DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

0427 '03 JAN 27 P2:20

Date: JAN 23 2003

From: Consumer Safety Officer, Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-821

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification:	*Lactobacillus delbrueckii* subsp. *bulgaricus* (resubmission)
Firm:	Pure Research Products Naturally LLC
Date Received by FDA:	July 16, 2002
90-Day Date:	October 14, 2002

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned substance should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Rhonda R. Kane, M.S., R.D.

Attachments

95S-0316

RPT144

Pure Research Products Naturally
6107 Chelsea Manor Court
Boulder, Colorado 80301

303 530-7761 Fax 303 530-0222

jsichel@ecentral.com

Ms Rhonda R. Kane
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, Maryland 20740

22 August 2002

Dear Ms Kane:

Here is the label that has been submitted to (HFS-810) for Del-Immune. Please note the label is completely revised from the example that was attached to Premarket Notification II. For this reason I feel it is important for you to see it so there are no surprises. If any of the information on the label would change your position on the PMN please contact me. If I don't hear from you I will assume what we have done is OK.

Mr Robert Moore (HFS-810) was contacted with a request to fax a label sample or two because the PDF file you directed me never completely downloaded. There has been no response. Therefore I visited the Vitamin Cottage Shop in Boulder on Wednesday and reviewed dozens of nutritional and food supplements to gain some insight into examples of labels.

The attached Del-Immune label was developed by carefully reviewing 101.36, 101.9, chatting with Ms Thompson (I think the name you provided wasThomas), and following the layout of a product called Sambucol...Immune System Formula.

Once again, thank you for your guidance and assistance. FYI I realize there are label consultants available, lawyers, and a zillion other experts. The facts are that I want to learn this procedure from the grass roots level...there will be other products that we may wish to market in the future.

What you have done is to convince me the FDA is not the "enemy", can provide some assistance, but that we must have the regulations, read and understand them, and be self reliant to achieve success. It's really the "Old Fashion American" way, isn't it!

Respectfully,

John A. Sichel, PD, RPh
Pure Research Products Naturally LLC

Lactobacillus *delbrueckii ssp bulgaricus* is one of several types of bacteria used to produce cheese and yogurt. In Russia, a unique strain of ***delbrueckii*** was discovered to have properties which support the immune system. Russian researchers culture the product, then use a process called *"lysing"*, which digests the cell wall. The resulting biomass is dry frozen to produce Del-Immune. The product has been used in Russia for more than 10 years.

This statement has not been evaluated by the Food and Drug Adminstration. The product is not intended to diagnose, treat, cure or prevent disase.

SUPPLEMENT FACTS

Serving Size 1 capsule
Servings per container 30

Amount Per Serving
Lactobacillus *delbrueckii* ssp bulgaricus lysate powder 125mg

Other Ingredients: brown rice powder filler, vegetable capsule.

Imported exclusively and distributed by:
Pure Research Products Naturally LLC
6107 Chelsea Manor Court
Boulder, Colorado 80301
USA
pure@ecentral.com

Pure Research Products Naturally LLC

Del-Immune

lactobacillus delbrueckii ssp bulgaricus lysed powder

A dietary supplement from St. Petersburg, Russia

immediate immune system support

Net Contents: 30 capsules

This statement has not been evaluated by the Food and Drug Adminstration. The product is not intended to diagnose, treat, cure or prevent disase.

Suggested Daily Usage:
1 or 2 capsules daily.

To preserve quality and freshness, keep tightly sealed and store in a cool, dry place.

Please keep out of the reach of children.

Safety sealed. Do not use if seal is broken or missing.

LOT#:
EXP DATE:

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

AUG 15 2002

Mr. John A. Sichel, R.Ph.
President
Pure Research Products Naturally LLC
6107 Chelsea Manor Court
Boulder, Colorado 80301-3148

Dear Mr. Sichel:

This is to inform you that the notification, dated July 15, 2002, you submitted pursuant to 21 U.S.C. 350b(a)(2) was received and filed by the Food and Drug Administration (FDA) on July 16, 2002. Your notification concerns the substance "*Lactobacillus delbrueckii* subsp. *bulgaricus* lysate" that you assert is a new dietary ingredient and that you want to market in a dietary supplement capsule called Del-Immune™ (Trademark is pending).

This notification represents a resubmission of the earlier notification you sent FDA in April 2001. On July 28, 2002, we responded in a letter to your first notification stating that it contained disease claims associated with the recommended conditions of use for Del-Immune that represented your product as a drug. Your first notification also did not comply with all the requirements of a new dietary ingredient notification specified in Federal regulations at 21 CFR 190.6.

