DEPARTMENT OF HEALTH & HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Public Health Service

Memorandum

Date NOV 12 1999

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From Senior Regulatory Scientist, Regulatory Branch, Division of Programs & Enforcement Policy (DPEP), Office of Special Nutritionals, HFS-456

Subject 75-day Premarket Notification for New Dietary Ingredient

To Dockets Management Branch, HFA-305

New Dietary Ingredient:	L-Se-methylselenocysteine
Firm:	PharmaSe, Inc.
Date Received by FDA:	October 20, 1999
90-day Date:	February 17, 2000

In accordance with the requirements of section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification for the aforementioned new dietary ingredient should be placed on public display in docket number 95S-0316 after February 17, 2000.

Robert J. Moore, Ph.D.

95S-0316

RPT 59

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington, DC 20204

NOV 12 1999

Julian E. Spallholz, Ph.D.
President & CEO
PharmaSe, Inc.
3416 Knoxville Avenue
Lubbock, Texas 79413

Dear Dr. Spallholz:

This is in response to your letter to the Food and Drug Administration (FDA) dated October 6, 1999 (received on October 20, 1999), making a submission for a new dietary ingredient pursuant to 21 U.S.C. 350b(a)(2) (section 413 of the Federal Food, Drug, and Cosmetic Act (the Act)) and 21 CFR 190.6. Your letter notified FDA of your intent to market a dietary supplement containing L-Se-methylselenocysteine (SeMC), a substance you assert is a new dietary ingredient.

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement that contains 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 deemed 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.

Your submission contained information that you believe establishes that the new dietary ingredient SeMC, when used under the conditions recommended or suggested in the labeling of the dietary supplements, will reasonably be expected to be safe. The information in your submission does not meet the requirements of 21 CFR 190.6 (copy enclosed). The submission required under the Act must contain a description of the dietary supplement or dietary supplements that contains, among other things, the level of the new dietary ingredient in the dietary supplement and the conditions of use recommended or suggested in the labeling of the dietary supplement, or if no conditions

of use are recommended or suggested in the labeling of the dietary supplement, the ordinary conditions of use of the supplement (see 21 CFR 190.6(b)(3)). You may submit an amended notification that cures the defects described above. If you market your product without submitting an amended notification that meets the requirements of 21 CFR 190.6, or less than 75 days after submitting such a notification, your product is considered 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).

Please contact us if you have any questions concerning this matter.

Sincerely,

Lynn A. Larsen, Ph.D.
Director
Division of Programs and Enforcement Policy
Office of Special Nutritionals
Center for Food Safety
and Applied Nutrition

Enclosure

6 1748

Office of Special Nutricuticals
HFS 450
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C St. SW.
Washington, DC 20204

October 6, 1999

Dear Sir:

PharmaSe, Inc would like to introduce into the health food market a non-protein amino acid, L-Se-methylselenocysteine (SeMC), following the 75 day waiting period as provided by law. This seleno-amino acid is naturally synthesized and is found in a number of plants commonly consumed in the human diet. Garlic, onions, leeks and broccoli are known to synthesize most notably this seleno-amino acid. Since selenium is not known to be an essential trace nutrient by plants of any kind, the concentration of selenium generally and Se-methylselenocysteine specifically in plants is totally dependent upon the distribution and concentration of selenium in the soils from which the plants are harvested. It is likely that many other plant species, as well as yeast, synthesize L-Se-methylselenocysteine as has been shown for Astragalus.

The major human dietary sources of selenium are animal meats and poultry, as well as fish. A secondary source of human dietary selenium is cereal grains. Many animal feeds, cattle, swine and poultry are fortified with selenium and therefore animal foods, as well as seafoods are an excellent source of bioavalible selenium for humans. Cereal grains are also good sources of human dietary selenium, but because the selenium is not a requirement for plant growth, the selenium content of cereal grains is also reflective of the soil selenium content in which the plant is grown and harvested. A third form of selenium for humans is from dietary supplements. Selenium supplements for humans followed that of animals (begun in 1973) beginning about 1978. Dietary selenium, an essential trace nutrient, ingested by humans is metabolized and incorporated into a number of selenoproteins now numbering 13, most notably the selenoenzymes of the glutathionine peroxidase family. These selenoenzymes provide an antioxidant function in vivo of reducing metabolic hydrogen peroxide to water and organic hydroperoxides to alcohols.

The chemical forms of selenium consumed by humans from animal foods are L-selenocysteine and L-selenomethionine. The forms of selenium consumed in plant foods are L-selenomethionine followed by lesser amounts of L-Se-methylselenocysteine. Lesser amounts of other selenium species likely exist in foods. Dietary supplements of selenium for humans have included sodium selenite, sodium selenate, L-

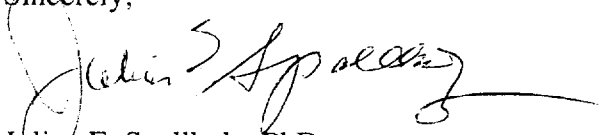
selenomethionine and a selenium containing yeast. These selenium supplements have been consumed for many years without any reports of human toxicity when ingested at levels of 200 ug selenium/day or less. A recent long term human study of 1312 persons with non-melanoma skin cancer were given 200 ug/Se/day of selenium yeast (mostly selenomethionine) for 4.5 years and revealed no toxicity and the epidemiological data suggested a reduction in lung, prostate and colorectal cancer in the selenium supplemented population. An even more recent report of humans consuming 200 ugSe/day reduced prostate cancer risk by one-third in 33,737 cohort members over seven years without adverse effects. The present Recommended Dietary Allowance (1989) for selenium is 70 ugSe/day for men and 55 ugSe/day for women.

The literature suggests and our own research shows that L-Se-methylselenocysteine has low toxicity relative to inorganic selenium compounds in animals and the toxicity of L-Se-methylselenocysteine is comparable L-selenomethionine toxicity. Tissue culture data reveals L-Se-methylselenocysteine toxicity to be far less toxic than inorganic selenium and again shows L-Se-methlyselenocysteine toxicity to be on a par with L-selenomethionine. The MSDS for L-Se-methylselenocysteine provides little toxicological information about the nutrient.

Dr. Clement Ip of Roswell Park Cancer Research Hospital will be or he may already have filed an IND with the FDA for the use of Se-methylselenocysteine in humans. Research plans are in place for eventual human research under a FDA approved IND.

We would appreciate any comments you may have on this natural selenoamino acid prior to its introduction into the health food industry.

Sincerely,



Julian E. Spallholz, PhD
President and CEO

PharmaSe.Inc.
3416 Knoxville Ave
Lubbock, TX 79413

Enclosures