Power Co. v. E.P.A.*, 208 F.3d 1015, 1020 (D.C. Cir. 2000). Moreover, legislative rules "grant rights, impose obligations, or produce other significant effects on private interests;" "narrowly constrict the discretion of agency officials by largely determining the issue addressed"; and "have substantive legal effect." *Batterton v. Marshall*, 648 F.2d 694, 701–02 (D.C. Cir. 1980).

(2) **Interpretive Rules:** An "interpretive rule" is "merely a clarification or explanation of an existing statute or rule." *Guardian Fed. Sav. & Loan Assn.*

[10] Certain criteria in section 101.9(j)(8) mirror the statutory requirements that a food must satisfy to be a medical food. For example, both the statutory definition and the nutrition labeling exemption require that medical foods be used under medical supervision. *See* 21 C.F.R. § 101.9(j)(8)(iv); 21 U.S.C. § 360ee(b)(3).

[11] A "rule" includes "the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy[.]" 5 U.S.C. § 551(4).

> *v. Fed. Sav. & Loan Ins. Corp.,* 589 F.2d 658, 664 (D.C. Cir. 1978) (citing *e.g., Pickus v. U.S. Bd. of Parole,* 507 F.2d 1107, 1113 (D.C. Cir. 1974)). For a rule to be interpretive, "the rule must be interpreting something. It must 'derive a proposition from an existing document whose meaning compels or logically justifies the proposition. The substance of the derived proposition must flow fairly from the substance of the existing document.'" *Cent. Tex. Tel. Coop., Inc. v. Fed. Commun. Commn.,* 402 F.3d 205, 212 (D.C. Cir. 2005) (quoting Robert A. Anthony, *"Interpretive" Rules, "Legislative" Rules, and "Spurious" Rules: Lifting the Smog,* 8 ADMIN. L. REV. 1, 6 n. 21 (1994)).

(3) **General Statements of Policy:** "General statements of policy" are "'statements issued by an agency to advise the public prospectively of the manner in which the agency proposes to exercise a discretionary power.'" *Chrysler Corp. v. Brown,* 441 U.S. 281, 302, n. 31 (quoting Attorney General's Manual on the Administrative Procedure Act 30, n. 3 (1947)).

According to FDA, the Draft Guidance represents the agency's current thinking on the topic, but "does not create or confer any rights for or on any person and does not operate to bind FDA or the public." *See* Draft Guidance. Similarly, FDA also claims that the Draft Guidance "do[es] not establish legally enforceable responsibilities . . . and should be viewed only as recommendations." *Id*. FDA's characterization of the Draft Guidance misleads and is not controlling. *See Gen. Motors Corp. v. Ruckelshaus*, 742 F.2d 1561, 1565 (D.C. Cir. 1984) (an "agency's own label, while relevant, is not dispositive").

FDA's assertion to the contrary notwithstanding, the Draft Guidance is a legislative rule subject to notice-and-comment rulemaking procedures under the APA. The Draft Guidance is a legislative rule because it has effectively amended the definition of a medical food by stating that a food is a medical food only if it satisfies the criteria contained in 21 C.F.R. § 101.9(j)(8), including the criterion that the dietary management of the disease or condition "cannot be achieved by the modification of the normal diet alone." It is a legislative rule because FDA intends it to govern the regulated class and to be relied upon by its own enforcement agents in their review of regulatee compliance. It is a legislative rule because even before finalization of the draft guidance, FDA is in fact using the criteria therein to guide its present enforcement against the regulated class. Rather than merely clarifying or explaining an existing statute or rule, e.g., 21 U.S.C. § 360ee(b)(3) or 21 C.F.R. § 101.9(j)(8), FDA has effectively amended the statute with newly required elements, elements that conflict with the plain meaning of the Orphan Drug Amendments and the nutrition labeling regulation, and thus, the Draft Guidance

takes the form of an illegal legislative rule. *See*, *e.g.*, *Am. Mining Cong. v. Mine Safety & Health Admin.,* 995 F.2d 1106, 1112 (D.C. Cir.1993) (a rule that effectively amends a prior legislative rule is a legislative, not an interpretative rule); *U.S. Telecom Assn. v. F.C.C.*, 400 F.3d 29, 34–35 (D.C. Cir. 2005) ("[N]ew rules that work substantive changes . . . or major substantive legal additions . . . to prior regulations are subject to the APA's procedures.") (citations omitted); *Shalala v. Guernsey Meml. Hosp*., 514 U.S. 87, 100, (1995) (if an agency adopts "a new position inconsistent with" an existing regulation, or effects "*a substantive change* in the regulation," notice and comment are required. (emphasis added) (quotation marks omitted); *Natl. Family Planning & Reprod. Health Assn. v. Sullivan*, 979 F.2d 227, 235 (D.C. Cir.1992) ("If a second rule repudiates or is irreconcilable with [a prior legislative rule], the second rule must be an amendment of the first; and, of course, an amendment to a legislative rule must itself be legislative." (alteration in original) (quoting Michael Asimow, *Nonlegislative Rulemaking and Regulatory Reform,* 1985 DUKE L.J. 381, 396).