Your current notification indicates that there are no live bacteria in *Lactobacillus delbrueckii* subsp. *bulgaricus* lysate that provides 125 mg of the lysate per capsule. You identify the intended users of Del-Immune as those who can swallow a size #1 capsule, and you state that the recommended intake level is 1-2 capsule per day as needed for "immediate immune system support." Your notification acknowledges that the quoted statement is a structure/function claim. As a reminder, no later than 30 days post marketing of a dietary supplement that contains any structure/function claims in the product's labeling, the distributor or manufacturer must submit to FDA certain information that complies with Federal regulations at 21 CFR 101.93. The label claim notification requirements are separate from those for the new dietary ingredient premarket notification program and are handled by another FDA staff.

The FDA Internet site http://www.cfsan.fda.gov/~dms/ds-labl.html#structure provides details on the types of claims that are allowed for dietary supplements, including structure/function, health, and nutrient content claims. Federal regulations at 21 CFR 101.36 address the general labeling requirements of all dietary supplements whether or not claims are made.

In addition, all dietary supplement claims made in both product labeling and advertising must be substantiated with scientific evidence, be truthful, and not be misleading. For your reference, the FTC Internet site http://www.ftc.gov/bcp/conline/pubs/buspubs/dietsupp.htm provides details on Federal requirements concerning the advertising of dietary supplements.

As a procedural matter in accordance with 21 CFR 190.6(c), this letter confirms FDA receipt of your notification for a new dietary ingredient. For 75 days after the filing date (i.e., until after September 29, 2002), you must not introduce or deliver for introduction into interstate commerce any dietary supplement that contains *Lactobacillus delbrueckii* subsp. *bulgaricus* lysate.

The lack of any follow-up FDA response during this 75-day period does not constitute a finding by the agency that *Lactobacillus delbrueckii* subsp. *bulgaricus* lysate or a dietary supplement containing it is safe or is not adulterated under 21 U.S.C. 342. Further, FDA is not precluded from taking action in the future against a dietary supplement containing *Lactobacillus delbrueckii* subsp. *bulgaricus* lysate if it is found to be unsafe, adulterated or misbranded. It is the responsibility of the manufacturer or distributor of a dietary supplement to ensure that it is safe, properly labeled and complies with all applicable requirements of the Federal Food, Drug and Cosmetic Act. Importantly, any new dietary ingredient for use in a dietary supplement that FDA has reviewed through the premarket notification process is not "approved" or "authorized" by the agency.

As another procedural matter, your notification will be kept confidential for 90 days after the filing date. Therefore, after October 14, 2002, the notification and this response will be placed on public display at FDA's Dockets Management Branch in docket number 95S-0316. However, any trade secret or otherwise confidential commercial information that is in the notification will not be disclosed to the public.

You identified in your notification what information you believe is proprietary. FDA will consider your request to withhold this information from public disclosure. Nevertheless, our Center's Freedom of Information Officer has the authority to make the final decision about what information in the notification should be redacted before it is posted at Dockets.

Please contact me at (301) 436-2371 if you have any questions concerning this matter.

Sincerely yours,

Rhonda R. Kane

Rhonda R. Kane, M.S., R.D.
Consumer Safety Officer
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

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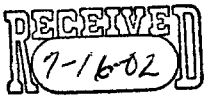

15 July 2002

Dear Ms Kane:

Here are three signed copies of the Del-Immune Premarket Notification II. Your helpful comments have been included in the revised edition. The Regulations provided have also been followed as required.

The Clinical Information section includes an affidavit to attest to the accuracy of the data presented. Copies of email and fax communications to Russia are enclosed to verify the information presented in the PMN II.

The information, as presented, is complete and will comply with the FDA Regulations for nutritional supplements.

Your assistance is genuinely and greatly appreciated.

