

Memorandum

2012 NOV 20 P 2:16

Date: September 4, 2012

From: Fred Hines, Consumer Safety Officer, New Dietary Ingredient Review Team,
Division of Dietary Supplement Programs, Office of Nutrition, Labeling and
Dietary Supplements, HFS-810

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

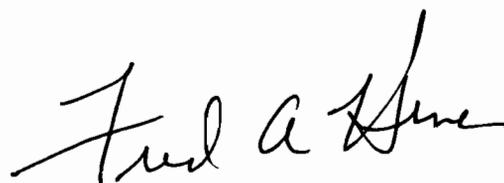
Subject of the Notification: Apoeaquorin (trade name: Prevagen)

Firm: Quincy Bioscience

Date Received by FDA: June 4, 2012

90-Day Date: September 2, 2012

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 **FDA-1995-S-0039** as soon possible since the 90-day date is September 2, 2012. Thank you for your assistance.



Fred A. Hines, DVM, CSO



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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

JUL 25 2012

Dan Moran, Ph.D.
Director of Manufacturing Sciences
Quincy Manufacturing
2010 Pinehurst Drive
Middleton, Wisconsin 53562

Dear Dr. Moran:

This is to inform you that the notification, dated May 30, 2012, which you submitted pursuant to 21 United States Code (U.S.C.) § 350b(a)(2) (section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was received and filed by the Food and Drug Administration (FDA) on June 4, 2012. Your notification concerned "Apoaequorin" which you identify as a new dietary ingredient derived from fermentation of recombinant bacteria expressing a protein from the jellyfish *Aequorea victoria* that you intend to market in a dietary supplement product under the trade name "Prevagen".

According to your notification, "Apoaequorin will be marketed as a dietary ingredient with a daily intake of 20mg in [a vegetarian] capsule form with suitable excipients [rice flour and magnesium stearate]."

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 21 U.S.C. 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.

It is not readily apparent whether the substance 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). For example, your new dietary ingredient is derived from a recombinant bacterial fermentation product which has no history of use as human food.

Nevertheless, 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 “Prevagen” containing “Apoaequorin” will reasonably be expected to be safe under the conditions of use described in your notification.

FDA is unable to establish the identity of your ingredient “Apoaequorin” because your notification does not provide adequate information on the specifications or the manufacturing of your ingredient. For example, it is unclear how impurities are controlled to acceptable levels to ensure the reproducibility of your final product manufactured by recombinant bacteria. Without such information, it is unclear how the product you intend to market is qualitatively and quantitatively similar to the substances described in the information that you rely on as evidence of safety or how that information forms the basis for a reasonable expectation of safety under the intended conditions of use.

FDA is unable to establish the safety of your ingredient “Apoaequorin” based on the history of use provided in your notification. For example, *Aequorea victoria*, which produces apoaequorin, is not one of the jellyfish species that was identified by your referenced articles as a jellyfish that is traditionally consumed by humans. In addition, you did not provide the identity relationship between jellyfish consumed by humans and your ingredient. Moreover, you did not relate serving levels, consumption frequencies, and duration of uses of “Apoaequorin” with that of jellyfish that are typically consumed by humans. Therefore, it is unclear, from your notification, how the history of use provided in your notification can be used to establish the safety of your ingredient under the intended conditions of use.

FDA is unable to establish the safety of your ingredient, “Apoaequorin”, based on the animal study provided in your notification. For example, your safety data is based on only a single 90-day toxicology rat study. In the absence of sufficient history of use or sub-chronic toxicology data from a second species, it is unclear how the history of use and other evidence of safety in your notification form a basis for a reasonable expectation of safety of daily chronic consumption of your ingredient at the proposed serving level.

It is possible that a recently enacted law may affect the legal status of dietary supplements containing “Apoaequorin”. Section 301(l) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(l)) prohibits the introduction or delivery for introduction into interstate commerce of any food (including a dietary supplement) that contains a drug approved under 21 U.S.C. 355, a biological product licensed under 42 U.S.C. 262, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(l)(1)-(4) applies. In our review of your notification, FDA did not consider whether section 301(l) or any of its exemptions apply to

dietary supplements containing "Apoaequorin". Accordingly, this response should not be construed to be a statement that a dietary supplement containing "Apoaequorin", if introduced or delivered for introduction into interstate commerce, would not also violate section 301(ll).

Your notification will be kept confidential for 90 days after the filing date of June 4, 2012. After the 90-day date, the notification will be placed on public display at FDA's Division of Docket Management in docket number FDA-1995-S-0039 (formerly docket number 95S-0316) as new dietary ingredient notification report number 763. Prior to that date, you may wish to identify in writing specifically what information you believe is trade secret or confidential commercial information and an explanation of the basis for this belief.

If you have any questions concerning this matter please contact Dr. Fred Hines, Consumer Safety Officer, New Dietary Ingredients Review Team, at (240) 402-1756.

Sincerely yours,



Ramadevi Gudi, Ph.D.

Acting New Dietary Ingredient Review Team Leader
Division of Dietary Supplement Programs
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