



Memorandum

Date DEC - 4 1996

From Acting Director, Division of Programs and Enforcement Policy, Office of Special Nutritionals, HFS-455

Subject 75-Day Premarket Notification for New Dietary Ingredients

To Dockets Management Branch, HFS-305

2233 '96 DEC 17 PM 2:47

New Dietary Ingredient: Trigonella foenum-graeceum  
(Debitterized fenugreek powder)

Firm: Kentucky Biosafety Consultants Inc.

Date Received by FDA: September 17, 1996

90-Day Date: December 15, 1996

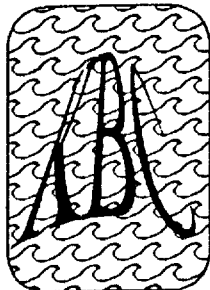
In accordance with the requirements of section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification for the aforementioned new dietary ingredient should be placed on public display in docket number 95S-0316 after December 15, 1996.

Sincerely yours,  
*James Tanner*  
James Tanner, Ph.D.  
Acting Director,  
Division of Programs and  
Enforcement Policy  
Office of Special Nutritionals  
Center for Food Safety  
and Applied Nutrition

Attachment

95S-0316

RPT 6



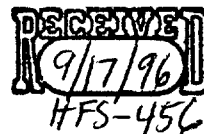
# Kentucky Biosafety Consultants Inc.,

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Consultants for Product Development, and Sourcing & Marketing Quality Herbal & Natural Consumer Products, Pharmaceutical, Fine & Industrial Chemicals, Diagnostics, Medical & Laboratory Equipment and Supplies.

Mr. Robert Moore, PhD, Sr. Regulatory Scientist  
MAILSTOP: HFS-450,  
FDA, FOB 8, Rm. 2804, 200 C Street, SW  
WASHINGTON, DC 20204



September 15, 1996

Subject: Trigonella foenum-graeceum (L) (Linn.)- [= fenugreek] for Dietary Fiber Supplement; PREMARKET notification of Debitterized Defatted powder as a dietary fiber supplement as required under Dietary Supplement Health & Education Act of 1994, Sec 8 "New Dietary Ingredient" (2)

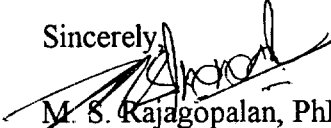
Dear Dr. Moore:

Personally, as a consultant to the manufacturers, and on behalf of KBC Inc, the authorized representative in USA, I present the following facts in support of the subject noted above, and submit the enclosed package of information material. I have enclosed a summary sheet herewith.

Apparently, Fenugreek has never been presented to FDA as a source of dietary fiber. Fenugreek is not only a good source of dietary fiber, it is also biologically better acceptable than other fiber supplements currently used, such as psyllium. Fenugreek was 'preserved' from animals by nature with the inherent bitterness and strong flavor. With persistent scientific advancement the manufacturers have remove the bitterness at commercial scale, without altering any of the other natural qualities of Fenugreek. Debitterized fenugreek powder has all its natural fiber, protein and mineral contents preserved through the process. It is shown to be safe by animal toxicology studies and human volunteer studies. Fenugreek has good quality protein, with NPU 64. Debitterized fenugreek is suitable for various presentations and blending to optimize the fiber intake per dose. The powder is manufactured in a cGMP compliant facility in India, and the laboratory analytical data show absence of any pathogenic or heavy metal contamination. When taken with 8 oz of liquid, it gives about 5 g fiber and 30 calories, and no fat.

I request that based on the information provided herewith, FDA will approve the use of debitterized fenugreek powder as a dietary fiber supplement suitable for human consumption. I would appreciate receiving a communication in this regard. If you need additional information, please do not hesitate to call or fax me your question to (606) 269-2411 or Email KBC.USA@WORLDNET.ATT.NET or msraja1@ukcc.uky.edu

Sincerely,

  
M. S. Rajagopalan, PhD  
President.

Shipping Address: 3304 Montavesta Road E74, Lexington, KY 40502 USA

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**SUMMARY SHEET**

1. Dietary Fiber- Definition: Fiber is a part of plants and parts of a plant that gives the shape and structure to the plant and hence are exclusively found only in plants. Some of the fibers are edible, while others such as cotton fiber from the fruit, coconut fiber the shell of the fruit, are not edible. There are two forms of *edible fibers*: namely some which are *soluble* that dissolve in water and others which are *insoluble*. The rich sources of edible soluble fiber are legumes, fruits and vegetables and of insoluble fiber includes various brans. Chemically, gums, mucilages and pectin are *soluble fibers*. Cellulose, hemicellulose and lignin are *insoluble fibers*.