Respectfully,

John A. Sichel, RPh
Pure Research Products Naturally

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

Del-Immune

Lactobacillus *delbrueckii* ssp bulgaricus lysate

A Dietary Supplement
For
Immediate Immune System Support

Prepared by:
John A. Sichel
President
Pure Research Products Naturally LLC
6107 Chelsea Manor Court
Boulder, Colorado 80301

15 July 2002

303 530-7761
Fax 303 5630-0222

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES (CONTINUED)

PART 190—DIETARY SUPPLEMENTS

Subpart B—New Dietary Ingredient Notification

Sec. 190.6 Requirement for Premarket Notification

(a) This document is prepared in an original and two copies for review by the:

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, Maryland 20740

(b) (1) "Name of manufacturer": ELAN, Ltd
Valerie Vospyakov, President
21/2 Komandsky Avenue
Saint Petersburg, Russia 7812 511 7039

Final Encapsulation: Natures Supplements,Inc
Arturo Castillo, President
2270 Camino Byda Roble, Suite Q
Carlsbad, California 92009 USA
Telephone 760 476-0559

Name of distributor: Pure Research Products Naturally LLC
John A. Sichel, President
6107 Chelsea Manor Court
Boulder, Colorado 80301 USA
Telephone 303 530-7761

(2) "Name of new dietary supplement": Del-Immune™ (Trademark is pending) Lactobacillus delbrueckii ssp bulgaricus lysate.

Please refer to Exhibit #1 re: the name Lactobacillus delbrueckii and Lactobacillus delbrueckii ssp bulgaricus and the planned product label.

Alphabetical Index-All Microorganisms:L (169 species) Lactobacillus delbrueckii is a synonym for Lactobacillus delbrueckii subsp bulgaricus.

Please refer to Exhibit #1 re: the name Lactobacillus delbrueckii and Lactobacillus delbrueckii ssp bulgaricus.

Alphabetical Index-All Microorganisms:L (169 species) Lactobacillus delbrueckii is a synonym for Lactobacillus delbrueckii subsp bulgaricus. Re:http://www.ifo.or.jp//db/A/MicroorL1_e.htlm.

(3) "A description of the dietary supplement(s) that contain the new dietary supplement".

The following references relate to the established use of Lactobacillus delbrueckii ssp bulgaricus (refer to Exhibit #1) in products on the US market including a treatment for heartburn and also for use in the production of food products in the dairy and cheese industries. Del-Immune information may be found under item (4) of Sec 190.6

a. Lactobacillus delbrueckii in Gastro AD for relief of Occassional Heartburn.

This reference is provided as an example to demonstrate the established use and safety of Lactobacillus delbrueckii (see Exhibit 1) for an over the counter treatment of gastrointestinal discomfort.

Please refer to exhibit #2 for the printed web page printout describing the product.

b. Lactobacillus *delbrueckii* bulgaricus (L. bulgaricus)

From Lactobacillus bulgaricus-Complete genome http://www.genoscope.cns.fr/externe/English/Projets_DF/DF.htlm.

This reference is provided to confirm the use of Lactobacillus delbrueckii in the production of food products that are routinely and safely consumed.

"Lactobacillus delbrueckii ssp bulgaricus (L.bulgaricus) is a Gram-Positive bacterium with a low GC content. This lactobacillus ferments sugars mainly to lactic acid, and therefore belongs to the lactic acid bacterial group. L. bulgaricus is one of two bacteria required for the production of yogurt and fermented milk, it has an essential role in the development of the organoleptic, hygienic and perhaps probiobiotic qualities of food."

Please refer to Exhibit #3.

c. **Use in cheese production**

This is an ATTC listing ...number 7995 and has as the application: "active in .. American cheese production process."

This reference is provided as another example of safety with Lactobacillus delbrueckii ssp bulgaricus , the use in cheese production, and with the ultimate consumption of the product by consumers.

Please refer to Exhibit #4

d. **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, 120A Borland, University Park, PA 16802.
"From the 1999 IFT Annual Meeting.

This document is provided to demonstrate consumer safety and the use of Lactobacillus delbrueckii ssp bulgaricus in cheese whey production for the manufacture of cheddar cheese.

Please refer to Exhibit #5

e. **SCIENCE YEAR-food technology-bio yogurt**

This reference demonstrates the safety and use of Lactobacillus delbrueckii ssp bulgaricus in the production of yogurt, a major consumer product.

This reference was located on an internet search and states "all yoghurt is made from milk using bacteria. The milk is heated up and a sample of bacteria is added to the milk while it is cooling. The bacteria live off the lactose (a type of sugar) in the milk and they convert it into a substance called lactic acid. And it's the lactic acid that makes the yoghurt set.

Most of the yoghurts you see in the shops are made using Lactobacillus delbrueckii bulgaricus and Streptoccus thermophilus. These bacteria are used because they grow quickly and turn milk into yoghurt in just a few hours.

