



Memorandum

 = FEB 06 2004

Date: _____

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

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Subject of the Notification: *Tricreatine Orotate*
Firm: *JNC NutraChem, Inc.*
Date Received by FDA: *July 14, 2003*
90-Day Date: *10/14/03*

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.

Maria Cheng

955-0316

RPT201



SEP 25 2003

Mr. Sal Abraham, M.S., R.D., L.D.N.
Technical Consultant for JNC NutraChem, Inc.
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 your client, 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 July 14, 2003. Your notification concerns the substance called Tricreatine Orotate that you intend to market as a new dietary ingredient.

You state that your substance is "tricreatine orotate" and consists of pure creatine molecularly bonded to pure orotic acid, in a molecular ratio of 3:1. You also state that the new dietary supplement containing your substance is 100% pure creatine orotate. The recommended condition of use is 3-6 grams (g)/day taken in three 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 Tricreatine Orotate will reasonably be expected to be safe.

The notification did not provide adequate information about the chemical identity of "Tricreatine Orotate". In the notification, "Tricreatine Orotate" is described as pure creatine molecularly bonded to pure orotic acid in a molecular ratio of 3:1. The notification also states that the new dietary supplement is composed of 100% creatine orotate. Since the notification does not provide sufficient information regarding the chemical identity of "tricreatine orotate" or "creatine orotate" (e.g., molecular weights, structural formulas; methods of synthesis, CAS Registry numbers, etc.), the new dietary ingredient (or ingredients) contained in your dietary supplement is (are) not clear.

The notification cited one reference for tricreatine orotate. However, the citation is a two paragraph personal testimonial rather than published data in a peer-reviewed journal. Thus, the notification does not contain a safety assessment for the chronic human consumption of tricreatine orotate.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that Tricreatine Orotate, 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 July 14, 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.

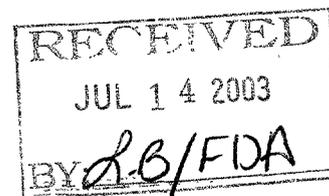
Sincerely yours,

Handwritten signature of Susan J. Walker in black ink. The signature is cursive and includes the word "FOR" written below it.

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



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 Tricreatine Orotate

Dear Sir:

Notice is hereby given to the requirements Section 413(a)(2) [(21 U.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 Tricreatine Orotate ("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:

Tricreatine Orotate

3. Dietary Supplement:

- a. The new ingredient contains pure Creatine molecularly bonded to pure Orotic acid, in a molecular ratio of 3:1.

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- b. The new dietary supplement is composed of 100% Creatine Orotate.
 - 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) Creatine in humans with special reference to creatine supplementation. Balsom, PD. Sports Med. 1994 Oct;18(4):268–80.
 - (ii) Long-term oral creatine supplementation does not impair renal function in healthy athletes. Poortmans, JR et al. Med Sci Sports Exerc 1999 Aug 31:8 1108–10.
 - (iii) Effects of long-term creatine supplementation on liver and kidney functions in American college football players. David, L et al. Int J Sport Nutr Exerc Metab. 2002 Dec 12(4):453–60
 - (iv) Effects of creatine supplementation on performance and training adaptations. Kreider RB. Mol Cell Biochem. 2003 Feb;244(1–2):89–94.
 - (v) Long-term creatine supplementation does not significantly affect clinical markers of health in athletes. Kreider, RB et al. Mol Cell Biochem. 2003 Feb;244(1–2):95–104.
 - (vi) Safety data (MSDS) for Orotic acid. Physical & Theoretical Chemistry Laboratory Oxford University. Dec. 2002: 1–2.
 - (vii) Metabolic supplementation with orotic acid and magnesium orotate. Rosenfeldt FL. Cardiovasc Drugs Ther 1998 Sep 12 Suppl 2:147–52.
 - (viii) Effects of orotic acid ingestion on urinary and blood parameters in humans. Robinson, JL et al. Nutrition Research 1983. 3: 407–415.

- (ix) Bovine milk orotic acid: Variability and significance for human nutrition. Robinson, JL et al. *J. Dairy Sci.* 1983. 63: 865-871.
- (x) Orotic acid content of infant formulas. Durschlag RP, et al. *Am. J. Clin. Nutr.* 1980 33: 2192-2193.
- (xi) Tricreatine Orotate 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

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

Enclosures

Cc: JNC NutraChem, Inc.