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March 20, 2003

Constance J. Hardy
Center for Food Safety and Applied
Nutrition (HFS-811)
Food and Drug Administration
5200 Paint Branch Parkway
College Park, MD 20740

Re: Comments to the Dietary Supplement Committee of the Food Advisory Committee on the Definition of "Metabolite"

Dear Ms. Hardy:

The National Nutritional Foods Association ("NNFA") is submitting these comments to the Food and Drug Administration ("FDA") in response to the March 4, 2003 Notice "Dietary Supplement Subcommittee of the Food Advisory Committee: Notice of Meeting."

NNFA is a trade association representing the interests of more than 3,000 retailers and 1,000 manufacturers, suppliers and distributors of natural foods, dietary supplements and other natural products throughout the United States. NNFA has consistently supported FDA's ability and efforts to enforce the Dietary Supplement Health and Education Act of 1994 ("DSHEA") and to ensure that dietary supplements continue to be safe.

NNFA appreciates FDA's solicitation of comments on the definition of "metabolite." NNFA believes that the term has a clear scientific definition and was explicitly included in the DSHEA definition of dietary supplement on those terms. NNFA therefore takes the position that there is no need for FDA to redefine or narrow the category.

I. The Definition of Dietary Supplement in DSHEA Includes "Metabolites"

As written in 21 U.S.C. 321(ff)(1), the DSHEA definition of dietary supplement includes the "metabolite" of a vitamin, mineral, herb or other botanical, amino acid, or dietary substance.

Specifically, 21 U.S.C. 321(ff)(1) states:

[t]he term "dietary supplement" means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(A) a vitamin;

(B) a mineral;

(C) an herb or other botanical;

(D) an amino acid;

(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or

(F) a concentrate, **metabolite**, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E) (emphasis added).

II. The Definition of "Metabolite" is not Contested

"Metabolite" is uniformly defined in scientific and general use dictionaries as "any substance produced by the body's metabolism or by one of the body's metabolic processes." A metabolite thus includes any substance that is created by the body as it builds upon, breaks down, or converts the nutrient.

This inclusion of the term "metabolite" in the DSHEA definition of dietary supplement indicates that the drafters of DSHEA contemplated allowing any compound that results from metabolism of one of the other defined "dietary ingredients" to be marketed in dietary supplements.

The range of "metabolites" is potentially broad, including what are called intermediary metabolites – molecules that are not identical to the original nutrient/supplement but are created to get to another step along a chain of alterations that lead to the molecule the body is trying to make or excrete.

III. A Wide Array of Dietary Supplements Are Already On the Market as "Metabolites"

A wide range of dietary supplements already on the market as "metabolites" of dietary ingredients:

- Ester-C ("Ester-C includes the vitamin C metabolites, L-hreonic acid, L-lyxonic acid and L-yloric acid. A special manufacturing process is employed to form a unique calcium ascorbate metabolite complex"),
- MSM ("MSM is a metabolite of DMSO, the garlic-oyster smelling substance")
- Glucosamine Sulfate, a metabolite of Chondroitin Sulfate
- Pantethine, a metabolite of pantothenic acid; and
- Co-B-Enzyme, a metabolite of CoQ10

IV. Like Other Dietary Supplements, "Metabolites" Must Meet the Statutory Safety Standard

The definition of metabolite is therefore very clear and there is no reason FDA should move to re-define or narrow the category.

At the same time, all dietary supplements – including metabolites – are subject to the statutory safety standard, which NNFA urges FDA to continue diligently enforce. Under this standard, dietary supplements must not present a: "significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling, or under ordinary conditions of use." 21 U.S.C. §342(f)(1)(A). Some products on the market clearly fail that standard, regardless of their definitional status under 21 U.S.C. 321(ff).

V. New Dietary Ingredient Provisions Also Apply

The New Dietary Ingredient ("NDI") provisions of DSHEA, 21 U.S.C. 350b, apply to all dietary supplement ingredients, including metabolites.

An NDI is defined as "a dietary ingredient that was not marketed in the United States before October 15, 1994." 21 U.S.C. §350b(c). DSHEA requires that manufacturers of dietary supplements containing an NDI file a notification establishing the safety of the ingredient 75 days before it is placed on the market. 21 U.S.C. §350b(a).[1]

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[1] Dietary ingredients which were not specifically marketed as such before October 15, 1994, but which have been "present in the food supply" as ingredients of food that have not been chemically altered, may be exempt from the NDI filing requirements. 21 U.S.C. §350b(a)(1).

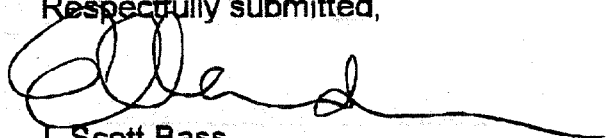
The safety of a dietary supplement containing an NDI is established if there is a:

> [H]istory of use or other evidence of safety establishing that the dietary ingredient when used under the condition recommended or suggested in the labeling of the dietary supplement will reasonably be expected to be safe. 21 U.S.C. §350b(a)(2).

Thus, manufacturers of dietary supplements containing NDIs are subject to both the general safety standard noted above, as well as the NDI standard. NNFA believes that these safety standards, together with FDA enforcement, are adequate to ensure that "metabolites" are adequately regulated.

Based on these comments, we urge FDA not to modify its interpretation of the term "metabolite."

Respectfully submitted,



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