.....Paragraph 4. With bio-yoghurts, the bacteria used in the production process aren't killed by the acid in our stomachs. The bacteria avoid being digested themselves and stick to your gut wall and they help your digestion of other foods. They also boost your immune system by reducing the amount of bad bacteria in your gut...

This document may be found in reference #6.

CHR Hansen Human Health
http://www.ch-humanhealth.com/probios.htm

This reference is included to demonstrate the availability of Lactobacillis delbrueckii ssp bulgaricus in bulk quantities for the commercial production of dairy products.

Please note in exhibit #7.

In review: Lactobacillus delbrueckii ssp bulgaricus is a bacteria found in in an over the counter stomach treatment. Additional references document the use of L. delbrueckii (see Exhibit #1) for the production of yogurt and cheese products that are safely and widely consumed in the United States.

(i) "The level of the new dietary ingredient in the dietary supplement."

Del-Immune will be formulated as a 125 milligram capsule. Size Number 1 vegetable capsules will be used for encapsulation of the Del-Immune powder (Lactobacillus delbrueckii lysate powder).

Approximately 125 milligrams of brown rice powder will be used as the filler for each individual capsule.

(ii) "The conditions of use recommended or suggested in the labeling of the dietary supplement...the ordinary conditions of use."

The condition of use is: immediate immune system support.

The product is available to all age groups . A warning statement will be included on the label as follows "WARNING: Keep out of the reach of children." **This warning is being used as a responsible pharmaceutical practice and good advice to consumers. It does not relate to nor restrict use of the product to any segment of the population.** Since the product will be manufactured and marketed as a capsule only persons capable of swallowing a size#1 capsule is the logical market .

The ordinary conditions of use will be for persons who feel their immune system is in need of support. These persons are thought to be consumers of natural and nutritional supplements that are to be found in health food outlets, internet marketing, and by direct mail marketing.

(4) "The history of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement , will reasonably be expected to be safe....."

Four major historical areas describe the key events in developing the product. They are:

a. **Biopreparate**
b. **History of Extrabiolat /Del-Immune**
c. **Production of Lactobacillus delbrueckii lysate**
d. **Clinical Use**
e. **Questions and answers from PMN #1**

The following events cover the period 1980 through 2002.

a. Biopreparate:

History of Lactobacillus delbrueckii ss bulgaricus as an immunotherapeutic agent.

The history of the product started in 1980 in Saint Petersburg at the State Research Center for Ultra Pure Biopreparations. As background, this facility was one of six leading weapons institutes in the former Soviet where 4,500 staff and about 500 senior scientists with biological weapons backgrounds were employed by the Russian government. "Following its ratification of the Biological and Toxin Weapons Convention in 1972, the Soviet Union established "Biopreparate" as a civilian pharmaceutical company and biotechnology enterprise, which also served as the civilian focal point of the Soviet biological weapons program."

For additional background, the State Research Center, in St Petersburg, was visited by senior US officials from the Departments of State, Defense, and Energy in December 1999. A report of their activities relating to bio-warfare agents is available in the GAO Report to Congressional Requesters. The report is titled BIOLOGICAL WEAPONS-Effort to reduce former Soviet threat offers benefits, poses new risks. GAO/NSIAD-00-138. (See Exhibit#8-First 4 pages only). This report offers an understanding of the impressive caliber of research performed at the State Research Institute as well as research performed at other former Soviet bio-warfare centers.

Under Biopreparate ,in 1980 USSR government officials with representatives from the Russian military requested a research group located at the State Research Center for Ultra Pure Biopreparations to develop products that could provide protection to Russians in the event of an enemy attack with anthrax or other biohazard agent. Concern was expressed about the need to also help the Russians in the event of a second Chernobyl disaster.

Subsequently a microbiological research team and laboratories were established in 1980 at the State Research Center for the purpose of developing immuno-therapeutic agents. The research was conducted by a group of six senior scientists (Exhibit #9) and staff of 50 employees. Approximately 600 different microbiological and other type products were investigated for their immunogenic activity. Many strains of Lactobacillus were collected and investigated as part of this study.

The system for evaluating the potential efficacy of products was the use of "in vivo" tests with laboratory rats. Controls and infected animals were tested by inoculation with various pathogens and part of the group given the immunotherapeutic test agent. Products showing promising results were moved into clinical testing. The clinical trials were

performed by physicians at the Saint Petersburg Research Institute of Hematology and Transfusiology (the main cancer hospital in St Petersburg).