"The agency may not use documents or other means of communication that are excluded from the definition of guidance document to informally communicate new or different regulatory expectations to a broad public audience for the first time." 21 C.F.R. § 10.115(e). Accordingly, FDA cannot reinvent the statutory definition of a medical food for political or administrative purposes through the Draft Guidance. The federal courts have been increasingly critical of FDA's use of so-called "Guidance Documents" to implement changes to the legal requirements that bind industry. *See, e.g., Sierra Club v. Johnson*, 541 F.3d 1257, 1265 n.3 (11th Cir. 2008) (holding that so-called "interpretations not the product of adjudication or notice-and-comment rulemaking … which lack the force of law do not warrant *Chevron*-style deference"); *Christensen v. Harris County*, 529 U.S. 576, 587 (2000); *Wilderness Watch v. Mainella*, 375 F.3d 1085, 1091 n.7 (11th Cir. 2004). When regulating through informal guidance documents, the FDA's decisions are reviewed under a more exacting standard, and the courts will examine whether the FDA's new policies are "consisten[t] with earlier and later pronouncements." *See Skidmorev. Swift & Co.*, 323 U.S. 134, 140 (1944). The federal courts examine whether the FDA policy has the "power to persuade." *Id.*

Based on the new substantive definition of a "medical food" first appearing in FDA's second edition of the draft guidance, FDA has excluded entire classes of diseases and conditions. *See* Draft Guidance (explaining that FDA does not consider diabetes to be a condition for which a medical food can be labeled and marketed, even though there are nutrient requirements associated with its management, because a regular diet can be modified to meet the needs of an individual affected by diabetes). That substantive change conflicts with FDA's historic regulation of medical foods in ways that exceed its discretion under its enabling statute. For example, FDA traditionally permitted a host of medical foods under the statutory definition, including, e.g., (1) nutritionally complete formulas for patients receiving no other sources of

nourishment; (2) nutritionally incomplete formulas that provide certain nutrients and are intended to be mixed with other products; and (3) formulas for metabolic (genetic) disorders (this last category being the category that FDA now focuses on in the Draft Guidance for the IEMs). *See* Talbot, 15 J. of Parenteral and Enteral Nutrition.

In other contexts, the FDA has defined "disease" as "damage to an organ, part, structure, or system of the body such that it does not function properly (e.g., cardiovascular disease), or a state of health leading to such dysfunctioning (e.g., hypertension)…" *See* 21 CFR 101.14(a)(5); *see also* 65 Fed. Reg. 10000, 1000-01 (Jan. 6, 2000).[12] Medical foods are inherently distinct from other food categories in that they are (1) "intended for the specific dietary management of a disease" with (2) "distinctive nutritional requirements," and (3) based on recognized scientific principles. *See* 21 U.S.C. § 360ee(b)(3). Those essential elements provide ample prophylactic authority to limit medical foods only to those ingredients or products proven effective by a consensus in the medical community. It is recognized that some diseases may be asymptomatic and others may not have abnormal objective laboratory or radiographic findings. Another, perhaps broader and more meaningful definition of disease would be a loss of *homeostasis,* this being defined as "[t]he state of dynamic equilibrium of the internal environment of the body that is maintained by the ever-changing processes of feedback and regulation in response to external or internal changes."[13] All organisms are genetically programmed to maintain homeostasis (health) or restore it when disturbed (disease) using environmentally available materials for regulation of the metabolic processes needed to provide structure, growth, energy generation and all the other myriad functions required for life. Medical foods are specially formulated from such environmental materials; often acting with pleiotropic activities that are designed to restore metabolic imbalances or, more accurately, restore homeostasis, when and for whatever reason such imbalances have developed and homeostasis is disturbed. While inborn errors of metabolism (IEMs) obviously represent a pre-programmed impairment of homeostasis, they constitute only a tiny fraction of the variety of disease etiologies that medical foods can successfully manage. Meanwhile the therapeutic benefit medical foods provide through dietary management has very wide applicability in the universe of disturbed homeostatic mechanisms.

Although FDA failed to follow notice-and-comment rulemaking procedures prior to amending the medical food definition, it is enforcing the new definition featured in the Draft Guidance. *See*, *e.g.*, FDA Ltr. to Metagenics, Inc. (Aug. 13, 2013) (a food is a medical food only if it complies with the five criteria in 21 C.F.R. § 101.9(j)(8) and concluding that a diabetes product did not qualify as a medical food because "FDA is not aware of any distinctive

[12] According to Taber's Encyclopedic Medical Dictionary, a disease is "A condition marked by subjective complaints, a specific history, and clinical signs, symptoms and laboratory or radiographic findings." *See* Donald Venes, *Taber's Cyclopedic Medical Dictionary* (19th ed. 1997).

