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Date: February 7, 2005

To: Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling, and Dietary Supplements (HFS-820)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD, 20740-3835

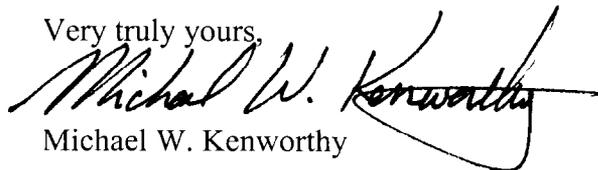
From: Michael W. Kenworthy
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To Whom It May Concern,

Pursuant to the Code of Federal Regulations, 21CFR190.6, Technology Commercialization Corp. is issuing this premarket notification of its intent to manufacture and market a product (herein described "Fermented Supernatant" or "Probiotic Booster") as a new dietary ingredient. Technology Commercialization Corp. will not market this product for a period of at least 75 days succeeding this notification and acceptance by the agency.

Please note that part of the text of the attached premarket notification is considered Confidential Information, and we respectfully request that this information not be published. Such Confidential text is shaded and marked as Confidential.

Very truly yours,


Michael W. Kenworthy

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RATIONALE FOR SAFE USE OF LACTIC ACID FERMENTED PRODUCTS

The art of fermentation, i.e. the transformation of organic compounds with the aid of enzymes produced by microorganisms, is very old. Fermentation has been used widely in the production of alcoholic beverages (beer, wine, brandy, etc.) and dairy products (yogurt, cheese, cream, etc.). Mankind has safely been using lactic acid fermentation for centuries. Yogurt was known in Persia, kefir in Caucasia. Many people in Korea, Africa, India and other countries and continents have been using lactic acid fermentation for various Oriental food products (roots of plants, beverages, etc.) [1]. Various fermented milk products have traditionally played an important role in the nutrition of people inhabiting Japan, Europe and Northern Europe.

Actually, nature lays the foundation for the safe use of lactic acid bacteria (LAB), *Lactobacilli* and *Bifidobacteria*. Babies are bacteria-free until they pass through the birth canal, the time when they are inoculated with *Lactobacilli*, which are dominant bacteria in the vagina in most healthy women [2].

Thus, this long history of human exposure and consumption of Lactic acid bacteria has led to the reasonable conclusion that they are generally safe [3].

Benefits of probiotics:

Since the early 1900's, when Metchnikoff first suggested that fermented milk could be consumed to eliminate putrefactive intestinal bacteria, there has been much interest in the potential health benefits of probiotic "living microorganisms, which upon ingestion in certain numbers, exert health benefits beyond inherent basic nutrition". There are some prophylaxis and therapeutic effects associated with starter microorganisms and their metabolites [5, 6, 7, 8].

Modulation of the gut microflora (populations and activities) and influence on mucosal immunity are mechanisms of probiotic function with potential to broadly influence human physiology [6, 9, 10, 11, 12]. Friendly lactobacteria maintain control of the normal vaginal ecology and administration of the probiotic organisms may normalize vaginal flora (2, 5).

Many basic biological functions can be assisted by probiotic bacteria. Probiotic bacteria produce enzymes [13, 14] that: 1) break down proteins into amino acids and peptides, 2) break down fats and complex sugars, and 3) improve the adsorption/bio-availability of calcium and other minerals. Some strains produce B-complex vitamins. Lactobacilli produce lactase, helping the lactose-intolerant digest lactose. Lactobacilli are able to predigest proteins, fats, or carbohydrates in such form that is more readily absorbed and digested in mammals.

Probiotic-microorganism containing foods and supplements, including yogurts, fermented milk products, capsules, and powders, now comprise a worldwide market with annual sales exceeding several hundred million dollars. And prebiotics - otherwise indigestible food ingredients that, when consumed, fuel the growth of beneficial bacteria in the intestines - also represent a similar product sector.