Human clinical trials involved patients who were jointly selected by the State Research Center research group and hospital physicians. The patients selected for clinical trials suffered from flu, colds, a garden variety of common infections and cancer. Participants were instructed to take their "medicine" and report back to the physicians. Based upon the patient response the investigational products were either rejected or selected for further investigation. (This protocol would obviously never "fly" in the US but it is necessary to remember the times in Russia!)

The products demonstrating the greatest immuno-therapeutic efficacy were from the group of Lactobacilli. Within the group of Lactobacilli the optimal responses were observed with Lactobacillus delbrueckii (Lactobacillus delbrueckii ssp bulgaricus). Through a process of elimination one product was selected to represent the preferred immuno-therapeutic agent.

This selected Lactobacillus delbrueckii product was tagged with a variety of names by different staff doing different types of clinical investigations at different periods of time. The same lactobacillus acquired names like Matrix E, Lactofluor, Vitafluor, Preparate, and the latest name of Extrabiolat. The difference between product names related to the evolving manufacturing techniques starting with bench top mini-quantities (Matrix E) to the present commercial quantities of about 3 to 5 kilograms in 48 hours. The point of this discussion is to affirm the Lactobacillus manufactured currently is the same as the original Lactobacillus delbrueckii ssp bulgaricus discovered back in the 1980's but manufactured quite differently.

The various names of the product employed during different periods obviously leads one to think there were many products but in reality there was only one product....the original.

b. History of Extrabiolat and Del-Immune

During the political, economic, and social changes in the USSR there was a period of almost 2 years when workers were not paid their salaries. This was in 1992 when Biopreparate was terminated (See Exhibit #8). Work simply stopped.

During this period Mr Valerie Vospyakov, (see Exhibit #9) one of the original immuno-therapeutic scientists requested permission to continue research on the Lactobacillus delbrueckii using the State Research Center laboratory but his personal equipment. (Mr Vospyakov personally purchased and salvaged used equipment from a salvage depot in St Petersburg.) He and his two sons, both college students, built a new laboratory and "clean room" in space provided and approved by the President of the State Research Center.

Mr Vospyakov and his two sons assembled the necessary equipment to culture the Lactobacillus, centrifuge the biomass, transfer the product to a sterile flask, lyse the biomass, and dry freeze the lysed product. He then formed a company and called it "ELAN,Ltd". During the period of no income he worked on purifying the product, building production, producing and packaging small quantities of powder and tablets. The product was made available to "friends" in relatively small quantities to provide some income for his

family. Valerie Vospyakov named the product "Extrabiolat" meaning Extra Bullet in Russian. The same product will be named Del-Immune in the United States.

c. Lactobacillus delbrueckii ssp bulgaricus lysate production

Two documents relating to the lysate process are enclosed (Please refer to Exhibit # 10). The first document is the comprehensive method for culturing the Extrabiolat and the lysate. It is a **"confidential"** document, is a translation from Russian, and shows production "secrets".

The second document is a publication from the Russian Journal of HIV and Related Problems, "2000" . The article is titled Peptidoglycans from Different Types of Lactobacilli:Isolation Methods, Identification, and Biological Activity. Please note the underlined paragraph. The general description discussing the lysing procedure for lactobacillus is the first of two steps for extracting peptigoglycans. These Lactobacillus products are unrelated to this submission however the lysing technique is directly related to this project!

d. Clinical History in Patients

Please refer to Exhibit #11 as evidence of human safety. Because of a delay that could take months, and require another trip to St Petersburg by Sichel, two documents relating to human use (clinical use) were obtained from the US Patent Application. The information was verified to be correct and accurate by Dr Vassilli Kravets (Exhibit#9) as noted in the affidavit, attached. This information is offered and requested to serve as evidence of human safety for Del-Immune. The product is not intended to be used for the indications in the attached documents nor will it be marketed for these indications .

Copies of all of the e-mails and faxes required to obtain the affidavit are attached for review. If there is any doubt about the validity of the information the FDA is invited to contact Dr Vassilli directly to verify the clinical information. His St Petersburg telephone number is 7812 274-5715.

"Results of Clinical Investigations in Bronchopulmonary Diseases".
(Please to Exhibit # 12)

This document is a summary of 300 patients participating in the use the Lactobacillus delbrueckii (Preparate) and was prepared by Dr Victor Rugal, MD,PhD and Dr Vassilli Kravets MD, PhD Medical Director of the Hospital for Transfusiology and translated for the purpose of preparing and submitting a Patent Application for the US Patent Office. (The patent application was rejected by the US Patent Office because they claim a bacteria cannot be patented).

