

Eco Terra Ltd.

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Office of Special Nutritionals
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
200 C Street, S.W. (HFS-450)
Washington, D.C. 20204

December 17, 1995
Our Ref: USFDA.9512171r

Re: Notice of Statements of Nutritional Support

Dear Persons,

Enclosed is a 2-page information sheet on Brain Bow®, a phosphatidylserine dietary supplement product produced by Lipogen Ltd. of Haifa, Israel. Eco Terra Ltd. has commenced importation of Brain Bow® into the United States in bulk form for supply to companies acting as wholesalers to the American nutritional supplements industry. We expect that retail products containing the Brain Bow® manufactured by Lipogen Ltd. will enter the American retail market during the First Quarter 1996.

We are therefore submitting on behalf of Lipogen Ltd. as manufacturer and Eco Terra Ltd. as import distributor, the enclosed information sheet pursuant to Section 6 of the Dietary Supplement Health and Education Act [DSHEA] [21 U.S.C. § 343(r)(6)] pertaining to statements of nutritional support. Our intention in providing the enclosed information sheet is to meet the requirements of the DSHEA in this regard.

Please feel free to contact me should you have any questions.

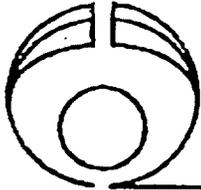
Respectfully yours,

Jerry M. Kosanovich
Executive Director

Encl: 2-page Brain Bow® Product Profile

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BRAIN BOW® PHOSPHATIDYLSERINE (PS) A Brain Nutrient Dietary Supplement For The People Who Can't Afford To Forget....

Indications are presented in the literature to implicate phosphatidylserine (PS) in neural processes where catecholamines and acetylcholine are released.¹⁻⁴ This natural phospholipid might therefore be of rehabilitation potential in memory and behavioral dysfunctions associated with deficits in cerebral neurotransmissions. In studies where brain PS was given intraperitoneally or intracerebro-ventricularly to aged rats, a significant improvement in learning and memory was observed.^{3,4} In over 20 American and international clinical studies with various patients, where PS was given orally, marked improvement was documented. A list of these studies, many of which were double blind, is available upon request.

The human clinical trials where PS dosage was 200-300mg per day clearly report the positive effects of PS upon memory and learning performance functions. This is especially so as regards tasks associated with daily living such as learning and remembering faces and names, recall of frequently misplaced items, maintaining concentration and remembering new information and procedures. By supplementing the body's natural supply of PS, which is most heavily concentrated in the membrane of brain cells, Brain Bow® as a dietary supplement is implicated as improving memory and cognitive functions in older adults. Memory performance appears to begin to improve to a noticeable and statistically significant degree, as measured by standard neuropsychological tests, starting in about 2 weeks.

The reason PS is only now available to the general public has to do with supply source. Prior to the 1992 Israeli market introduction of the soy lecithin derived PS made by Lipogen Ltd., the only commercially available PS was derived from cow's brain - Bovine Cortex Phosphatidylserine (BCPS). The danger of viral contamination in an animal derivative presented insurmountable regulatory obstacles.

Lipogen's Brain Bow® on the other hand is a mixture of phospholipids from soy beans which is enriched with phosphatidylserine (PS) by the reaction of phospholipase-D.⁵⁻⁶ It has the advantage of being a natural product of plant phospholipids which presumably retains the same anti-aging activity as PS from bovine brain. Brain Bow® was clinically tested in a double-blind study. The results of the clinical study using Brain Bow® showed a large and significant influence of treatment on both memory and mood and are therefore very much in line with other published clinical trials in the field. Even as Lipogen was the pioneer in the development of soy lecithin PS, Brain Bow® is today the only soy lecithin PS product being freely sold within the European Union.

BRAIN BOW® PHOSPHATIDYLSERINE (PS)

The implications of the availability of the Lipogen Brain Bow® PS product in terms of the American market is significant. Consider the product's appeal and usefulness as a dietary supplement for a larger, often younger and otherwise neurologically healthy population defined by the concept of "Age-Associated Memory Impairment" or AAMI.

The US Census Bureau showed that in 1994 there were 53.1 million people in the USA aged 40 - 59 years. These are individuals the majority of whom are daily active in the work force and subject to the tremendous strains and pressures that now require almost constant adaptation and the learning of new skills. The same census figures show that there are 28.7 million Americans aged 60-74 years of age, and 13 million aged 75+ years. These older Americans are the most susceptible to Age-Associated Memory Impairment at the same time that the changing socio-economic and governmental environments in which they live are becoming more stringent and less supportive. The premium on continued independence and staying in the work force longer makes the ability to cognitively function even more important today for these older Americans.

Brain Bow® is available as a dietary supplement in bulk liquid and powder forms for customer encapsulation, manufactured to deliver 100mg of phosphatidylserine per recommended encapsulation dose. Brain Bow® is also available in bulk soft gel capsules and 2-part hard gel capsules for customer packaging. Each capsule supplied contains 100mg of phosphatidylserine.

References:

- 1 Drago, F. et al. Behavioral effects of phosphatidylserine in aged rats. *Neurobiology of Aging* 2, 209-213, 1981.
- 2 Drago, F. et al. Phosphatidylserine facilitates learning and memory processes in aged rats. in *Aging of the Brain*. (D. Samuel, ed.) Raven Press, New York, pp. 309-316, 1983.
- 3 Aporti, F. et al. Computerized EEG and behavioral effects of brain cortical phosphatidylserine (PS) in young and aged rats. in *Aging of the Brain*. (D. Samuel, ed.) Raven Press, New York, pp. 317-328, 1983.
- 4 Corwin, J. et al. Behavioral effects of phosphatidylserine in the aged Fischer rat: amelioration of passive avoidance deficits without changes in psychomotor task performance. *Neurobiology of Aging*, 6, pp. 11-15, 1985.
- 5 Confurins, P. and Zwaal, R.F.A. The enzymatic syntheses of phosphatidylserine and purification by CM cellulose column chromatography. *Biochem. Biophys. Acta.* 488, pp. 36-42, 1977.
- 6 Eibl, A. and Kovatchev, S. Preparation of phospholipids and their analogs by phospholipase D. *Methods Enzymology*, 7, pp. 632-639, 1981.

The statements made herein have been neither evaluated nor approved by the U.S. Food and Drug Administration. The Brain Bow® phosphatidylserine is not a medicine and is not intended to diagnose, treat, prevent or cure any disease.

