DEPARTMENT OF HEALTH & HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Public Health Service

Memorandum

Date APR 29 1998

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:	Seaprose-s (semi-alkaline protease from *Aspergillus melleus*
Firm:	General Nutrition Corporation
Date Received by FDA:	April 28, 1998
90-day Date:	July 11, 1998

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 June 28, 1998.

Robert J. Moore, Ph.D.

95S-0316

RPT 29

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington, DC 20204

APR 29 1998

John P. Troup, Ph.D.
Vice President, Scientific Affairs
General Nutrition Corporation
300 Sixth Avenue
Pittsburgh, Pennsylvania 15222

Dear Dr. Troup:

This is to notify you that your submission pursuant to section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act) dated April 20, 1998, concerning the marketing of a substance that you assert is a new dietary ingredient (i.e., seaprose-S) was received by the Food and Drug Administration (FDA) on April 28, 1998. Your submission will be kept confidential for 90 days from the date of receipt, and after July 11, 1998, your submission will be placed on public display at Dockets Management Branch (Docket No. 95S-0316). Commercial and confidential information in the notification will not be made available to the public.

Please contact us if you have questions concerning this matter.

Sincerely,

Robert J. Moore, Ph.D.
Senior Regulatory Scientist
Division of Programs and Enforcement Policy
Office of Special Nutritionals

GNC LiveWell™

John P. Troup, Ph.D.
Vice President,
Scientific Affairs

April 20, 1998

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

Pursuant to Section 8 of the Dietary Supplement Health and Education Act of 1994, General Nutrition Corporation ("GNC") located at 300 Sixth Avenue, Pittsburgh, PA 15222 wishes to notify the Food and Drug Administration that GNC will market a new dietary ingredient, Seaprose-S (Semi-Alkaline Proteinase) a homogeneous crystalline proteinase originated from Aspergillus Melleus. Accordingly, enclosed please find two (2) copies of this notification.

The dietary supplement which contains Seaprose-S, will consist of fifteen (15) mg of Seaprose-S in a tablet or capsule which will be suggested to be taken two (2) times per day.

Attached please find the scientific studies and other information which establish that this dietary ingredient, when used under the conditions suggested in the labeling of the dietary supplement, is reasonably expected to be safe. This information includes:

(1) Development and manufacturing chemistry

(2) Toxicity studies (including absorption and excretion, acute, subacute, chronic, toxicology and antigenicity studies)

(3) Product stability data

(4) Physiological studies

Very truly yours,

John P. Troup, Ph.D.

Enclosures

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General Nutrition Corporation, 300 Sixth Avenue, Pittsburgh, PA 15222
Tel: (412) 338-8844 Fax: (412) 338-8954

SECTION 1 - Seaprose-S

Development and Manufacturing Chemistry

Background

Proteinases, such as α-chymotrypsin originated from animals, bromelain from plants, or semi-alkaline proteinase, serrapeptase and pronase from microorganisms, have been observed to exert clinically anti-inflammatory, anti-swelling and expectoration activities by an oral administration, and have been widely used for "improvement of post-operative and post-traumatic swelling, sinusitis, mammalian congestion and difficulty in expectoration associated with respiratory diseases", and so on. Proteinases having anti-inflammatory effect was confirmed of its effectiveness in "difficulty in expectoration associated with respiratory diseases" as well as "remission of swelling".

Seaprose-S is a homogeneous crystalline semi-alkaline proteinase originated from *Aspergillus melleus* with a molecular weight of about 30,000. It is stable within a range of pH 5.0 - 9.0, optimum pH being 8.0 and active center being serine.

Semi-alkaline proteinase (SAP) was confirmed of its anti-inflammatory and anti-swelling activities in an experimental inflammatory swelling and its clinical effect by an oral route on "remission of traumatic swelling and inflammation", and was approved in August 1967. These approved indication, "remission of post-operative and post-traumatic swelling" was published as a result of drug re-evaluation (No.11) in May 1977 and the efficacy was confirmed.

In vitro and *in vivo* studies confirmed that Seaprose-S has activities of lysing sputum, reducing viscosity, reducing dynamic viscosity/dynamic elasticity of sputum and increasing expectoration volume. Moreover, oral serving of Seaprose-S was confirmed of its usefulness in "difficulty in expectoration associated with respiratory diseases" through the double blind clinical study. Based on this result, an application for modification of approved indications was filed in December 1978, and in January 1980 an additional indication was approved with respect to "difficulty in expectoration in the following disease - bronchitis, pulmonary tuberculosis, bronchiectasia, pulmonary emphysema, bronchiolitis and bronchial asthma". On August 1, 1988, the above additional indication was appointed to be re-evaluated and confirmed on March 9, 1995, with restriction of applicable diseases (SAP should be applied to severe cases of the above diseases.). Moreover, on February 1, 1990, the indication of "remission of post-

Analysis of Seaprose-S

Seaprose-S is a semi-alkaline proteinase originated from Aspergillus melleus, and has a proteolytic activity. When assayed, it contains 1900 - 2500 units per mg. Seaprose-S has been listed as a semi-alkaline proteinase in Monograph of the Japanese Standards of Pharmaceutical Ingredients.

Description
Identification
Purity
Loss on drying
Residue on ignition
Assay

} See the attached JSPI 1991.