This document discusses the clinical use of the Lactobacillus delbrueckii, with the name Preparate, (please refer to section 4. a "History of Lactobacillus delbrueckii as an immunotherapeutic agent". The document states "This Preparation does not engender an side effects and is not toxic".

"Preparate Clinical Trials"

This document (Exhibit 11) was also prepared by Doctors Kravets and Rugal for the for the Patent Application. The information discusses selected clinical cases, the use of Lactobacillus delbrueckii (Preparate) and dosages. It is an example to demonstrate safety with human use on a case by case basis. Although the sample is small it documents the absence of side effects when consumed.

e. Questions asked by the FDA Review Team

1. Provide confirmation that Del-Immune (Extrabiolat) is made by Elan, Ltd.

(Exhibit #12) is the Russian package insert for Extrabiolat and shows ELAN as the manufacturer...note the circled area. The Russian letter H is an N in English.

2. Confirmation the Extrabiolat does not contain live cells. Exhibit #13

3. Is Extrabiolat Lactobacillus delbrueckii ssp bulgaricus. Exhibit #13

A fax was sent to Mr Vospyakov requesting answers to the four questions that were suggested to be addressed. A telephone was subsequently made with the request to answer the questions and return them to Sichel...this failed. (Vospyakov is terribly afraid of the government in spit of efforts to reassure him that the USA and the FDA do not have relationships with the KGB.) A copy of the fax and Russian translation of the fax is attached. An answer was not forthcoming so the same questions were asked to Dr Vassilli by e-mail...please note his response. "The product does not contain live cells."

Mr Vospyakov was telephoned by Valentina Mouravych, Assistant Director of "Doctors Without Walls" and formerly a professional translator. (Please see Exhibit #14) She served as the translator for Sichel during the first meeting with the research team in the Cancer Hospital. Valentina has assisted in translating messages to and from the Russians since the hospital meeting.

Sichel contacted Valentina by email with the request to call Mr Vospyakov and ask if Extrabiolat contained live cells and what bacteria is used for making Extrabiolat. Please refer to the copies of email that follow.

My Vospyakov reported to Valentina that Extrabiolat does not contain live cells and is Lactobacillus delbrueckii.

In summary, this Pre-Market Notification presents the information requested in Sec 190.6, Subpart B, Part 190, Chapter 1, Title 21-FOOD AND DRUGS.

The information presented demonstrates the current use of Lactobacillus delbrueckii ssp bulgaricus as an over the counter stomach medication. Other strains/variants of the

Lactobacillus are used for the production of cheese and dairy products. In all cases the Lactobacillus delbrueckii is safe for human consumption.

The Russian history of the Lactobacillus delbrueckii development weaves through many periods of cultural, economic, and sociological changes. The product acquired a variety of names over time however the bacteria has remained the same. The only changes have been in manufacturing procedures from bench top production to commercial production.

The product has been in continuous clinical use since 1986 at the State Institute for Hematology and Transfusiology for the treatment of lung, breast, and liver cancer. Procuring information has been extremely difficult because the research group is now into the development of the immunomodulating component of the Lactobacillus delbrueckii. There is also great concern about any relationship with the government...Russian or US.

The clinical documentation presents information taken directly from the US Patent Application and that had been originally prepared by Dr Vissilli Kravets, Head Physician and other staff members at the State Institute for Hematology and Transfusiology in St Petersburg. The clinical information was faxed to St Petersburg and presented to Dr Kravets for his review by Anatoly Plikh, a professional translator. After his review Dr Kravets signed an affidavit testifying that the clinical information presented is true and correct.

Ms Valentina Mourayvk, formerly a professional translator and now the Assistant Director for "Doctors Without Walls" assisted by contacting Mr Valerie Vospyakov by telephone in St Petersburg to collect information re: the presence of live cells in the product and to confirm the product is 100% Lactobacillus delbrueckii.

Dr Kravets also confirms there are no live cells in the product. Copies of e-mails and faxes are attached to confirm the communications.

If acceptable the product will be made available for the "structure/function" use as an "immediate immune system support" product.

The assistance of Ms Kane and other FDA members is greatly and genuinely appreciated.

I hereby state the information and claims made in this FDA Premarket Notification II are true and accurate in every detail.

John A. Sichel, RPh
President
Pure Research Products Naturally LLC
Boulder, Colorado 80301

15 July 2002
Date