Date: MAR 03 2004

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: Piracetam

Firm/Person: David Tolson

Date Received by FDA: October 27, 2003

90-Day Date: 1/25/04

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 955-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Gloria Chen 03/10/04

955-0316 RP1 215
Mr. David Tolson  
1420 Turk Street # 1208  
San Francisco, California  94115

Dear Mr. Tolson:

This is to inform you that the notification 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 27, 2003. Your notification concerns the substance "Piracetam" also known as 2-oxo-pyrrolidone or 2-oxo-1-pyrrolidine acetamide, that you intend to market as a new dietary ingredient.

The notification states that the product will contain Piracetam only and that the suggested dosage will be 2.4-4.8 grams (g) daily. You state that your product will not have specific conditions for use and that consultation with a physician will be recommended if any medical condition is present.

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 Piracetam will reasonably be expected to be safe.
Your product is excluded from the definition of “dietary supplement” under 21 U.S.C. 321(ff)(3)(B). Piracetam is an article authorized as an investigational new drug (IND) for which substantial clinical investigations have been instituted in the United States, and the existence of such investigations has been made public. The results of at least two clinical studies conducted under authorized INDs were published in peer reviewed journals\textsuperscript{1,2}. In addition, there is no evidence that Piracetam was marketed as a dietary supplement or a food prior to the authorization to investigate Piracetam as a new drug. Therefore Piracetam is excluded from the statutory definition of a dietary supplement under 21 U.S.C. 321(ff)(3)(B).

In summary, Piracetam is not a dietary supplement under the Federal Food, Drug, and Cosmetic Act. Moreover, the product appears to be a drug under the Act and thus subject to the regulatory requirements of drugs.

Under 21 U.S.C. 321(g)(1)(B), an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease in man is a drug. The information contained in your submission, namely the inclusion of a list of documents setting forth diseases for which Piracetam may be an effective treatment, suggests that it is intended to treat, prevent, or mitigate diseases. See 21 CFR 101.93(g). These representations suggest that this product is intended for use as a drug within the meaning of 21 U.S.C. 321(g)(1)(B), and that it is 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), Office of Compliance, HFD-310, Montrose Metro II, 11919 Rockville Pike, Rockville, Maryland 20852.

Your notification will be kept confidential for 90 days after the filing date of October 17, 2003. 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 Victoria Lutwak at (301) 436-2375.

Sincerely yours,

Susan J. Walker, M.D.
Division Director
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling and Dietary Supplements
Center for Food Safety
and Applied Nutrition
Premarket notification for new dietary ingredient: Piracetam

(1) Distributor of new dietary supplement

Mike McCandless
Unlimited Nutrition
1332 Plaza Drive
Burlington, NC 27215

(2) Name of dietary ingredient

Piracetam (?-oxo-pyrrrolidone; 2-oxo-1-pyrrolidine acetamide)

(3) Description of dietary supplement

(i) Level of ingredient in dietary supplement

The new dietary supplement will contain piracetam only, and the suggested dosage will be 2.4-4.8 g daily.

(ii) Conditions of use of new dietary supplement

The new dietary supplement will not have specific conditions for use; consultation with a physician will be recommended if any medical condition is present

(4) History of use and evidence of safety

History: Piracetam has a wide history of use and an excellent safety record. Clinical investigation of piracetam began in 1965 [1], and it reached clinical use in France in 1971 [2]. It was established that piracetam enhanced learning and memory and protected the brain from a variety of physical and chemical insults in animal models, and that it lacked sedative, stimulant or other CNS side effects [3]. In various countries of the world, it has been approved for use for the treatment of alcohol withdrawal, alcoholism, head injuries, learning disorders, vertigo, dyslexia, post-traumatic vertigo and coma, sickle-cell anaemia, epilepsy, Raynaud's disease, and Parkinson's disease; it also has a history of use in treatment of brain disturbances and intellectual disorders caused by tranquilizers, neuroleptics, depressants, barbiturates, electroconvulsive therapy, and agents that impair brain circulation, as well as treatment of mild cognitive impairment (MCI), cortical myoclonus, Alzheimer's disease, intrauterine hypoxia in prematurely born infants, ischemic stroke, and aphasia; finally, it has been investigated with promising results in treatment of schizophrenia, depression, congestive heart failure, myocardial infarction, arrhythmia, hypertension, fetal alcohol syndrome, sudden deafness, neuropathic pain, viral neuroinfections, breath holding spells, burn wounds, hypoxia associated with altitude and hazardous jobs, motion sickness, bronchitis, gastric ulcers, cancer, and cerebral palsy [2, 5-7]. No serious side effects have occurred, even with doses as high as 24 g daily (which are commonly used in treatment of myoclonus) and no significant drug interactions have been reported [2, 8].
Animal safety data: Piracetam has exhibited no signs of toxicity or teratogenicity in animal models, even at extremely high doses. Acute administration of 8 g/kg IV in rats and 10 g/kg orally in rats, dogs, and mice (about 150 times the recommended dose in humans) have been tested without reaching an LD50, and dogs treated with 10 g/kg orally for a year showed no signs of toxicity [3, 9].

When the extensive history of safe use of piracetam and the animal safety data are taken into consideration, piracetam can be reasonably expected to be safe.

References (full texts attached)


(5) Individual responsible for notification

David Tolson
1420 Turk St. #1208
San Francisco, CA 94115
415-238-2291