DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: JAN 27 2004

5190 '04 FEB -3 [illegible]

From: Interdisciplinary Scientist/Pharmacist , Division of Dietary Supplement Programs , Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification: **β-hydroxy-β-methylbutyrate (HMB)-L-arginine**

Firm: **ISC (Innovative Supplement Concepts)**

Date Received by FDA: May 05, 2003

90-Day Date: August 5, 2003

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned substance should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Gloria Chang

95S-0316

RPT192

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740-3835

JUL 18 2003

Sal Abraham, M.S., R.D., L.D.N.
ISC (Innovative Supplement Concepts)
1304 Electric Street
Dunmore, Pennsylvania 18509

Dear Mr. Abraham:

This is to inform you that the notification you submitted on behalf of the manufacturer JNC NutraChem, Inc. pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on May 5, 2003. Your notification concerns the substance, β-hydroxy-β-methylbutyrate (HMB)-L-arginine, that you intend to market as a new dietary ingredient. You state that the ingredient contains pure L-arginine molecularly bonded to pure β-hydroxy-β-methylbutyrate (HMB) in a molecular ratio of 1:1. You state that the recommended condition for use is 3-6 grams (g)/day taken in 3 equal doses, with a beverage.

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully considered the information in your submission, and the agency has significant concerns about the evidence on which you rely to support your conclusion that a dietary supplement containing β-hydroxy-β-methylbutyrate (HMB)-L-arginine will reasonably be expected to be safe.

It is unclear in which definition of a dietary ingredient under 21 U.S.C. 201(ff)(1) your substance is included. Please provide a basis for your determination. The notification states that the synthesis of HMB-L-arginine "forms a covalent bond which is the same type of bond found in various peptides." This statement is not consistent with the Classification Code of the substance as an amino acid salt of HMB and is not consistent with the structure or the molecular weight of the compound that you provided. Because of these inconsistencies, it is not possible to identify the compound that is the subject of the notification. It is difficult to ascertain adequate safety information from the limited information on the synthesis and the metabolism of HMB and L-arginine. The notification contains several references that describe studies with either HMB or L-arginine. None of the studies used your substance as the test substance. There is no information provided that relates the referenced information to a safety assessment of the substance that is the subject of your notification.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that β-hydroxy-β-methylbutyrate (HMB)-L-arginine, when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. Therefore, your product may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such an ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such a product into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Your notification will be kept confidential for 90 days after the filing date of May 5, 2003. After the 90-day date, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

IF you have any questions concerning this matter, please contact Victoria Lutwak at (301) 436-2375.

Sincerely yours,

Susan J. Walker, M.D.
Acting Division Director
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

ISC
INNOVATIVE SUPPLEMENT CONCEPTS
Sports Nutrition Consulting

Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling, and Dietary Supplements (HFS-820)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835
Telephone Number: (301)-436-2371

Re: Premarket Notification of New Dietary Ingredient HMB-L-Arginine

Dear Sir:

Notice is hereby given to the requirements Section 413(a)(2) [(21U.S.C. 350b)] of the Federal Food and Drug Cosmetic Act of the intent of JNC NutraChem, Inc. to introduce into interstate commerce in 75 days herefrom a new dietary ingredient Beta-Hydroxy-beta-methylbutyrate (HMB)-L-arginine ("the ingredient"). In accordance with 21 CFR Section 190.6 the following information is provided:

1. Manufacturer:

   JNC NutraChem, Inc.
   Room 401-4,
   Honghai Commerce & Trading Building,
   Ningbo Free Trade Zone,
   Zhejiang 315800, China

2. New Dietary Ingredient:

   Beta-Hydroxy-beta-methylbutyrate-L-arginine

3. Dietary Supplement:

a. The new ingredient contains pure L-arginine molecularly bonded to pure beta-hydroxy-beta-methylbutyrate (HMB), in a molecular ratio of 1:1.
b. The new dietary supplement is composed of 100% HMB-L-arginine.
c. The recommended condition for use is 3-6 grams / day taken in 3 equal doses, with a beverage.

4. JNC NutraChem, Inc. has concluded that the dietary supplement containing the new dietary ingredient will reasonably be expected to be safe under the recommended conditions of use based on numerous studies and other information, including the following documents, copies of which are appended hereto:

(i) Beta-hydroxy-beta-methylbutyrate ingestion, part II: effects on hematology, hepatic and renal function. Gallagher PM. et al, Med Sci Sports Exerc. 2000 Dec; 32(12):2116-9.

(ii) Beta-hydroxy-beta-methylbutyrate (HMB) kinetics and the influence of glucose ingestion in humans. Vukovich MD. Et al, J Nutr Biochem. 2001 Nov; 12(11):631-639.

(iii) Beta-hydroxy-beta-methylbutyrate (HMB) supplementation in humans is safe and may decrease cardiovascular risk factors. Nissen S. et al, J Nutr. 2000 Aug; 130(8):1937-45.

(iv) Nutritional supplementation of the leucine metabolite beta-hydroxy-beta-methylbutyrate (hmb) during resistance training. Nutrition. Panton LB. et al, 2000 Sep; 16(9):734-9.

(v) l. Arginine. Tapiero H. et al, Biomed Pharmacother. 2002 Nov; 56(9):439-45.

(vi) Endocrine and lipid effects of oral L-arginine treatment in healthy postmenopausal women. Blum A. et al, J Lab Clin Med. 2000 Mar; 135(3):231-7.

(vii) L-arginine reduces exercise-induced increase in plasma lactate and ammonia. Schaefer A. et al, Int J Sports Med. 2002 Aug; 23(6):403-7

(viii) L-Arginine - Continuing Education Module. Maher TJ. New Hope Institute of Retailing. 2000 Feb; 1-8.

(ix) Beta-hydroxy-beta-methylbutyrate (HMB)-L-Arginine and its application as a Dietary Supplement. Abraham S. 2003 Apr; 1-7.

Please direct all correspondence regarding this matter to the undersigned. Please feel free to call me if you have any questions.

Sincerely

Sal Abraham

For JNC NutraChem, Inc.
Sal Abraham M.S., R.D., L.D.N.
Innovative Supplement Concepts
Outside Technical Consultant

Enclosures

Cc: JNC NutraChem, Inc.