DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

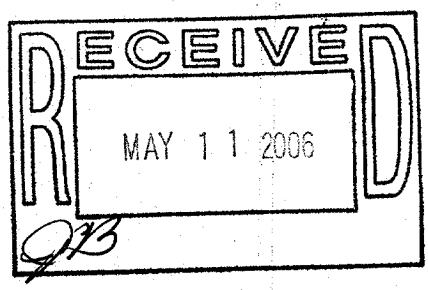
Memorandum

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



Subject of the Notification: **Pacific Yew tips extract**

Firm: **Vitabio, Inc.**

Date Received by FDA: 1/31/2006

90-Day Date: 5/1/2006

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

RPT 336

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

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

Arthur Wu, Ph.D.
General Manager
Vitabio, Inc.
969G Edgewater Boulevard #168
Foster City, California 94404

APR 13 2006

Dear Dr. Wu:

This is to inform you that the notification, dated January 27, 2006, you submitted pursuant to 21 U.S.C. 3501b(a)(2) (section 413 of the Federal Food, Drug, and Cosmetic Act (the Act)) was received by the Food and Drug Administration (FDA) on January 31, 2006. Your notification concerns the new dietary ingredient Pacific Yew tips extract (*Taxus brevifolia* Nuttall), that you intend to market as a dietary supplement product called "VitaBio Spirit".

According to your notice the conditions for use for Pacific Yew tips extract contained in "VitaBio Spirit" are the following: "The directions for usage as one to two times daily, each time 5 to 10 drops with mixing about 100 ml of water.... The product is not intended for use during pregnancy and for child usage...."

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 21U.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 significant concerns about the evidence on which you rely to support your conclusion that a dietary supplement containing "VitaBio Spirit" extract will reasonably be expected to be safe. FDA was unable to determine the identity of your new dietary ingredient, Pacific Yew tips extract.

For example, your notification did not provide any information that would support the statement that the toxic taxine alkaloids which are found in virtually all yew trees, whose needles are the source of the extract, are "almost absent" from Pacific Yew tips extract contained in "VitaBio Spirit." It is unclear to FDA whether the Pacific Yew tips extract that is the subject of your notification contains poisonous constituents extracted from the *Taxus brevifolia* Nuttall used to manufacture the dietary supplement product you call "VitaBio Spirit".

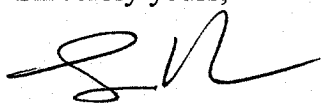
In addition, the relationship between your Pacific Yew tips extract contained in "VitaBio Spirit." and the information described in your notification is unclear. For example, your notification contains information about the external use of different parts of the Pacific Yew by Native Americans. However, this history of use information does not describe the amounts of Pacific Yew extract consumed, the parts of the plant used or the manner in which the plant was processed prior to consumption. It is unclear how the constituents of your Pacific Yew tips extract are qualitatively or quantitatively similar to the *Taxus brevifolia* Nuttall described in the history of use information that you rely on as a basis for the safety for your new dietary ingredient.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that "VitaBio Spirit," 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 31, 2006. After the 90-day date, the notification will be placed on public display at FDA's Division of Docket Management 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,



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

Qims
2006-685

Division of Standard and Labeling Regulations
Office of Nutritional Products, Labeling, and Dietary Supplement (HFS-820)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835
Tel: (301) 436-2371

January 27, 2006

Dear Food and Drug Administration:

Pursuant to 21 CFR Section 190.6 requirement for interstate commerce pre-marketing notification, VITABIO, Inc. wishes to notify the Food and Drug Administration that it prepares and will market the following list of botanical as dietary supplement:

Scientific Name: *Taxus Brevifolia* tips extract
Common Name: Pacific Yew tips extract
The dietary supplement will be distributed by VITABIO, Inc., under the proprietary trade name as VitaBio Spirit.

Attached please find an overview summary and reports that established the dietary ingredient, when used under ordinary recommended conditions suggested in the labeling of the dietary supplement, is reasonably expected to be safe. These reporting and studies include:

(1) The history of use or other evidence of safety establishing that the dietary ingredient will reasonably be expected to be safe.
(2) The toxicity issues surrounding the dietary ingredient based upon the published articles and their reprints that support the dietary ingredient will reasonably be expected to be safe.

Respectfully yours,

Arthur Wu, Ph.D., General Manager

RECEIVED
JAN 31 2006
BY: HFS 810 - N

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969G Edgewater Blvd. #168
Foster City, CA 94404
Tel: (650) 578-8936, Fax: (650) 578-1307
Email: vitabio@yahoo.com

Overview Summary

Pacific Yew (*Taxus brevifolia*) became a well-known botanical after National Institutes of Health (NIH) announced the tree bark portion contained a complex chemical that has unusual anti-cancer property. Since then, lots of Pacific Yew related botanical products flushed into market to meet the consumer's demand. However, the taxus toxicity reputation has confused the general consumers and even among the groups of professional.

This submission lists the Pacific Yew tip extract as the new dietary ingredient. In the Section of The Background of Pacific Yew, several references are cited to establish that Pacific Yew is part of food source. The evidence of historical usage, particularly botanical usage in Native American, has been clearly listed in the reference and other historical documents as well. Pacific Yew also is an important food source for wild life animals in part of North West region of United States.

In the Section of Toxicity, the toxicity issues related to Pacific Yew (*Taxus brevifolia*) are discussed. A reference from Journal of the American Pharmaceutical Association is cited to show the taxine fraction is almost absent in *Taxus brevifolia* (Pacific Yew). To our current knowledge, there are no documented poisonings of humans or animals with *Taxus brevifolia*. Additionally, a reference of an acute oral toxicity study in rats is quoted.