2. Health Benefits Dietary Fibers: Soluble and insoluble fibers contribute differently to a healthy diet. Several studies have shown that when combined with a low-fat diet, *soluble fiber decreases the blood cholesterol level*, especially the 'bad' cholesterol (LDL, VLDL, Triglycerides) levels in blood and thus help in preventing heart disease. In addition, soluble fiber also *help regulate blood sugar level*, and thus may help diabetes patients as an adjuvant to other forms of management. Soluble fiber also is recognized to influence bile secretion and steroid metabolism. *Insoluble fiber* act as bulk, they help the digestive system run smoothly, aiding in treatment or prevention of constipation, hemorrhoids and other intestinal problems. Some studies have indicated that diets rich in insoluble fiber may lower risk of some types of cancer like colon cancer. In addition to the recognized benefits, high fiber foods displaces fat and other such calorie-rich components of a meal, increases satiety, reduces craving for feed, and thus help in control of weight gain. Most high fiber diets are shown to be rich in vitamins and minerals while being low in fat.

3. Recommended daily amount for Total Dietary Fiber: Although there are no US official guidelines on the amount of total dietary fibers yet, many health organizations recommend **20 to 35 grams of fiber per day**. The World Health Organization has recommended 22 g/1000 Calories. Scientific studies have shown that a combination of 60% of fibers as soluble and the rest as insoluble fibers offer best health benefit.

4. Sources of Dietary Fiber: Copy of public education pamphlets (a) Fiber Facts from American Dietetic Association, and (b) New Buyer's Guide to Dietary Fiber from California Fig Advisory Board<sup>1,2</sup>. They show the fiber content of dietary components such as fruits and vegetables, which range from a fraction of 1% to about 15% of the total weight. It is not surprising that normal American diet contains only about 5 grams of fiber a day, against 20 g to 35 g considering the 2000 Calorie intake. Unlike any other source of dietary fiber, Fenugreek seeds (fruits of *Trigonella foenum-graeceum (L)*) contain almost 50% it weight in the form of edible fiber. Further, Fenugreek seeds contain significant quantity of both soluble and insoluble fiber. (U. Rao & R. D. Sharma, Food Chemistry, 1987, 24:1-9<sup>3</sup>).

5. Nutritional Support of Dietary Fiber: While there is no dispute over the need for dietary fiber in our diet, the quantity of food items that need to be taken considerably increases if a given food contains only 3 or 5%. Taking 10 g of Fenugreek equals (= 4.5 g fiber). To get this amount of fiber we must consume 500 g of white Thompson grapes, or 100 g of cabbage or 150 g of banana. A 10 g fenugreek powder less than 20 Calories whereas 500 g of grapes has 250 Cal., and 150 g of banana has 100

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Calories. Therefore Fenugreek provides a low calorie, high fiber concentrate, allowing an individual to obtain adequate amount of dietary fiber without enormously increasing the volume of food items in order to reach the recommended 20 to 35 g a day.

6. Current use of *Trigonella foenum-graeceum* (L) in USA: Fenugreek seeds are already used as food, as spice, as pest repellent. 21 CFR part 182 lists Fenugreek as a GRAS spice, oleoresin, extract and flavoring. Fenugreek has been used in oriental culinary for several millennia, as well as a medicinal plant (copy of Indian Materia Medica, 1976, 1: 1240-1243<sup>4</sup>). Fenugreek seed and powder are safe and have been in use for a long time. In fact Fenugreek extract contains the alkaloids which is imported into USA as oleoresin and absolute extracts, and used for flavoring.

7. Composition of Fenugreek- Fenugreek has been studied very carefully for its composition. It contains about 30% protein, which has an Net Protein Utilization value of 64, coming close to meat. It contains about 45% carbohydrates all of which are in the form of soluble (28% ) and insoluble (17%) fiber. It also contains minerals which are beneficial to humans. Fenugreek seed is very bitter, and also has a strong flavor. These are due to the two alkaloids as well as volatile fatty acid. The plant uses these bitterness and strong flavor to repel herbivorous animals that may harm the propagation of the species. The extracts of Fenugreek listed under GRAS ( part 182) is a mixture of plant saponins and steroids, alkaloids such as choline and trigonellin, and the essential fat. (relevant pages from "Wealth of India"<sup>5</sup>).

8. Safety of Fenugreek seed powder: Toxicological studies were conducted in rats using the powder from fenugreek seeds at the National Institute of Nutrition, Hyderabad, India. Fenugreek even used up to 20% of total diet by weight, caused no toxic effects. Male rats showed a significant reduction in the cholesterol levels. A pre-publication manuscript of a scientific paper accepted for publication in Nutrition Research 1996, title: "Short term Nutritional and Safety Evaluation of Fenugreek" by U. Rao et al<sup>6</sup>. In addition, Fenugreek has been used for several centuries and no adverse side effects have been noted. In fact, FDA permits use of Fenugreek as spice in USA. Fenugreek seeds are freely available in all oriental and even some supermarkets in most part of USA.

9. Chemical composition of processed seed powder. By employing a patented method of extraction using permitted solvents, the bitter principles, the saponins, alkaloids and fat have been removed from fenugreek powder. (U. Rao & R.D. Sharma, Food Chemistry 1987, 24:1-9<sup>3</sup>). The resultant powder is free of the solvents, and has been analyzed for composition, safety and tested in small and large animals for efficacy in regulating blood glucose levels, and blood cholesterol levels. The debitterized fenugreek powder manufactured by Sterling Home Products, Madras, India, is an improved and commercial version of the methods elaborated in several publications listed here. A patent application has been filed in USA elucidating the processing of fenugreek seed powder.

