



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

NOV 22 2004

Mr. Richard Conant  
V.P. Technical and Regulatory Affairs  
Life Science Division  
AIBMR Life Sciences, Inc.,  
4117 S. Meridian  
Puyallup, WA 98373

Dear Mr. Conant:

This is to inform you that the notification you submitted, dated September 2, 2004, on behalf of your client, Medical Research Institute, 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 September 7, 2004. Your notification concerns the substance called "N-Acetyl-L-Hydroxyproline" that you intend to market as a new dietary ingredient.

The notification informs FDA that Kyowa Hakko Kogyo Co., Ltd. intends to market the new dietary ingredient, "N-Acetyl-L-Hydroxyproline", in tablets or capsules. The notification states that "the level of the new dietary ingredient in a dietary supplement will be in the range of 50 mg to 100 mg per tablet or capsule." For directions of use, the notification states "take three capsules daily (daily intake not to exceed 300 mg of N-Acetyl-L-Hydroxyproline)." The conditions of use of "N-Acetyl-L-Hydroxyproline" as described in your notification includes a statement that "This product is not intended for use by pregnant women and children. This product should be taken for a maximum period of 8 months. If you take any medication, consult with a physician before using this product." Additionally, the notification contains a structure-function claim and label wording: "A dietary supplement for healthy joints" and a disclaimer "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."

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.

It is not readily apparent whether the "N-Acetyl-L-Hydroxyproline" 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 "N-Acetyl-L-Hydroxyproline" is a "dietary ingredient" within the meaning of 21 U.S.C. 321(ff)(1). Therefore, notwithstanding the discussion below of the information you rely upon as evidence that your product is reasonably expected to be safe, FDA cannot determine, at this time, whether your product contains a dietary ingredient that may lawfully be marketed as 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 "N-Acetyl-L-Hydroxyproline" when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. "N-Acetyl-L-Hydroxyproline" is not a natural product. "N-Acetyl-L-Hydroxyproline" is not a constituent of human or animal cells and is not a product of mammalian proline or hydroxyproline metabolism.

Moreover, all of the information and reports included in the notification appear to involve test materials variously described as the pharmaceutical AHYP 200, a product of Chem.-pharm Fabrik GmbH, Germany; N-Acetyl-L-Hydroxyproline, manufactured by Kyowa Hakko Kogyo., Ltd., Japan; N-Acetyl-L-Hydroxyproline, a trade-marketed product of Merrell-Pharma, Germany; Oxaceprol 200, a product of Chephasaar, Germany; and Jonctum. The relationships among these materials are not stated. Therefore, it is not evident that the test substances used in the referenced studies are qualitatively or quantitatively similar to your "N-Acetyl-L-Hydroxyproline" or how these studies are relevant to evaluating the safe use of your new dietary ingredient under the recommended conditions of use.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that "N-Acetyl-L-Hydroxyproline", 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 September 7, 2004. 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.

Sincerely yours,



*Linda S. Pellicore*  
for Susan J. Walker, M.D.

Director  
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