

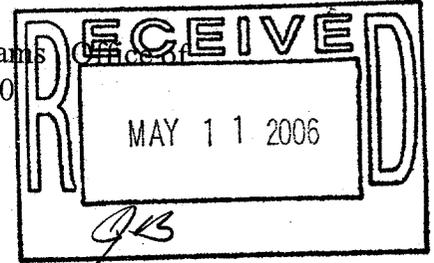
Memorandum

Date: MAY 3 2006

From: Consumer Safety Officer, Division of Dietary Supplement Programs
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: **“A symbiosis of Streptococcus faecalis T-110, Bacillus mesentericus TO-A, and Clostridium butyricum TO-A”**

Firm: Global Asia LLC

Date Received by FDA: January 26, 2006

90-Day Date: April 26, 2006

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.

—Victoria Lutwak—

1995S-0316

RPT335



APR 11 2006

Albert Wai-Kit Chan
Law Offices of Albert Wai-Kit Chan, LLC
World Plaza, Suite 604
141-07 20th Avenue
Whitestone, New York 11357

Dear Mr. Chan:

This is to inform you that the notification, dated January 24, 2007 that you submitted pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) on behalf of your client, GlobalAsia LLC, was filed by the Food and Drug Administration (FDA) on January 26, 2006. Your notification concerned the substance that you identified as "a symbiosis of Streptococcus faecalis T-110, Bacillus mesentericus TO-A, and Clostridium butyricum TO-A" that you intend to market in a new dietary supplement product that you call BIO-THREE™.

Your notification states that "The typical composition for one (1) tablet..." of your product includes 5 mg of Streptococcus faecalis T-110, 25 mg of Bacillus mesentericus TO-A, and 25 mg of Clostridium butyricum TO-A as well as several other non-dietary ingredients such as lactose and magnesium stearate. Your notification also states that "The recommended daily dosage for adults: 2 tablets, three times a day. The recommended daily dosage for children ... over 5 and under 15 years: half the adult dose a day." Your notification further informs FDA that the conditions of use stated on the label or the ordinary conditions of use are that the product will be "[r]ecommended as a dietary supplement for maintaining normal gastrointestinal function to be consumed orally as a tablet, three times a day before meals, after meals, between meals or whenever convenient. To obtain the highest efficacy, take between meals. If experiencing constipation take the dietary supplement with a glass of water or luke-wam water. The dietary supplement should not be administered to infants less than 3 months old."

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 to be 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.

Federal regulations found at 21 CFR 190.6 specify the requirements for a pre-market notification for a new dietary ingredient. Your notification does not comply with the requirements of 21 CFR 190.6 and is incomplete. Your submission did not include an original and two copies of the notification. In addition, the safety information in your notification consists of a bibliography and several English translations of abstracts of articles which were originally published in Japanese. This information does not meet the requirement in 21 CFR 190.6(b)(4) that "...any reference to published information offered in support of the notification shall be accompanied by reprints or photostatic copies of such references. If any part of the material submitted is in a foreign language, it shall be accompanied by an accurate and complete English translation."

Moreover, it is not readily apparent whether the organisms that are combined to produce the ingredient that is the subject of your notification are "dietary ingredients" within the meaning of 21 U.S.C. 321(ff)(1) that may be lawfully used in dietary supplements. The term "dietary supplement" is defined in 21 U.S.C. 321(ff). A dietary supplement means, among other things, 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)."

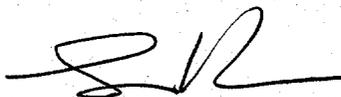
Based on the information in your submission, it is unclear that *Streptococcus faecalis* (now called *Enterococcus faecalis*), *Bacillus mesentericus* or *Clostridium butyricum* is a "dietary ingredient" within the meaning of 21 U.S.C. 321(ff)(1). Therefore, FDA can not determine, at this time, whether your product contains a dietary ingredient(s) that may lawfully be marketed as a dietary supplement.

FDA is unable to determine whether the information cited in your notice provide an adequate basis for a conclusion that the dietary supplement will reasonably be expected to be safe because the information contained in your notice is incomplete. If you market your product without submitting a notification that meets the requirements of 21 CFR 190.6 (<http://www.cfsan.fda.gov/~lrd/cfr190-6.html>), or market your product less than 75 days after submitting such a notification, your product is considered 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 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 January 26, 2006. 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 Linda S. Pellicore, Ph.D. at (301) 436-2375.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'S. Walker', written over a horizontal line.

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

Law Offices of Albert Wai-Kit Chan, LLC

World Plaza, Suite 604, 141-07 20th Avenue • Whitestone, NY 11357 • USA
Tel: (718) 799-1000 • Fax: (718) 357-8615 e-mail: chank@kitchanlaw.com

January 24, 2006

2006-593

VIA EXPRESS MAIL (Label No. EL 969230060 US)

Office of Nutritional Products
Labeling and Dietary Supplements (HFS-820)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Pkwy.
College Park, MD 20740

JAN 24 2006
HFS 810

Re: 75-Day Premarket Notification for a New Dietary Ingredient

On behalf of our client, GloboAsia LLC, and pursuant to 21 CFR 190.6, GloboAsia LLC is filing this premarket notification of its intent to market a product consisting of a symbiosis of *Streptococcus faecalis* T-110, *Bacillus mesentericus* TO-A, and *Clostridium butyricum* TO-A (described herein as BIO-THREE™; tablet) as a new dietary ingredient. GloboAsia LLC is aware that it is unable to market this product for a period of at least 75 days following the acceptance of this notification by the Food and Drug Administration ("FDA").