[13] *See* Taber's Cyclopedic Medical dictionary, *supra* at n.12.

nutritional requirement or unique nutrient need for patients with Type 2 Diabetes that cannot be met through dietary modification alone").[14] Thus, the Draft Guidance binds industry despite FDA's statements to the contrary. *See Appalachian Power Co. v. E.P.A.*, 208 F.3d 1015, 1020-21 (D.C. Cir. 2000) ("If an agency acts as if a document issued at headquarters is controlling in the field, if it treats the document in the same manner as it treats a legislative rule, if it bases enforcement actions on the policies or interpretations formulated in the document, if it leads private parties or State permitting authorities to believe that it will declare permits invalid unless they comply with the terms of the document, then the agency's document is for all practical purposes 'binding.'").

Instead of using an informal guidance illegally to redefine medical foods, FDA should follow the notice-and-comment procedures required by the APA and act only in strict accord with its enabling statute. Failure to do so in this instance renders its actions unlawful and invalid. *See* 5 U.S.C. § 706(2)(D) (requiring reviewing courts to hold unlawful and set aside agency actions, findings, and conclusions found to be without observance of notice and comment procedure required by the Administrative Procedure Act). Those procedural protections are significant because in a rulemaking proceeding, unlike in the sua sponte issuance of an FDA guidance, the FDA must explain its bases for decision sufficient to provide the regulated class with notice of the agency's deliberative process. *See Chemical Mfrs. Assn. v. E.P.A.*, 885 F.2d 253, 265 (5th Cir. 1989), cert. denied, 495 U.S. 910 (1990) (holding that the agency has the burden of producing a reasonable basis on the record for its rule, and a failure to provide adequate information could result in a failure to meet the arbitrariness standard). Absent that crucial notice and opportunity for comment, the industry lacks a meaningful opportunity to discern the precise rationale for the agency's move and to participate meaningfully in agency deliberations. Moreover, the law contemplates a detailed administrative record, replete with submissions from the regulated class, to form the record on any appeal of agency action. For instance, the rule in *Chenery* states that an agency decision can only be upheld on the "basis of arguments and evidence provided by the agency during the rulemaking proceeding." *See Safe Food and Fertilizer v. E.P.A.*, 365 F.3d 46, 50 (D.C. Cir. 2004). Here, the FDA's decision to limit medical foods to specific types of diseases is a substantive change in the pre-existing law and a change critical for the industry, forcing cessation of certain product sales, relabeling of others, and reformulation of many. Despite that fact, the regulated class cannot pinpoint the precise grounds for challenge without sufficient notice of the evidentiary and legal bases by which FDA supports its new standard.

[14] *Available at* http://www.fda.gov/iceci/enforcementactions/warningletters/2013/ucm367142.htm (last accessed Oct. 8, 2013).

Rulemaking must also incorporate impact statements that justify the administration's policy through cost-benefit analyses. *See Mathews v. Eldridge*, 424 U.S. 319 (1976). Courts will therefore review whether the procedural or administrative benefit outweighs the costs of those procedures as part of the overall "arbitrariness" review. *Id.*; *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co*., 463 U.S. 29 (1983); *Thompson v. Clark*, 741 F.2d 401, 405 (D.C. Cir. 1984) (explaining that "if a defective regulatory flexibility analysis caused an agency to underestimate the harm inflicted upon small business to such a degree that, when adjustment is made for the error, that harm clearly outweighs the claimed benefit of the rule, then the rule must be set aside"). Here, because the FDA has implemented new legislative changes through guidance documents only, the agency fails to fulfill its obligation to weigh the costs of its new rule. Of course, a policy that erects a categorical bar to certain medical foods used by patients in the dietary management of disease likely has dramatic costs for both industry and patients. Those costs are reflected in the reduction of markets, economic losses for business, resulting unemployment, reduction in treatment options for patients, and, ultimately, the increase in patient health consequences and health care expenses.

The FDA has not explained, as it lawfully must under the APA, why patients should suddenly be expected to manage disease without reliance on certain medical foods now in the market and instead through complicated "modifications to their diet," all with limited physician interaction, and without the benefit of public information concerning the association of nutrition and disease. In short, the FDA's decision to avoid formal (or even informal) rulemaking while promulgating a new definition of medical foods harms the public and is prejudicial to the regulated class.

In sum, we recommend that FDA cease enforcing the Draft Guidance, including its rule that prohibits medical foods from being marketed for diseases or conditions that can be managed by changes to the normal diet alone. We also recommend that FDA formally propose regulations amending the Code of Federal Regulations in accordance with the APA to ensure that the substantive and procedural protections of the APA are implemented.