10. Safety of debitterized Fenugreek powder: Acute toxicity studies conducted with the processed fenugreek powder in mice and rats showed NO Toxic effect in the animals. The highest dosage was 5 g/ kg body weight (see "Interim Progress Report- Toxicological Studies on Debitterized Fenugreek Powder, conducted by Dr. S. P. Pillai, at the Central Food Technology and Research Institute, Mysore,

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India<sup>7</sup>). In another study, NO toxic effect was observed even with debitterized fenugreek powder at 40% total dietary volume (Unpublished data- report: "Short term safety Evaluation of Debitterized Fenugreek" by N. Prabhakar et al, from University of Madras, India<sup>8</sup>). These studies confirm the safety of the debitterized powder.

11. Animal Studies with Debitterized Fenugreek powder: When diabetic model rats were fed debitterized powder with glucose, a significant hypoglycemic effect was observed, and was shown to be due to the soluble fiber content of the processed fenugreek (L. Ali et al, *Planta Med*, 1995, 61: 358-60<sup>8</sup>). Similar studies conducted in dogs observed hypoglycemic effect (Ribes et al, 1986, *Proc. Soc. Exp. Biol. Med*, 182:159-166, Not enclosed). In addition, Hypolipidaemic effect of debitterized fenugreek was shown in dogs by Vallette et al., 1984, *Atherosclerosis* 50:105-11, Not enclosed). Effect of debitterized fenugreek on the cholesterol levels in dogs was reported by Stark and Madar (*Brit J Nutrition* 1993, 69:277-87<sup>9</sup>).

12. Clinical studies using processed seed powder: Hypolipidaemic effect of debitterized fenugreek powder in humans was shown by R.D. Sharma et al (*Phytotherapy Res* 1991, 5:145-147<sup>10</sup>). This study had a cross-over design on volunteers, and each subject was fed a total of 100 g of the powder per day. The experimental diet reduced Cholesterol, LDL, VLDL and triglyceride levels in 80% of the subjects. Glycemic index of fenugreek recipes and its beneficial effects on regulating blood glucose levels was reported in a study on volunteers by Raghuram et al (*Intl. J Diab Dev Countries*, 1992, 12:45-9<sup>11</sup>).

13. References of scientific publications using the processed seed powder: A Medline search result showing 12 abstracts<sup>12</sup>, as well a list of 9 references<sup>13</sup> is provided. These references cite use of defatted powdered fenugreek. Some of these citations may be duplicate. However, the short list illustrates that the chemically treated fenugreek powder is safe and functionally useful as a source of dietary fiber.

14. Ingredients of the Fenuber: Sterling Home Products Limited, a division of Sterling Healthcare Limited, Madras, India, manufacture the debitterized fenugreek powder as per the standardized and published methods in Bangalore, India. They incorporate debitterized fenugreek powder into a proprietary blend containing Guar gum (21 CFR part 184.1339) and wheat bran and named this powder "Fibernat" for Indian market, and "Fenuber" for export market. The name difference is due to the unavailability of 'Fibernat' for registration in US and Europe.

15. Safety of the blended product: On my advice, the manufacturers submitted Fenuber as well as debitterized fenugreek powder to independent laboratories in India for analysis. The analytical reports are enclosed<sup>14</sup>. There were NO pathogens in the finished product. Microbial load was low. Analysis was conducted from different batches. Only representative reports are enclosed. Critical analysis revealed that the microbial load was mainly contributed by wheat bran, and the fenugreek powder is relatively sterile. In fact, fenugreek is permitted in USA as a supplement to insect repellents and pesticides. Fenugreek seldom spoils, and seldom supported microbial growth.

16. Double Blind Controlled Clinical Trials : Multi-center double-blind controlled clinical trials on

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Fenuber (blend) as a beverage are in progress in 6 leading teaching hospitals affiliated with different Universities in India. The studies were initiated on my approval in February 1996. Microcrystalline cellulose is the control used in the studies. No subject has reported with adverse effects as due to the experimental supplement or with the placebo/control diet. A statement from Sterling Home Products is *enclosed*<sup>15</sup>.

17. Public Health Authority certification: The product is manufactured under acceptable sanitary conditions. Indian authorities do not have regulations similar to cGMP. They consider sanitary and healthful production facility as compliant. A certificate from the Local authority for sanitary and health enforcement is enclosed<sup>16</sup>.

18. Compliance with FDA- cGMP standard: I initiated cGMP standard of sanitary and production compliance during my inspection trip in Feb 1996. An affidavit from the President of Sterling Home Products regarding compliance with cGMP are *enclosed*<sup>17</sup>. The manufacturer has a contractual agreement with a physician who cares for the health of the employees, as well as provide adequate preventive medical care. Though rodent infestation is a problem in most parts of the world, including Madras, I have personally inspected this factory, and am satisfied with their standard of protection of stocks and inventory, as well as the manufacturing plant area.

19. Sample available for FDA opinion: I have in my possession samples of Fenuber as well as debitterized Fenugreek powder for examination by FDA.

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