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**U.S. Food and Drug Administration  
Pre-market Notification**

**Preparate Capsules**

The lysate powder of  
***Lactobacillus delbrueckii subsp bulgaricus***

A Dietary Supplement  
For  
Immediate Immune System Support

Prepared by:

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USFDA Pre-market Notification**

The format employed for this submission was provided by Ms Shelley Maifarth, USFDA Compliance Officer, Denver, Colorado. The USFDA document supplied was updated September 20, 2001. Special thanks to Ms Maifarth for her assistance and time.

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**Name of new dietary supplement:** *Lactobacillus delbrueckii ssp bulgaricus* lysate

**Trade name of new product:** Preparate (USA) Extrabiolat (Russia)

**Description of the dietary supplement:** This is a cultured lactobacillus product that is manufactured like yogurt. When the fermentation is complete the biomass is lysed, and then dry frozen to produce a powder similar to dry milk (A translation of the lysing process is included with this submission. The information is a trade secret and highly CONFIDENTIAL. The USFDA document dated September 10, 2001 states confidential information will not be revealed to public. The information is provided with the caveat it will not be released. Thank you!).

Capsules are manufactured containing 125 mg of the active *Lactobacillus delbrueckii ssp bulgaricus* lysate powder. Brown rice powder is used as a filler. Either #0 or #1 gelatin capsules will be filled to produce the final commercial product.

The label will state the product is for "immediate immune system support".

Re: safety Acute and chronic toxicity studies were conducted under the supervision of Vasilli N. Kravets, MD. PhD. Medical Director of the Russian Institute of Hematology and Transfusiology. The study is enclosed for review. Dr Kravets stated "Matrix E has been consumed by thousands of Russian patients, in large dosages, over the past 16 years without evidence of toxicity."

Re: safety of *Lactobacillus delbrueckii ssp bulgaricus*. This specific bacterium is extensively used in yogurt and cheese production in the United States. In cheese the bacteria lends a sweet flavor and attractive color according to the literature review.

## A History of Use:

(The following synopsis has been obtained through discussions with the principle investigators in St Petersburg, Russia, and reviewing a number of translated documents.)

In 1980 the Russian military challenged (ordered) a medical research team comprised of members from the Russian Institute of Hematology and Transfusiology and the State Research Institute of Highly Pure (Refined) Biopreparations, both located in St Petersburg, to develop a new product to protect Russians against the anticipated American use of bio-terrorism products including anthrax, small pox, tularemia, etc. The new product was ordered to be highly effective in providing immune system protection, inexpensive to produce in large quantities, and absolutely safe to ingest in the required dosage.

The St Petersburg medical research team reviewed products that allegedly boosted the immune system to protect against infectious bio-warfare invaders. One of many areas for investigation were Russian farmers who for years consumed unpasteurized milk and have traditionally experienced long and healthy lives. With time, the focus of their research effort turned to the comprehensive investigation of *Lactobacillus* strains found in unpasteurized milk.

Hundreds of *Lactobacillus* strains were collected, cultured, harvested, processed and laboratory/clinically tested against a variety of infections. Most of the strains were clinically unimpressive. A few strains looked promising, but the "shining star" was identified as a specific variant of *Lactobacillus delbrueckii ssp. bulgaricus*. The product was given the name "Matrix E" (now called Preparate in the USA and Extrabiolat in Russia).

A small production laboratory was assembled at the Institute of Hematology, and limited quantities of the Matrix E were produced. The product was cultured like yogurt, lysed, and dry frozen like powdered milk. The research team claims lysing increases the immuno-modulating effects by exposing more of the cell components to the immune system, facilitates opportunities for biopharmaceutical formulations, and enhances shelf life.

Clinical testing of Matrix E, (Preparate/Extrabiolat) proved the product to be highly efficacious in "stimulating" the immune system, inexpensive to produce, and have extraordinarily low toxicity. The project was successfully concluded in 1986. Subsequent political and economic changes in the USSR eliminated the need to mass produce and distribute the product after 1986.

After completion of the project in 1986 the Medical Director and Assistant Medical Director of the St Petersburg Hospital cautiously prescribed the Matrix E (Preparate/Extrabiolat) for new cancer patients and patients receiving chemotherapy and radiation therapy. The results were impressive in both types of patients. Since then thousands of patients have been given the product in doses exceeding 10 grams a day for protracted periods of time... in excess of 3 years. The doctors reported side effects to be almost negligible in the past 15 years.

Matrix E (Preparate/ Extrabiolat) is commercially produced , distributed, and marketed in Russia and the Ukraine by Elan, Ltd of St Petersburg, Russia.

**Reference and Published Materials:** In order or presentation the following reference and published materials are provided to document the consumer safety of *Lactobacillus delbrueckii ssp bulgaricus* when used as a dietary supplement. An internet search produced 256 *Lactobacillus delbrueckii bulgaricas* references . Most all of the references relate to cheese, yogurt, whey, and cultured milk production or research.

1. Confirmation of Safety in Human Use... Translated from Russian. Provided by Dr Vasilli Kravets, MD PhD, Medical Director, Russian Institute of Hemotology and Transfusiology, St Petersburg, Russia.
2. Complete genome-internet search- description of *Lactobacillus delbrueckii bulgaricus* stating it is one of two bacteria required in the production of yogurt and fermented milk.
3. Gastro-AD for relief of Occasional Heartburn... a *Lactobacillus delbrueckii* commercially marketed product.
4. Probiotic strains offered for sale by Chris Hansen Ltd, Denmark. *Lactobacillus delbrueckii ssp.bulgaricus*.
5. American Type Culture Collection Catalog...*Lactobacillus delbrueckii subsp.bulgaricus* Designation (USDA Lb7), Applications: active in American cheese production.
6. Exopolysaccharide production by *Lactobacillus delbrueckii ssp. Bulgaricus* RR grown in whey and whey permeate. E.M. Panko and R.F. Roberts, Food Science Department, Pennsylvania State University.
7. **CONFIDENTIAL:** Russian translation "Preparation of a food supplement with curative and prophylactic properties".
8. Russian translation. "INSTRUCTIONS" .
9. Original Russian Package Insert.
10. Proposed package labels for containers of 30 and 100 capsules. Labels are designer proofs and are greatly enlarged.

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