



Food and Drug Administration
Center for Food Safety and
Applied Nutrition
Office of Nutritional Products,
Labeling and Dietary Supplements

FACSIMILE TRANSMITTAL SHEET

DATE:

To: Mr Nicolas Coudurier	From: Lisa Barr-Thompkins Secretary
Company: Biocodex, Inc	Division of Dietary Supplement Programs
Fax number: 541 895 8913	Fax number: 301 436 2636
Phone number: 541 895 8910	Phone number: 301 436-2375

Subject:

NEW DIETARY INGREDIENT NOTIFICATION

Total no. of pages including cover: 4

Comments:

Document to be mailed: YES NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301 436-2375. Thank you.



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
5100 Paint Branch Parkway
College Park, Maryland 20740

Mr. Nicolas Coudurier,
General Manager
Biocodex, Inc.
300 North Mill Street
P.O. Box 387
Creswell, OR 97426

MAY 23 2005

Dear Mr. Coudurier:

This is to inform you that the notification, dated January 28, 2005, 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)) was filed by the Food and Drug Administration (FDA) on February 8, 2005. Your notification concerned the substance that you identified as "Lyophilised *Saccharomyces boulardii*" that you intend to market as a new dietary ingredient in a dietary supplement product that you call "Florastor®".

According to your notification, your new dietary ingredient will be marketed in capsules and sachets, each containing 250 mg of the ingredient, "Lyophilised *Saccharomyces boulardii*" and that consumers will be instructed to take one capsule or sachet in the morning and one in the evening.

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.

Page 2 - Mr. Coudurlier

Two sections of your notification are labeled "Biocodex Ref. #9": one in English and one in French. There is no statement as to the accuracy of the translation of this or any of the other foreign language materials in the notification and there are two pages of English language material that does not correspond to anything in the French portion of "Biocodex Ref. #9". Because the translation of the foreign language material is not accompanied by an accurate and complete English Translation, the notification does not comply with the requirements of 21 CFR 190.6(b)(4)¹.

Nevertheless, FDA has carefully considered the information in your submission and the agency has concerns about the evidence on which you rely to support your conclusion that a dietary supplement containing "Lyophilised *Saccharomyces boulardii*" will reasonably be expected to be safe.

Your notification fails to clearly identify the new dietary ingredient because the notification did not include an adequate description of the final composition of your new dietary ingredient, "Lyophilised *Saccharomyces boulardii*". For example, it is not clear if your ingredient is composed solely of the organism or also includes culture medium or other substances introduced during production. In addition, while most of the safety information included in your notification contains explicit references to "*Saccharomyces boulardii*", it is not clear how the test materials used in clinical trials for the treatment of diarrhea are related to your product. For example, it is not clear whether the studies published over a 25 year period all employed organisms that are otherwise related to the "Lyophilised *Saccharomyces boulardii*" that is the subject of your notification. Furthermore, while you state on page 2 that each capsule or sachet of your product will contain "250 mg (5 billion live freeze dried cells)" (2×10^{10} cells/1000 mg), material in reference 9 suggests that the contents of a sachet can vary from 4×10^8 to 4×10^{10} "freeze-dried live cells of *Saccharomyces boulardii*" per 200 mg. Most of the other references in your notification describe the administered dose in clinical trials in units of mass but not viable organisms. Therefore, it is not clear how the substances which were administered in clinical trials for treatment or prevention of diarrhea are qualitatively and quantitatively similar to "Lyophilised *Saccharomyces boulardii*" or how these trials are relevant to evaluating the safe use of your new dietary ingredient under the recommended conditions of use in a dietary supplement product.

Furthermore, you state on page 2 of your notification that "*S. boulardii* has been used extensively and safely in over 50 countries to relieve and prevent the symptoms of diarrhea... as either a dietary supplement or an over the counter (OTC) drug." The composition and conditions of use of the listed products are not described in the notification and thus it is unclear to FDA how these products are qualitatively and quantitatively similar to the dietary supplement product that you intend to market in the United States or how the history of use of

¹ Your notification also fails to correctly identify the botanical which is the subject of the notification. The notification erroneously uses the name "*Saccharomyces boulardii*" to describe what appears to be *Saccharomyces cerevisiae* Meyen ex E.C. Hansen var. *cerevisiae* (*S. cerevisiae*). Under the requirements of 21 CFR 190.6(b)(2) and of 21 CFR 101.4 (h) the Latin binomial name must be stated in accordance with the internationally accepted rules on botanical nomenclature.

Page 3 - Mr. Coudurier

these products is relevant to a determination that the product that you intend to market as a dietary supplement as defined in the United States by the Act can reasonably be expected to be safe under the conditions of use described in your notification.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that "Lyophilised *Saccharomyces boulardii*" 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 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 February 8, 2005. 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,



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