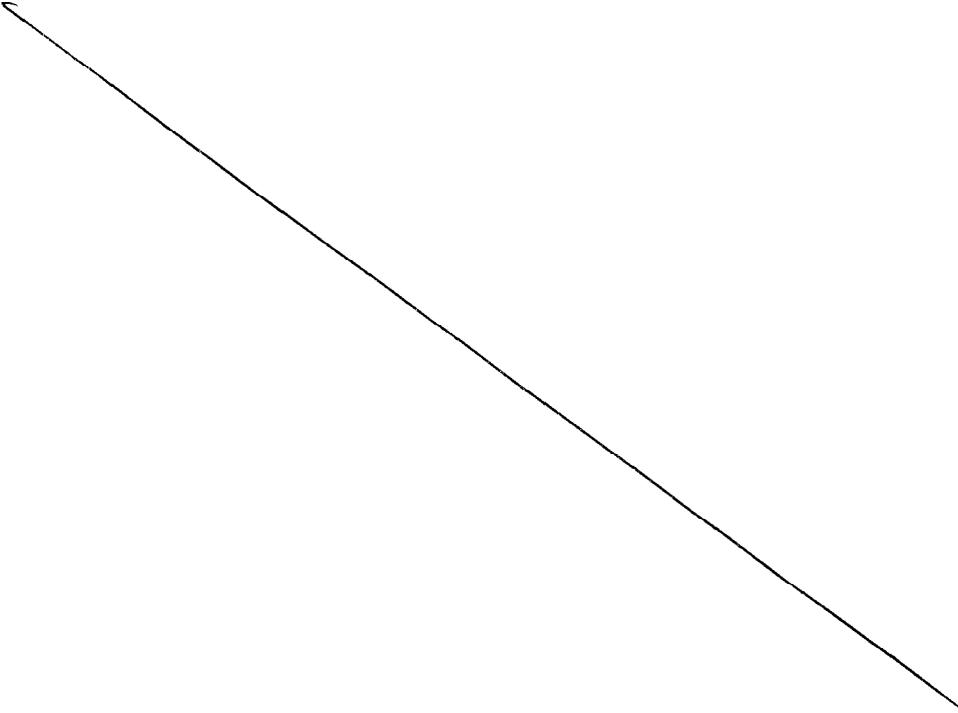
PRODUCT NAME:

“Probiotic Booster” or “Fermented Supernatant”

PRODUCT DESCRIPTION:

“*Probiotic Booster*” is comprised of natural food ingredients fermented using probiotic bacteria that are “generally regarded as safe” (GRAS) [15].

DETAILED DESCRIPTION OF PRODUCTION



At the end of the fermentation process, the liquid portion of *Probiotic Booster* is separated from the sediment. Some fine sediment is desirably retained in the liquid portion, which can be packaged in plastic or glass bottles for later sale. Such bottled *Probiotic Booster* can be stored for a minimum of eighteen months at 5 - 15 C⁰. The sediment byproduct, which consists of non-hydrolyzed food materials along with living probiotic bacteria, can be dried at 40 - 50 C⁰ and stored for up to 2 years at room temperature (or less) and consumed as a snack or for use in animal husbandry. Alternatively, the sediment can be utilized without drying, and in this case, it can be stored at 5 - 15 C⁰ for 2 - 4 weeks. The sediment is a non-hydrolyzed material (a prebiotic), and is beneficial for the growth of bifidobacteria and the host's microflora in the colon.

PHYSICAL AND CHEMICAL PROPERTIES

Physical description:

The *Probiotic Booster* is a liquid having a reddish or brownish color, depending on the quantity of fermented end products. By the end of the fermentation process, the hydrolyzed medium has high acidity (generally, from 800 to 900 T⁰, or lactate from 7.2 to 8.1%), low pH (from 3 to 4.5), and a high concentration of bacterial metabolic products and a relatively low concentration of GRAS strains of Lactobacilli (from 10⁵ to 10⁶ cells/ml) compared to traditional probiotic preparations, the latter having bacteria populations of from 10⁷ to 10⁹ cells/ml.

Probiotic Booster contains peptides (5 - 10 % by weight), all essential amino acids, nicotinic acid, all B vitamins, biotin (vitamin H), microelements, ferments with high proteolytic

activity and organic acids, predominantly lactate; these are naturally produced metabolic end-products of the fermentation process.

The smell of **Probiotic Booster** is full-flavored, and the taste is acidic due to the high concentration of lactate. The smell and taste can be improved by shortening fermentation time.