II. The Draft Guidance Is Arbitrary and Capricious Under the APA

Agency actions, findings, and conclusions are invalid under the APA if they are arbitrary, capricious, unlawful or an abuse of agency discretion. 5 U.S.C. § 706(2)(A). To survive judicial review under the arbitrary and capricious standard, an agency must have "examine[d] the relevant data and articulate[d] a satisfactory explanation for its action." *Motor Vehicle Mfrs. Assn. of U.S., Inc. v. State Farm Mut. Automobile Ins. Co.,* 463 U.S. 29, 43 (1983). When an agency action represents a change in administrative policy, this requirement means that an

agency must display awareness of that changing position and show good reasons for the new policy. *See F.C.C. v. Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009). An agency must also "evaluate parties' proposals of 'significant viable alternatives.'" *Shieldalloy Metallurgical Corp. v. Nuclear Regulatory Commn.*, 624 F.3d 489, 493 (D.C. Cir. 2010). In most instances, the agency need not demonstrate that its reasons for the new policy are better than the old ones. *Fox Television Stations, Inc*., 556 U.S. at 515. It must do so "when, for example, its new policy rests upon factual findings that contradict those which underlay its prior policy; or when its prior policy has engendered serious reliance interests that must be taken into account." *Id*.

Here, the Draft Guidance is arbitrary and capricious because FDA failed to acknowledge and adequately explain its promulgation of a new substantive standard for what constitutes a "medical food." For instance, FDA did not acknowledge that the Draft Guidance amends, as discussed above, the medical food definition by making the criteria in 21 C.F.R. § 101.9(j)(8)(i)-(v) part of that definition. Additionally, FDA previously regulated medical foods by focusing on scientific elements of the statutory definition, e.g., whether the disease had distinct nutritional requirements. That approach made good sense because it focused on the dietary management aspect, as opposed to FDA's contrived distinction among food sources as stated in the Draft Guidance.

More significantly, the Draft Guidance is arbitrary and capricious because FDA has not provided an explanation for its new substantive rule, including why it is now necessary to prohibit medical foods from being marketed and labeled for diseases and conditions that can be managed by modification of the normal diet alone. *See* Draft Guidance ("[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*.") (emphasis added). Pursuant to this new rule, a medical food cannot be labeled and marketed for pregnancy or diabetes. *See id*. Regarding diabetes, in particular, FDA said it can be managed by restricting calories, eating regularly, increasing fiber intake, and limiting intake of refined carbohydrates and saturated fats, or for pregnancy. *See id*. ("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 . . . Therefore, FDA generally would not consider a product labeled and marketed for DM to meet the regulatory criteria for a medical food."). FDA is currently enforcing this new rule. *See*, *e.g*., FDA Ltr. to Metagenics, Inc., *supra*. In so doing, FDA wholly disregards the practical effects of its rule on patients and doctors. The FDA has essentially commandeered physician's treatment decisions by (a) depriving those doctors of information concerning medical foods that might guide treatment decisions and (b) making uniform conclusions concerning the patients' abilities to find and purchase conventional foods suitable in the dietary management of disease.

Prohibiting manufacturers and distributors from disseminating information to consumers about how a product, which satisfies the definition of a medical food in 21 U.S.C. § 360ee(b)(3), can be used to manage a disease or condition simply because modification of the normal diet alone is also sufficient to manage the disease or condition unnecessarily harms patients by depriving them of critical options. Moreover, preventing the disclosure of such information deprives patients of vital data that can enable them to make the best, most well-informed choices among options. Even if some diseases or conditions can theoretically be managed with modifications to the normal diet alone, it does not necessarily mean such modifications are practical, advisable, or medically feasible for all patients. FDA provides no basis to conclude that most or all patients can acquire the nutrition they need from dietary changes alone. It is quite possible that a dietary supplement or conventional food may contain a nutrient that is necessary to manage a disease but is not ordinarily available or comfortably achievable in sufficient amounts when consumed in the daily diet. When that happens, a patient is either denied the optimum nutrient level or must consume far higher calories or uncomfortably large amounts of foods to achieve the optimum nutrient level. The number of servings will vary, but variable dosing is not always practical. For example, a patient may have to consume twenty servings of a food or multiple units of a dietary supplement to get the same amount a medical food provides. Often ease of use and comfort associated with use determines consistency of compliance and, thereupon, reliability of medically beneficial results. FDA's Draft Guidance thus creates unnecessary and harmful new barriers to the achievement of medical objectives in the dietary management of disease.

Even if modification to the normal diet alone is feasible, why must a patient be limited to that sole option? Why should this agency automatically foreclose medical foods, which logically help patients and their caregivers achieve the benefits of dietary disease management through more expeditious and cost-effective means? Without explanation, FDA's policy appears to challenge medical foods solely on the basis that FDA's new regulatory theory is more manageable for the agency when regulating conventional foods or dietary supplements that may resemble drug products because of disease language. FDA has provided no rationale or facts explaining why reliance on the Orphan Drug Act definition of a "medical food" is inadequate to police the market without FDA's new global restrictions. Nor has FDA explained precisely how those new global restrictions will redound to the benefit, or at least not harm or endanger, patients in all categories that require dietary management techniques to survive or cope with disease.

On its face, the agency's constrictive action, by eliminating numerous choices otherwise possible in the market, deprives patients and their caregivers of a plethora of needed means to combat nutritional deficiencies arising from or associated with the treatment of disease

conditions. Doing so limits therapeutic options and compounds the burdens that patients and their caregivers face. The benefit of the rule is apparently one of administrative convenience for the agency but the burden of the rule is immediately consequential for the health of patients and for the survival and success of markets endeavoring to satisfy ever changing patient and caregiver nutrient management demands.

