DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: MAY 3 2006

From: Consumer Safety Officer, Division of Dietary Supplement Programs , Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

RECEIVED
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Subject of the Notification: **"DIAM-H-04-02"**

Firm: AIMBR Life Sciences

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

RPT334

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

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

APR 11 2006

Alexander G. Schauss, Ph.D., FACN
Director
Natural and Medicinal Products Research
AIBMR Life Sciences, Inc.
4117 S. Meridian
Puyallup, Washington 98373

Dear Dr. Schauss:

This is to inform you that the notification, dated January 19, 2006 that you submitted on behalf of your client, Embria Health Sciences, 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 January 26, 2006. Your notification concerned the substance that you call "DIAM-H-04-2" that Embria Health Sciences prepares from *Saccharomyces cerevisiae Meyen ex E.C. Hansen var. cerevisiae* and intends to market in a dietary supplement product called "EpiCor™".

According to your notification, "DIAM-H-04-2" will be marketed as a capsule or tablet containing 500 mg of "DIAM-H-04-2". Your notification states that "The suggested daily intake on the product label will be 500 mg a day, in one serving....The directions for use will be: 'Take one capsule or tablet once a day with or without food.'"

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) (section 402(f)(1)(B) of the Act) 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 "DIAM-H-04-2" will reasonably be expected to be safe.

FDA was unable to determine the identity of "DIAM-H-04-2". For example, according to your notification the organism used to produce "DIAM-H-04-2" is *S. cerevisiae*. However, data included in appendix 11 indicates that the viable organisms in your product include other aerobic, non-yeast organisms said to be lactic acid bacteria, at up to 100 times the level of the viable yeast in your product. These organisms were not specified in your notification and their presence is inconsistent with the manufacturing process you have described.

In addition, the level of "DIAM-H-04-2" in "EpiCor™" is unclear. According to your notification, you recommend a daily intake of 500 mg of "DIAM-H-04-2". Based on the data and information in your notification, it is unclear to FDA how many viable organisms are present in your recommended daily serving of "EpiCor™". For example, your notification does not state the maximum number of colony forming units (cfu) of *S. cerevisiae* that will be present in a 500 mg serving of "EpiCor™", nor are the cfu of the unidentified organisms other than *S. cerevisiae* clearly identified.

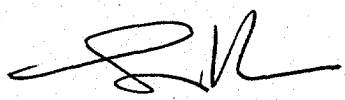
Because the identity of "DIAM-H-04-2" is unclear, and the level of "DIAM-H-04-2" in "EpiCor™" is unclear, it unclear how the product that you intend to market is qualitatively or quantitatively similar to the substances described in the information that you present as evidence of safety for your new dietary ingredient, or how that information is 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 "DIAM-H-04-2" 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 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,



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

(334)

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2006-592

January 19, 2006

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Dr. Susan Walker, PhD
Division of Supplement Programs and Compliance,
Office of Nutritional Products, Labeling, and Dietary Supplements (HFS-820),
Center for Food Safety and Applied Nutrition (CFSAN),
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740

HFS 810/VL

1046 6 MAY 11 P3:48

Re: Submission of New Dietary Ingredient Notification - DIAM-H-04-2 (EpiCor)

Dear Dr. Walker:

On behalf of Embria Health Sciences, LLC, ("Embria), the undersigned submits a New Dietary Ingredient ("NDI") Notification. Along with this letter, Embria is submitting the original and two copies of the NDI Notification.

The street mailing address for communications regarding this NDI Notification is:

Attention: Alexander G. Schauss, PhD, FACN

Director, Natural and Medicinal Products Research,

AIBMR Life Sciences, Inc.

