

Memorandum

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Date:

JAN 11 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

Subject of the Notification: ACAPHA

Firm: Global Cancer Strategies

Date Received by FDA: 10/17/2005

90-Day Date: 1/15/2006

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

19955-0316

RPT310



DEC 29 2005

Dr. T. P. Chiang, C.E.O.
Global Cancer Strategies Ltd.
113-990 Beach Avenue
Vancouver, British Columbia V6Z 2N9
Canada

Dear Dr. Chiang:

This is to inform you that the notification, dated October 14, 2005, that 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 October 17, 2005. Your notification concerned the substance that you identified as "ACAPHA" which you prepare from *Sophora tonkinensis* Gagnep., *Sonchus brachyotus* DC., *Prunella vulgaris* L., *Polygonum bistorta* L., *Dioscorea bulbifera* L. and *Dictamnus dasycarpus* Turcz. You intend to market "ACAPHA" as a new dietary ingredient in a dietary supplement product called "ProhibitRx".

Your notification states that "[t]he dietary supplement will contain 600mg of "ACAPHA" in film coated tablet form with a suggested daily dose of 1.8g, 600mg/ tablet to be taken three (3) times per day."

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.

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 "ACAPHA" will reasonably be expected to be safe.

FDA was unable to determine the identity of your new dietary ingredient, "ACAPHA". For example, according to your notification, the product will be standardized to the content of the alkaloid, matrine, which is described as being present only in *Sophora tonkinensis*. Since the other five botanical starting materials are extracted separately in the manufacturing process described in your notification, it is unclear how the constituents of the other botanicals contribute to the composition of your ingredient. In addition information in your notification (tab 17) describes the existence of multiple varieties of *Dioscorea bulbifera*, some of which are described as being cultivated for food use whereas other, uncultivated varieties are described as "slightly poisonous" and "bitter and even poisonous". It is unclear to FDA whether the "ACAPHA" that is the subject of your notification contains poisonous constituents extracted from the *Dioscorea bulbifera* used to manufacture the ingredient.

In addition, the relationship between "ACAPHA" and the botanicals described in your notification are unclear. For example, your notification contains information about the history of use as food or for medical treatments for each of the botanical starting materials used to manufacture your "ACAPHA". However, this history of use information does not describe the amounts consumed, the parts of the plants used and/or the manner in which the plants were processed prior to consumption. It is unclear how the constituents of your "ACAPHA" are qualitatively or quantitatively similar to the botanical materials described in the history of use information that you rely on as a basis for the safety for your new dietary ingredient.

In addition, the relationship of the test materials used in the animal safety studies of substances called ACAPHA to the "ACAPHA" that you intend to market is unclear. For example, the test materials used in mouse, rat and dog studies were obtained from at least two different sources, neither of which appears to be the same as Central Pharmaceutical Co., Ltd of Tianjin China, the company you have identified as the manufacturer of your new dietary ingredient. While the test material is called "ACAPHA" in each case, it is unclear if the starting materials and manufacturing process are the same for all substances bearing that name. Therefore, it is unclear how the test substances are qualitatively or quantitatively similar to the test substances described in the information that you rely on for the safety for your new dietary ingredient called "ACAPHA".

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

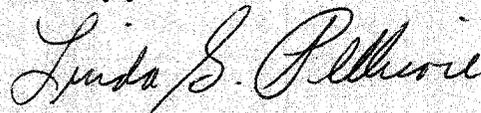
From the information submitted in your notification, it appears that "ACAPHA" is marketed outside of the United States to treat medical conditions. Please be aware that under 21 U.S.C. 321(g)(1)(B), if a product is implicitly or expressly represented as being intended for use in the

diagnosis, cure, mitigation, treatment, or prevention of a disease, it may be subject to regulation under the drug provisions of the Act. If you intend to make claims or representations of this nature, you should contact FDA's Center for Drug Evaluation and Research (CDER).

Your notification will be kept confidential for 90 days after the filing date of October 17, 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,



for

Susan J. Walker, M.D.

Director

Division of Dietary Supplement Programs

Office of Nutritional Products, Labeling

and Dietary Supplements

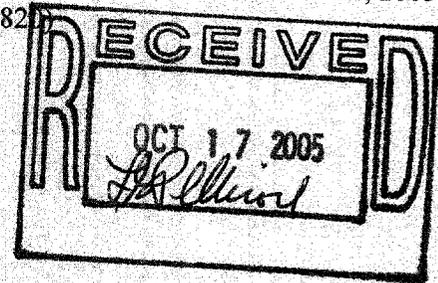
Center for Food Safety and Applied Nutrition



Global Cancer Strategies Ltd. *Preventive Health Division*

Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling, and Dietary Supplements (HFS-82)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD, 20740-3835
US

October 14, 2005



Dear Dr. Linda Pellicore:

Pursuant to Section 8 of the Dietary Supplement Health and Education Act of 1994, Global Cancer Strategies Ltd., Preventive Health Division, located at 113-990 Beach Avenue, Vancouver, BC, Canada V6Z 2N9, wishes to notify the Food and Drug Administration that it will market a new dietary supplement, ACAPHA, prepared from six commonly available botanicals: namely, Vietnamese Sophora (*Sophora tonkinensis* Gapnep), bistort (*Polygonum bistorta* L.), heal all (*Prunella vulgaris* L.), perennial sowthistle (*Sonchus brachyotus* DC), dense fruit dittany (*Dictamnus dasycarpus* Turcz), and air potato (*Dioscorea bulbifera* L.). Enclosed please find two (2) copies of this notification. Details of concentrations and content of the product, conditions of use stated in the labeling, and evidence of safety are documented in the enclosed attachment.

The dietary supplement will contain 600mg of ACAPHA in film coated tablet form with a suggested daily dose of 1.8g, 600mg/ tablet to be taken three (3) times per day.

FDA traditionally considered dietary supplements to be composed only of essential nutrients. The Nutrition Labeling and Education Act of 1990 added "herbs, or similar nutritional substances", to the term "dietary supplement". ACAPHA contains six herbs that have been used as food or herbs for centuries in Asia and Europe. Sophora tonkinensis, Polygonum bistorta, Prunella vulgaris, Dictamnus dasycarpus, and Dioscorea bulbifera are listed in the Herb of Commerce book. Safety and toxicity studies of ACAPHA have been performed in rats, mice, dogs and healthy volunteers. They include mutagenicity, acute and sub-chronic toxicity tests in rodents and dogs, and tolerance of healthy human volunteers. The maximum tolerable daily dose is greater than 20g/kg in mice, 833 times the intended human dosage. Healthy volunteers taking 4.8g of ACAPHA daily, 2.7 times the proposed dosage for the new dietary supplement for as long as 4 weeks did not reveal any adverse reaction. Safety and toxicity studies showed that ACAPHA did not have accumulative toxicity in animals, nor was it mutagenic in bacteria and mice.

The proposed new dietary ingredient is to be labeled ProhibitRx to have the same ingredients as ACAPHA but at a lower dosage (ProhibitRx vs ACAPHA is at a ratio of 1.8g vs 4.8g). Attached please find the detailed information which establishes that this dietary supplement, when used under the conditions suggested in the label, is expected to be reasonably safe.

Please direct all correspondence to me if you have any questions regarding this matter.

Very truly yours,

Dr. T. P. Chiang
CEO

2005-6965
AIMS

Confidential

New Dietary Ingredient Notification
Product name: ACAPHA
Global Cancer Strategies Ltd.
Preventive Health Division
Vancouver, British Columbia, Canada
Date: Oct. 14, 2005