For the above reasons, the new rule FDA announced in the Draft Guidance is inferior to the governing law in the agency's enabling statute, which the medical food industry has successfully relied upon as evidenced by the rapid growth in the industry for decades. As explained above, the new rule is legislative and unlawful because it conflicts with the relevant amendment to the Orphan Drug Act and was not adopted in accordance with APA notice and comment rulemaking. It is arbitrary and capricious and an abuse of agency discretion. It should be abandoned in favor of notice and comment rulemaking.

III. The Draft Guidance Is Not in Accordance with Law

Under the APA, a reviewing court must set aside agency actions that are "not in accordance with law." 5 U.S.C. § 706(2)(A). Both 21 C.F.R. §101.9(j)(8) and the Orphan Drug Amendments, 21 U.S.C. § 360ee(b)(3), define a medical food as follows:

> [A] 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.

The FDA's new "medical food" rule in the draft guidance exceeds the precise definition provided by Congress:

> 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.

(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.

In the Draft Guidance, FDA unlawfully provides that the criteria in 21 C.F.R. §101.9(j)(8)(i)-(v) are meant to modify the statutory definition of a medical food, something the FDA is not lawfully entitled to do, let alone by guidance. *See, e.g., Landstar Exp. Am., Inc. v. Fed. Maritime Commn.*, 569 F.3d 493, 498 (D.C. Cir. 2009) ("neither courts nor federal agencies can rewrite a statute's plain text to correspond to its supposed purposes"); *Barnhart v. Sigmon Coal Co., Inc.*, 534 U.S. 438, 462 (2002) ("We will not alter the text in order to satisfy the policy preferences of the Commissioner"); *Chevron, U.S.A. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 842-43 (1984) ("[i]f the intent of Congress is clear, that is the end of the matter, for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress"); *Legal Environmental Assistance Foundation, Inc. v. E.P.A.*, 118 F.3d 1467, 1477 (1997) ("no deference is due to agency interpretations at odds with the plain language of the statute itself" and "even contemporaneous and longstanding agency interpretations must fall to the extent they conflict with statutory language").

Rather than truncate the definition of medical food through criteria amending the statute, FDA's pre-existing regulation on point merely creates an exemption from nutritional labeling requirements for a medical food that satisfies the five criteria contained therein. *See* 61 Fed. Reg. at 60663 ("The regulation provides that a food may claim the exemption from nutrition labeling requirements only if it meets the following

criteria in §101.9(j)(8)[.]").[15] Therefore, by the express terms of section 101.9(j)(8), a product failing to satisfy all five criteria must display a nutrition facts panel; but failure to satisfy that definition does not cause the product to lose its status as a medical food. *See* 56 Fed. Reg. at 60377 ("In general, to be considered a medical food, a product must, *at a minimum*, meet the following criteria: The product must be a food for oral or tube feeding; the product must be labeled for the dietary management of a specific medical disorder, disease, or condition for which there are distinctive nutritional requirements; and the product must be intended to be used under medical supervision[.]") (emphasis added). Accordingly, the Draft Guidance announces a new legislative rule that conflicts with statutory and regulatory language because it presumes to limit the statutory universe of what may be sold as a "medical food" to one far narrower than the plain and intended meaning of the statute and far more constrictive than simply delimiting what may be put on the label of a medical food. As a result, it is unlawful under the APA.

Instead of stating that a food is a medical food only if it complies with the five criteria contained in section 101.9(j)(8), the FDA should clarify that those criteria are only applicable when determining whether a medical food is exempt from nutrition labeling requirements. Otherwise, the FDA must proceed through rulemaking to modify the medical foods definition, assuming FDA can do so within the confines of the law. FDA should further clarify terms used in the statutory definition as opposed to creating entirely new elements for the definition. Specifically, FDA should clarify the phrase "dietary management of a disease." By clarifying that term, FDA can help the regulated class better understand claim limitations and the distinctions among medical foods, foods for special dietary use, and drugs, all without depriving patients of beneficial or essential disease management options.

IV. The Draft Guidance Violates the First Amendment's Protection of Truthful and Non-Misleading Commercial Speech

The Draft Guidance violates the First Amendment of the United States Constitution because it prohibits truthful claims about medical foods. *C. Hudson Gas & Elec. Corp. v. Pub. Serv. Commn. of New York*, 447 U.S. 557, 561-63 (1980) (explaining that the First Amendment protects truthful commercial speech, i.e., expression related solely to the economic interests of the speaker and its audience, from unnecessary government intrusion, albeit to a lesser extent

[15] The federal register text suggests that the only reason FDA exempted "medical foods" from the nutrition labeling requirements contained in section 101.9 was because the agency had intended "to develop regulations covering these aspects of medical foods in the near future." *See* 56 Fed. Reg. at 60378.