4117 S. Meridian

Puyallup, WA 98373

Phone: 253-286-2888

FAX: 253-286-2451

In a letter dated December 6, 2005, you indicated that the NDI Notification, initially submitted by Embria on September 22, 2005, "did not provide an adequate basis to conclude that 'DIAM-H-04-2', when used under the conditions recommended or suggested in the labeling of [Embria's] product, will reasonably be expected to be safe." Accordingly, this new NDI Notification contains additional information that addresses the issues raised in your December 6, 2005 letter which formed the basis for the FDA's determination. We anticipate that this additional information, as summarized in the notification and documented in the referent appendices will alleviate any concerns expressed by the FDA and indicate that a dietary supplement containing DIAM-H-04-2 will reasonably be expected to be safe.

As expressed previously with the first NDI Notification, this NDI Notification contains trade secrets and confidential commercial information protected from disclosure by the

Freedom of Information Act, 5 U.S.C. § 552(b)(4) ("FOIA")(Exemption 4) and the Federal Trade Secrets Act, 18 U.S.C. §1905. In this submission, we have not included the trade secret information, but have indicated, by the following notice, where the trade secret information would otherwise be :

Confidential Commercial and Trade Secret Information

Embria is providing this public version of this NDI Notification for posting on the Docket No. 95S-0316 and public disclosure including, but not limited to, in response to FOIA requests and for the agency's public reading room. Please call me to discuss any concerns or questions that you have about this NDI Notification. I am ready, willing, and able to respond, promptly, to any such communication from you.

Sincerely,

Alexander G. Schauss, PhD, FACN
Director, Natural and Medicinal Products Research

Enclosures: One original and two copies of the resubmitted NDI Notification

Premarket Notification for

DIAM-H-04-2

as a New Dietary Ingredient

Table of Contents

I. Description of DIAM-H-04-2

i. Chemistry of DIAM-H-04-2

II. Stability and Self-life Studies of DIAM-H-04-2

III. Toxicology and Safety Studies of DIAM-H-04-2

IV. Summary

V. Appendices (1-19)

VI. References

The format of this Notification meets the requirements listed in 21 CFR 190.6 (b) (1 through 5) and follows the numbering system of that regulation.

(b) (1): The name and address of the manufacturer is:

Embria Health Sciences LLC
838 1st Street N.W.
Cedar Rapids, IA 52405

(b) (2): The name of the dietary supplement that is the subject of the premarket Notification is:

[redacted] *Saccharomyces cerevisiae* Hansen (hereinafter called "DIAM-H-04-2"), to be sold under the tradename EpiCor™.

(b) (3): This NDI may be sold for use as a dietary ingredient in a dietary supplement.

(b) (3) (i) and (ii): Level of the NDI in a supplement and conditions of use.

(1) The suggested daily intake on the product label will be 500 mg a day, in one serving.

(2) The serving size is one capsule or tablet containing 500 mg of DIAM-H04-2.

(3) The directions for use will be: "Take one capsule or tablet once a day with or without food."

Section I. Description (Appendices 1-5)

DIAM-H-04-2 is [redacted] *Saccharomyces cerevisiae* Hansen (*S. cerevisiae*) [redacted]

that may be sold for use as a dietary ingredient in a multi-ingredient dietary supplement or as a sole ingredient dietary supplement.

[redacted]

S. cerevisiae, is a species of budding yeast that has been a useful fungus for humans for millennia and has an extensive history of use in

the area of food processing. Other names for *S. cerevisiae* are "Brewer's yeast" and "Baker's yeast." It is used to make bourbon whiskey, apple cider, and a fermented rice beverage called "sake", all of which are consumed world-wide by humans. Brewer's yeast extract is already widely used as a flavor enhancer for soups, soy sauce, sausage, etc., and is also used as a dietary supplement.

