



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

MAY 31 2005

Miss Iris Meiri-Bendek, M.Sc.  
Regulatory Affairs  
Enzymotec Ltd.  
Hataasia 5 Street  
P.O. Box 6  
Migdal HaEmeg 23106  
Israel

Dear Miss Meiri-Bendek:

This is to inform you that the notification you submitted, dated January 17, 2005, on behalf of Enzymotec Ltd, 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 10, 2005. Your notification concerns the substance "CarDiabeat" that you intend to market as a new dietary ingredient.

According to the notification, you intend to market your new dietary ingredient, "CarDiabeat", as a dietary supplement in the form of capsules, liquids, and nutritional bars. Each tablet will contain 1.1g of "CarDiabeat." You recommend consuming two servings of "CarDiabeat" per day, or a total serving of 2.2 g "CarDiabeat" per day.

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement that contains 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 deemed 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.

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 "CarDiabeat" will reasonably be expected to be safe.

It is not readily apparent whether the "CarDiabeat" that is the subject of your notification is a dietary ingredient 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 "CarDiabeat" is a "dietary ingredient" within the meaning of 21 U.S.C. 321(ff)(1). Therefore, FDA cannot determine, at this time whether your product is a new dietary ingredient that may lawfully be marketed as a component of a dietary supplement.

Nevertheless, FDA has carefully evaluated the information in your submission and the agency has significant concerns about the evidence upon which you rely to support your conclusion that "CarDiabeat," when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. The ingredient, "CarDiabeat" is a preparation composed of phytosterol esters including DHA and EPA fatty acids. The Notification contains summaries of many studies conducted with phytosterols and with DHA and EPA. It is not clear whether these studies contribute to an assessment of the safety of "CarDiabeat." Your notification included summaries of two studies of products said to be similar to "CarDiabeat". Therefore it is not clear how the substances which were administered in these studies are qualitatively and quantitatively similar to "CarDiabeat" or how these studies are relevant to evaluating the safe use of your new dietary ingredient under the recommended condition of use in a dietary supplement product. Moreover, the notification does not present history of use or other evidence of safety for any material that is identical or similar to "CarDiabeat."

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that "CarDiabeat" 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

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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 10, 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 Pellicore, Ph.D. at (301) 436-2375.



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