than other varieties of speech.) (hereinafter "*Central Hudson*"). In *Central Hudson*, the U.S. Supreme Court established a four-part test for restrictions on commercial speech. First, the Court must "determine whether the expression is protected by the First Amendment. For commercial speech to come within that provision, it at least must concern lawful activity and not be misleading." *Central Hudson*, 447 U.S. at 566. Second, the Court must decide "whether the asserted governmental interest is substantial. Third, if the foregoing inquiries yield positive answers, [the Court] must determine whether the regulation directly advances the governmental interest asserted." *Id*. And fourth, the Court must determine "whether it is not more extensive than is necessary to serve that interest." *Id*. Under the Commercial Speech Doctrine, there is a "preference for disclosure over outright suppression" and for "less restrictive and more precise means" of regulating commercial speech. *Pearson v. Shalala*, 164 F.3d 650, 657-58 (D.C. Cir. 1999) (internal quotation marks omitted). Accordingly, when commercial speech is only potential misleading, there is an obligation to consider appropriate disclaimers. *Id*. at 655.

Here, the Draft Guidance restricts truthful commercial speech in several ways. Most notably it prevents regulated industry from disseminating accurate and beneficial health information to patients as well as physicians concerning medical foods.

FDA recognizes, as it must, that Congress defined a subcategory of foods ("medical foods") which are permitted to make claims associated with disease without the prior restraint contained in the health claims and drug provisions of the Act. *See* 21 U.S.C. § 360ee(b)(3) (allowing medical foods to make claims about "the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation"). For example, the Draft Guidance states that a medical food can be labeled and marketed for phenylketonuria, an inborn error of metabolism.

Although medical foods can make truthful claims about the management of diseases, the Draft Guidance categorically prohibits diabetes claims, regardless of their veracity. Specifically, the Draft Guidance prohibits a medical food, as defined under 21 U.S.C. § 360ee(b)(3), from making medical food claims when FDA makes an administrative determination that other products (i.e., conventional foods and dietary supplements) are already sufficient to manage a disease. *See* Draft Guidance (stating that although nutrient requirements are associated with the management of diabetes, diabetes is not a disease or condition for which a medical food can be marketed because diabetes can be managed by modification of the normal diet alone). At the same time, the FDA prohibits both conventional foods and dietary supplements from conveying that disease information on labels or labeling. *See*, *e.g*., *id*. at § 321(g)(1)(B) (categorizing a product as a drug if it is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease"); 21 C.F.R. § 101.93 (prohibiting dietary supplement label and labeling from bearing disease claims). The FDA's new rule therefore unconstitutionally censors the

speech of medical food manufacturers. The new policy deprives the speaker and the consumer and physician alike from communication on the dietary management of certain diseases. That blanket censorship of crucial market information therefore violates the First Amendment. There is an obvious, less speech restrictive alternative to the blanket ban, which is to allow the speech with agency mandated qualifications to avoid misleadingness. *See Pearson v. Shalala*, 164 F.3d 650, 652-59 (D.C. Cir. 1999).

FDA's categorical ban on truthful disease management claims in the medical food context serves no compelling or even substantial government interest. Indeed, by proceeding to adopt a regulation by fiat in its guidance, the FDA has failed to engage in the kind of detailed explanation required to establish a substantial governmental interest and proof that its means chosen are reasonably related to the end it seeks to achieve. Rather, the prior restraint announced in the guidance only harms the public because it removes all diabetes medical foods from the market. As a result, diabetes patients will be limited to conventional foods and dietary supplements for the dietary management of their disease, which are prohibited from bearing claims about diabetes under the FDCA lest they be regulated as unapproved new drugs. *See* 21 U.S.C. § 321(g). Yet, in the Draft Guidance, FDA stated that conventional foods and supplements can (and should) be used to manage diabetes. If those products cannot have disease associations under the law, it makes no sense to also prevent medical food labels from conveying the disease treatment information that FDA just *supported* in the Draft Guidance. After all, the FDA has admitted in the Draft Guidance that those conventional foods and dietary supplements can, in fact, treat disease or assist in the dietary management of disease (two uses the FDA has heretofore steadfastly rejected for those products). *See* 21 C.F.R. § 101.93; FDA Ltr. to Ancient Formulas, Inc. (Feb. 9, 2011) (therapeutic drug claims, including a diabetes management claim, rendered a product a drug).[16] The censorship announced in the guidance removes all beneficial information about the dietary management of diabetes from the marketplace, which makes it more difficult for diabetic patients to make fully informed decisions about their health, a regulatory end that directly conflicts with Congress's goal in enacting the medical food definition through the Orphan Drug Act. *See* 21 U.S.C. § 360ee(b)(3) (permitting claims about the dietary management of diseases).