In the Section of the Process, the manufacturing process is presented. In the Section of Proposed Use, the suggested usage quantity for the new dietary ingredient is presented. The usage quantity is much far less than the D_{50} value set in the oral toxicity study in rat.

It is expected that the submitted new dietary ingredient, when used with the suggested quantity, will reasonably be expected to be safe.

The Background of Pacific Yew

Pacific Yew, (*Taxus brevifolia* Nuttall), was famous for Taxol ingredient from its bark and other parts of this tree. (Note: Taxol is Bristol-Myers Squibb's registered trademark for paclitaxel. Paclitaxel is commonly referred to as "Taxol" in the press and conversation; the term will be used here.) Taxol derived from the Pacific Yew was approved by FDA for ovarian cancer treatment as well as other types of cancer treatments. [Ref. 1]

The natural habitat of mature Pacific Yew is located in the moist forest in the northwest region of North America. Before the Taxol Usage for the anticancer agent, Native American uses different parts of Pacific Yew in their daily life for various purposes. Some of the uses are listed here to show that Pacific Yew was part of the natural food source supply as their dietary supplement for Native American. [Ref. 2]

Reference 2 also indicated the following:
"The needles are chewed and put into wounds to promote healing. Peeled bark is made into a tea for the lungs and for internal pains."

Reference 3 indicated Pacific Yew usages by Native American as in the following:
"Yew also had many medicinal uses, many of a magical nature, using the tree to impart strength." Smooth sticks of yew are used by a Swinomish youth to rub himself to gain strength. The Swinomish use boughs to rub themselves when bathing. The Chehalis crush the leaves and soak them in water which is used to bathe a baby or an old person. It is supposed to make them perspire and improve their condition. While the Chehalis never drink this water, the Klallam prepare leaves of yew, grind them up, and apply the pulp to wounds. The Quinault chew the leaves and spit them in wounds. This stings, but is supposed to be very healing. They are the only tribe making medicinal use of the bark, which is peeled, dried, and boiled. The liquid is drunk as lung medicine. The Makah and Nootka also used the needles to brew an astringent bath. Yew was smoked, alone or with other plants, by the Klallam, Samish, Swinomish and Snohomish."

Additionally, Reference 4 indicated as:
"The people scraped the bark off the western Yew twigs and branches and made a tea by boiling it in water. Taken to relieve a stomachache, the decoction was also used for kidney problems. No formula or song was needed for its ingestion."

Furthermore, Reference 5 indicated as:
"Like other Native American cultures, the Kalapuya used the yew medicinally. According to Bill Burwell;
They used yew wood in a skin salve in which the needles and the bark were soaked in water and then prepared with grease into a concoction that was used on the skin as a protection against sunburn. The Yoncallas used it as a tonic for old people who would ingest a tea made out of the yew needles."

The Pacific Yew tree is considered as a critical for wild life animal survival and stated in the Reference 6 as:
"The several species of yew in both the western and eastern hemispheres are thought to have poisonous seeds and foliage. Incidents of livestock poisoning by yew have been reported in Europe and North America. Conversely, in both Europe and North America, domestic and wild animals are known to browse yew foliage without ill effects. If and under what conditions yew foliage is poisonous are not known. Pacific yew is browsed by moose in the South Fork of the Clearwater River basin in Idaho, where the tree is considered critical to the animals' survival. Pacific yew is also browsed heavily by elk and occasionally by deer in Oregon and Washington."

After the FDA approval of Taxol as an anticancer drug, the interest about Pacific Yew was blooming, lots of dietary supplement distributors and manufacturers have put the Pacific Yew related products as dietary supplements in the market before October 15, 1994.

In concluding the above references from Ref. 2 to Ref. 6, they show the evidence of history of use. The Pacific Yew tree was part of the Native American culture for botanical and herbal usage.

List of References

Ref. 1: FDA NEWS 11/18/1992 at http://www.fda.gov/bbs/topics/NEWS/NEW00307.html

Ref. 2: Ethnobotany – Taxus brevifolia, Washington State Department of Transportation at http://www.wsdot.wa.gov/environment/culres/ethbot/t-z/Taxus.htm

Ref. 3: Taxus brevifolia Nuttall 1849, Gymnosperm Database, http://www.conifers.org/ta/ta/brevifolia.htm

Ref. 4: Plants and the People – Ethnobotany of the Karuk Tribe, page 23. By Barbara J. Davis and Michael Hendric.

Ref. 5: The Yew Tree, A Thousand Whispers, page 139. By Hal Hartzell, Jr.

Ref. 6: Taxus brevifolia Nutt. by Charles L. Bolsinger and Annabelle E. Jaramillo http://www.na.fs.fed.us/spfo/pubs/silvics_manual/Volume_1/taxus/brevifolia.htm

Ref. 7: San Francisco State University, Geography 316: Biogeography by Mrs. Merrel (Alice) Ackley http://bss.sfsu.edu/holzman/courses/fall%2003%20project/PacificYew.htm

Ref. 8: Journal of the American Pharmaceutical Association, Scientific Edition - Note on the occurrence of taxine in *Taxus brevifolia*, Vol. 49, No. 10, Pages 683-684, October 1960. By V.E. Tyler

Ref. 9: Acute Oral Toxicity Study in Rats – Limit Test, by product safety labs, Study Number 7734. 1999

Ref. 10: Analysis Report, by Flora Research, sample# 990118006, 1999.