Brewer's yeast extract is "generally recognized as safe" (GRAS) as a direct food additive (21 CFR §184.1982). A compilation of GRAS affirmed substances listed in 21 CFR part 184 which are derived from microorganisms such as *S. cerevisiae* that are used in foods include protein derived from *S. cerevisiae* (21 CFR §172.325), yeast-malt sprout extract derived from *S. cervisiae* (21 CFR §172.590), glycan from *S. cervisiae* (21 CFR 21 CFR §172.898) and, dried yeast of *S. cervisiae* (21 CFR §172.896). S. cervisiae is not among the species of a few genera of yeasts (e.g. *Candida* and *Cryptococcus*) that cause illness in humans or other warm-blooded animals.[Ref. 1]

Despite the fact that yeasts have been used, albeit unknowingly, in the production of human foodstuffs for thousands of years, they were first described by van Leewenhoek in 1680. Pasteur first discovered their real nature in his experiments starting in 1859. Hansen initiated the classification of yeasts in the late 19th century and early 20th century. Today's modern classification is not dissimilar to his. So it has only been since the late 1800's that the *term Saccharomyces cerevisiae* has been used.[Ref. 2]

The early studies of yeast were concerned mainly with brewing and wine making, and it was from breweries that yeast was first sold as a by product, for use in baking, for animal consumption, and for human consumption. This was well established by the late 19th century. Work continued in the 20th century, with a number of German studies suggesting that yeast would be a useful nutritional supplement for humans and animals.[Ref. 2, 3]

The advent of food shortages during the First World War and again in the latter part of the 20th century, when concerns were raised about worldwide food shortages, stimulated a great deal of interest in the use of a variety of yeasts such as S. cerevisiae for protein production for both animals and humans (fodder and feed).[Ref. 3]

Hence, there is a history of thousands of years of consumption *of S. cerevisiae* by humans.

Manufacturing

Typically, yeast extract hydrolysate from *S. cerevisiae* is autolyzed by raising the temperature of the yeast while in an aqueous suspension and maintaining it at an elevated temperature. This causes the yeast to start digesting itself resulting in the rupturing of the yeast cell wall and release of the yeast cell content. If the suspension is centrifuged, the insoluble cell walls are spun down and the liquid yeast extract is left. That liquid is then concentrated.

i. Chemistry of DIAM-H-04-2 (Appendices 6-8).

DIAM-H-04-2 Is a Dietary Ingredient

DIAM-H-04-2 meets the definition of a dietary ingredient in 21 U.S.C. § 321 (ff) because it is a botantical prepared in a powdered form intended to supplement the diet.

Section II. Stability, Shelf-life, Pesticide Determination of DIAM-H-04-2 (Appendices 9-11).

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Section II. Toxicology and Safety Studies of DIAM-H-04-2 (Appendices 13-19)

PAGES 9 THROUGH 16

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VI. Summary

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COMMERICAL
INFORMATION

In summary, the studies presented in this Notification are an adequate basis upon which Embria has concluded that DIAM-H-04-2, when used under the conditions recommended or suggested in the labeling of its dietary supplement product, will reasonably be expected to be safe.

V. List of Appendices

Appendix 1.

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Appendix 4.

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Appendix 10.

Appendix 11.

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Appendix 19.

VI. References

1. Reed G. and Peppler HJ. *Yeast Technology*. AVI Publishing: Westport, CT, 1973, p. 10.
2. Rose AH and Vijayalakshmi G. *Baker's Yeasts*. In*: The Yeasts: Volume 5, Second Edition*. Rose AH and Harrison JS [eds.] Academic Press: New York, 1993, pp. 357-360,
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4. Diagram of refractance drying process. MCD Technologies' patent #4631837 (Magoon), "Method and apparatus for drying fruit pulp and the like."
5. Adamson GE, Lazarus SA, Mitchell AE, Prior RL, et al. HPLC method for the quantification of procyanidins in cocoa and chocolate samples and correlation to total antioxidant capacity. *J Agric Food Chem*, 1999; 47: 4184-4188.
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7. Dooley DC, Oppenlander BK, Xiao M. Analysis of primitive CD34- and CD34+ hematopoietic cells from adults: gain and loss of

8. CD34 antigen by undifferentiated cells are closely linked to proliferative status in culture. *Stem Cells*, 2004; 22:556-69.