The Draft Guidance also unlawfully restricts truthful commercial speech (and is arbitrary and capricious) by prohibiting medical foods from bearing the symbol "Rx only." According to the Draft Guidance, the "Rx only" symbol means that federal law prohibits the product bearing the symbol from being distributed without a prescription. Because medical foods can be distributed without a prescription, the Draft Guidance states that use of the "Rx only" symbol

[16] *Available at* http://www.fda.gov/iceci/enforcementactions/warningletters/2011/ucm244190.htm (last accessed Oct. 10, 2013).

misbrands the food under section 403(a)(1) of the FDCA [21 U.S.C. § 343(a)(1)].[17] FDA will not, however, object to a statement like, "must be used under the supervision of a physician" because medical foods are required "to be consumed or administered [orally or] enterally under the supervision of a physician." *See* Draft Guidance.

FDA's interpretation of the meaning of the "Rx only" symbol is based upon the history of prescription drug labeling. The Draft Guidance states:

> 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." 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.

[17] Section 403(a)(1) of the FDCA states that a food is misbranded if "its labeling is false or misleading in any particular[.]"

There is, of course, an alternative meaning that arises from "Rx only," one that is consistent with the agency goal of ensuring that a medical food is used as part of a physician's dietary management of disease (as opposed to a patient's independent use of such products). By listing the product as "Rx only," manufacturers often intend to convey in a simple and direct way that the patient should be adhering to a regimen specified, or prescribed by, a physician for the dietary management of the disease. To avoid any ambiguity on that point, the obvious, less speech restrictive alternative is, of course, either to allow "Rx Only" when medical foods are distributed by (or only with) a physician's prescription or a mandated qualification (e.g., "this product is not a prescription drug; however, the product should only be used in accordance with a physician's prescribed direction for the dietary management of disease").

FDA's failure to consider the inclusion of disclaimers to remedy its concerns about use of the "Rx only" symbol violates the commercial speech doctrine. *See Pearson v. Shalala*, 164 F.3d 650, 657 (D.C. Cir. 1999). Here, for all the reasons expressed in the *Pearson* decision and its progeny, FDA has a constitutional obligation to consider less speech-restrictive means such as those recommended here. *See*, *e.g.*, *id*. at 658; *Pearson v. Shalala*, 130 F. Supp. 2d. 105, 113 (D.D.C. 2001); *Pearson v. Thompson*, 141 F. Supp. 2d 105, 112 (D.D.C. 2001); *Whitaker v. Thompson*, 248 F. Supp. 2d 1, 9-10 (D.D.C. 2002); *Alliance for Natural Health v. Sebelius*, 714 F. Supp. 2d 48, 63 (D.D.C. 2010); *Alliance for Natural Health v. Sebelius*, 786 F. Supp. 2d 1, 15 (D.D.C. 2011). FDA could require clear disclaimers on all medical foods alerting consumers to the fact that changes to diet alone might provide the same health benefit as a medical food. Or, FDA could allow dietary supplements and conventional foods to advertise their benefits in the dietary management of certain diseases. If FDA accepts none of those less speech-restrictive measures, or fails to even investigate the merits of those approaches, the agency has chosen an unconstitutional path under the *Pearson* precedent. *See Pearson*, 164 F.3d at 657-60 By instead removing from the market beneficial and scientifically proven medical food products, the FDA has eliminated not just the products sold to consumers, but also the information provided to consumers attendant to those sales.

Moreover, FDA's rejection of the "Rx Only" symbol seems at odds with the agency's regulatory approach for medical foods in general. FDA has stated that medical foods should only be used under physician supervision. Yet the agency now limits labeling language that would help manufacturers and physicians ensure that such products are, in fact, provided under the guidance and direction of physicians. In a market where medical foods are available for purchase online and shipped directly to consumers, the FDA should permit all labeling statements that help encourage purchases that are informed by physician interaction. The "Rx only" symbol encourages patients to speak with a physician before purchasing the medical food. Accordingly, both constitutional law and regulatory policy favor use of the "Rx only" symbol, perhaps subject to reasonable disclaimers as discussed above.

FDA should consider guidelines to ensure medical foods are distributed and promoted under direct physician supervision. The most effective way to avoid misuse and incidental usage is to distribute via physician dispensing, pharmacy with a prescription, or through a hospital or long-term care facility with physician orders. FDA should also remove prohibitions against making claims about diseases or conditions that can be managed by modification of the normal diet alone. Additionally, the Draft Guidance should allow medical food labels to bear the "Rx symbol" when a disclaimer is used that remedies any potential for misleadingness.

V. The Draft Guidance Violates the Regulatory Flexibility Act and Executive Order 12866

Both the Regulatory Flexibility Act ("RFA") and Executive Order 12866 require FDA to evaluate the costs of its regulation. Specially, the RFA requires FDA to prepare a regulatory flexibility analysis and an assessment of the economic impact of a final rule promulgated under 5 U.S.C. § 553 on small business entities, unless the agency certifies that the proposed rule will not have a "significant economic impact on a substantial number of small entities" and provides a factual basis for that certification. *See* 5 U.S.C. §§ 604-605; *N.W. Mining Assn. v. Babbitt,* 5 F.Supp.2d 9, 15–16 (D.D.C. 1998). Similarly, Executive Order 12866 states that "[i]n deciding whether and how to regulate, agencies should assess all costs and benefits of available regulatory alternatives, including the alternative of not regulating." *See* Exec. Order No. 12866, Sec. 1(a) (Sept. 30 1993). Further, federal agencies "should select those approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity), unless a statute requires another regulatory approach." *Id*. FDA must adhere to the following principle: "Each agency shall assess both the costs and benefits of the intended regulation and, recognizing that some costs and benefits are difficult to quantify, propose or adopt a regulation only upon a reasoned determination that the benefits of the intended regulation justify its costs." *Id*. at Sec. 1(b)(6).