Stability and reactivity:

The shelf-life of **Probiotic Booster** is exceptionally long. If not diluted, it is stable for several weeks at room temperature; and when refrigerated at 2-12 degree C, it can be stored for a minimum of eighteen months without deterioration. No preservatives need to be added given that **Probiotic Booster** naturally inhibits the growth of pathogenic bacteria and viruses because of its high acidity and the presence of other probiotic bacterial metabolites.

Quantity of LAB per Unit:

A relatively low number of bacteria are living in **Probiotic Booster** (around 2×10^5 cfu/ml) when compared to other probiotic products (as measured by volume and by recommended daily intake). This may be due to cell autolysis, which has been attributed to the lipoteichoic acid present on the cell surface. Starter activity in the liquid leads to the production of lactic acid, as well as flavor and aroma compounds and CO₂.

RECOMMENDED USE

Directions for use:

Oral Administration: mix 1 tablespoon (or 0.15 ml per kg body weight) of **Probiotic Booster** with (preferably, fruit-flavored, fat-free) yogurt, juice or water (in proportion 1:3 to 1:5), and take 2 to 3 times per day after meals. For stronger effect, use undiluted.

For intensive administration, the dose can be increased to 2 tablespoons (or 0.3 ml per kg body weight) 2 to 3 times per day after meals.

Other relevant information:

The **Probiotic Booster** contains approximately 60 kilocalories /100g (one kilocalorie equals one "food calorie") and is low in fat. Given a daily recommended intake of 20-30 g., this equates to 12-18 food calories / day. **Probiotic Booster** contains live active probiotic bacteria assimilated to an acidic environment.

Warning:

Because of the acidity (high lactate and other organic acids) of undiluted **Probiotic Booster**, it should not be ingested in undiluted form by people with an ulcer or any intestinal or stomach inflammation. For such people, the **Probiotic Booster** should be diluted in yoghurt (in proportions of 1:5), not acidic juice or water, immediately before consumption.

Store in refrigerator. When stored at 34 - 45° F, shelf life is 18 months or more.

Do not freeze.

NUTRITIONAL CLAIMS

- 1) Low fat
- 2) Low salt
- 3) No additives

- 4) No cholesterol
- 5) No alcohol
- 6) High in calcium
- 7) High in fiber
- 8) All natural
- 9) Organic

Note: Nutritional claims categories are not cumulative, as new products may carry more than one claim.

STRUCTURE / FUNCTION CLAIMS:

Probiotic Booster is a unique product [15]. It is a probiotic liquid medium (a supernatant) containing a high concentration of fermented metabolites along with several strains of highly active living “generally regarded as safe” (“GRAS”) *Lactobacillus* bacteria. A wide variety of natural food ingredients is fermented intensively using a patented process to produce a high concentration of beneficial metabolites (organic acids, hydrogen peroxide, amino acids, vitamins, bacteriocins and many secondary metabolites). The various ingredients and bacteria are selected specifically to produce a broad array of favorable metabolites. Probiotic bacterial metabolites help produce an environment favorable to friendly bacteria of the host organism, stimulating their growth. Probiotic bacteria living in their natural medium (their supernatant) are more active and viable than those in a lyophilized (freeze-dried) state. **Probiotic Booster** is formulated to re-populate and promote the growth of beneficial bacteria.

- 1) **Probiotic Booster** stimulates the growth of beneficial bacteria in the gastrointestinal tract and in the uro-genital tract [2, 5, 6, 7, 9].
- 2) **Probiotic Booster** helps maintain desirable micro-organisms in the vaginal tract [2, 5]. Supportive for menopausal women when take orally.
- 3) **Probiotic Booster** effectively helps maintain intestinal flora [5, 7, 9].
- 4) **Probiotic Booster** contains nutrients that are easily absorbed by the body, and is especially beneficial for the elderly and those with a weakened digestive system [8, 13, 14].
- 5) **Probiotic Booster** supports the immune system [3, 4, 5, 6, 7, 11, 12].
- 6) **Probiotic Booster** improves overall health [3, 5, 6].

DISCLAIMER: "These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, mitigate, cure or prevent any disease"

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