As per the requirements, we are enclosing two copies of this premarket notification for your reference.

1. Name and complete address:

GloboAsia LLC
11427 Potomac Oaks Drive
Rockville, MD 20850
Contact person: Albert Wai-Kit Chan, Esq.
Phone (718) 799-1000

2. New dietary ingredient:

Symbiosis of:
Streptococcus faecalis T-110
Bacillus mesentericus TO-A
Clostridium butyricum TO-A

3. Description of the dietary supplement that contains the new dietary ingredient:

A. Taxonomy:

1. Introduction:

BIO-THREE™ (Tablet) is a dietary supplement for balance of intestinal flora.

The active ingredient is a symbiosis of three probiotic bacteria strains: Streptococcus faecalis T-110, a lactic acid bacteria; Bacillus mesentericus TO-A, an amyolytic bacillus; and Clostridium butyricum TO-A, a butyric acid bacteria. This product has been used overseas in Japan for many years.

2. Formulation:

B. Level of the new dietary ingredient in the product:

5 mg of Streptococcus faecalis T-110, 25 mg of Bacillus mesentericus TO-A, 25 mg of Clostridium butyricum TO-A per one (1) tablet.

The recommended daily dosage for adults: 2 tablets, three times a day. The recommended daily dosage for children for over 5 and under 15 years: half the adult dose a day.

C. Conditions of use if the product states in the labeling, or if no conditions of use are stated, the ordinary conditions of use:

Recommended as a dietary supplement for maintaining normal gastrointestinal function to be consumed orally as a tablet, three times a day before meals, after meals, between meals or whenever convenient. To obtain the highest efficacy, take between meals. If experiencing constipation take the dietary supplement with a glass of water or luke-warm water. The dietary supplement should not be administered to infants less than 3 months old.

D. History of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe:

1. Reference to published materials attached:

*® was added in the original Japanese articles. BIO-THREE™ is not a federally registered mark.

- a. Igari, H., S. Suzuki, K. Yogogi, and K. Ishibashi. 1989. **Clinical Reports of Treating Abnormal Bowel Movement with Bio-three®** Journal: *Iyaku no Mon* 29(4): 221~224. Original Article in Japanese; Summary in English.
- b. Joh, K., T. Seki, T. Oh-ishi, T. Arai, K. Fukaya, K. Tago, and G. Seo. 1993. **The Effect of Treating Bacterial Diarrhea Caused by *Salmonella* with Bio-three®** Journal: *Prog. Med.* 13: 621~626. Original article in Japanese; Summary in English.
- c. Kato, H., R. Hayashi, T. Miwa, M. Kobayashi, K. Sakamoto. 1994. **The Effect of the Administration of Bio-three® on Abnormal Bowel Movement Caused by Endocrine and Rheumatic Disease.** Journal: *Medicine and Pharmacy* 31(6):1483~1487. Original article in Japanese; Summary in English.
- d. Kosuke, J., S. Takashi, O. Tsutomu, and A. Tadashi. 1993. **A Case That Demonstrates the Elimination of Drug Resistant *Salmonella* by the Administration of A Living Bacterial Preparation.** Journal: *Medicine and Pharmacy.* 29(4): 1027-1030. Original article in Japanese; Summary in English.
- e. Nakamine, K. 2003. **Effectiveness of Treating Cases of Drug-Induced Hypersensitivity Syndrome (DIHS) With Bio-three®--a Combination Product Consisting of *Streptococcus faecalis*, *Clostridium butyricum*, and *Bacillus mesentericus*--Anti-aging and Probiotex--.** Journal: *Research Bulletin of Hakujuikai Foundation Geriatric Hospital* Vol. 12: 63~72. Original article in Japanese; Summary in English.
- f. Sakuma, I. 1999. **Nutrition Management on Low Birth Weight Infants with Infection** Journal: *JJPEN* 12(2): 89~92. Original article in Japanese; Summary in English.
- g. Sakuma, I. 2000. **A Review of Neonatal Infection in the NICU.** Journal: *Perinatal Medicine* 30(12): 1687~1691. Original article in Japanese; Full text translated into Chinese; Summary in English.

h. Yamaoka, M. 1992. **Clinical Records Using Bio-three ® Combined with Other Medications to Treat Various Symptoms of Irritable Bowel Syndrome.** Journal: Diagnosis and Therapy 80 (Suppl.): 702~704. Original article in Japanese; Summary in English.

Please send all correspondence to:

Albert Wai Kit Chan

Albert Wai-Kit Chan

Attorney

Law Offices of Albert Wai-Kit Chan, LLC

World Plaza, Suite 604

141-07 20th Avenue

Whitestone, New York 11357

AKC/lis

Enclosures

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