As explained above, the Draft Guidance is a final, legislative rule under section 553 because it amends the medical food definition and is already being enforced. Rather than prepare a regulatory flexibility analysis, the Draft Guidance remains silent on its effect on small entities in violation of the RFA. The Draft Guidance also does not indicate that FDA weighed its costs and benefits, or even evaluated how consumers and physicians as well as hospitals and care facilities will be harmed by the removal of products from the market that do not fit within FDA's new medical food definition. An essential element in a full rulemaking proceeding is the need to justify the economic burdens when compared with the regulatory goal. *See* Exec. Order No. 12866, Sec. 1 (b)(6). By proceeding through the Draft Guidance, FDA bypasses those key

obligations—obligations which serve as procedural safeguards against unduly oppressive administrative action.

We anticipate that the costs to consumer health will alone substantially outweigh any benefit to FDA's constrictive rule. Medical foods do not replace drugs or serve the same function as drug products, but FDA should promote innovation and development of nutritional products that help aid patients currently suffering from disease, rather than limiting patients to nutritional products designed for healthy population groups (e.g., dietary supplements and conventional foods). That approach is particularly important here where FDA concedes that diseases can be alleviated or "managed" though dietary habits (i.e., "modification of the normal diet"). The Centers for Medicare & Medicaid Services (CMS) has likewise emphasized the role of nutrition in patient management. In February 2013, CMS proposed to expand hospital ordering privileges to Registered Dieticians (RDs) who would be permitted to order "therapeutic diets." *See Medicare and Medicaid Programs; Part II—Regulatory Provisions To Promote Program Efficiency, Transparency, and Burden Reduction*, 78 FR 9216-01 (Feb. 27, 2013). According to CMS, the provision of "therapeutic diets" contributes to "improved patient outcomes and overall cost savings…" *Id.* at 9222.

By failing to observe the significant patient costs and health consequences, the Draft Guidance also conflicts with national priorities of disease prevention, health promotion, and lower health care costs memorialized in the Patient Protection and Affordable Care Act. *See* Title IV, Subtitle A of the Patient Protection and Affordable Care Act ("PPACA"), Pub. L. No. 111-148. The PPACA includes provisions aimed at those priorities. *Id.* For example, section 4002(a) of the PPACA established the Prevention and Public Health Fund "to provide for expanded and sustained national investment in prevention and public health programs to improve health and help restrain the rate of growth in private and public sector health care costs." Section 4004 of the PPACA requires the Secretary of Health and Human Services to "provide for the planning and implementation of a national public–private partnership for a prevention and health promotion outreach and education campaign to raise public awareness of health improvement across the life span." Under Section 4004(a)(1), HHS's program must include dissemination of information concerning "the importance of utilizing preventions services to promote wellness, reduce health disparities, and mitigate chronic disease[.]" The FDA's Draft Medical Foods Guidance therefore directly conflicts with widely publicized regulatory goals in the PPACA. It does not promote wellness or mitigation of chronic diseases because it limits the market for medical foods specifically formatted for the dietary management of those very diseases. That policy, in turn, reduces information available to patients and physicians concerning the dietary management of disease, and stifles innovation and research in the area.

FDA should revoke the Draft Guidance, and proceed only after having performed a complete regulatory flexibility analysis or complied with the principles outlined in Executive Order 12866. FDA should not drastically alter the medical food marketplace until after it has sufficiently weighed the costs and benefits, particularly after the agency took almost no significant action in the area for decades.[18] 61 Fed. Reg. 60661 (No. 29, 1996)

VI. Conclusion

For the foregoing reasons, ANH respectfully requests that FDA rescind the Draft Guidance and halt all enforcement action based on the legislative rule contained therein, which has not been lawfully promulgated in APA mandated notice and comment rulemaking.

Respectfully submitted,

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[18] For instance, the FDA has repeatedly moved to address medical foods through proper rulemaking procedures only to withdraw or abandon those efforts. *See, e.g., Regulation of Medical Foods*, 61 Fed. Reg. 60661-01 (Nov. 29, 1996); *Regulation of Medical Foods; Extension of Comment Period*, 62 Fed. Reg. 7390 (Feb. 19, 1997) (extending comment period); *see also* 66 Fed. Reg. 61593 (Dec. 3, 2001); *Withdrawal of Certain Proposed Rules and Other Proposed Actions; Notice of Intent*, 68 Fed. Reg. 19766 (Apr. 22, 2003) (withdrawing medical foods guidance because the proposal was "no longer considered [a] viable candidate[] for final action").