

Memorandum

9246 6 JUL 18 12:04

Date: JUL 10 2006

From: Consumer Safety Officer, Division of Dietary Supplement Programs, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification: **“Alkaplex®”**

Firm: pH Sciences

Date Received by FDA: 4/12/06

90-Day Date: 7/11/06

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.

Victoria Lutwak

1995S-0316

RPT346



JUN 14 2006

Mr. Steve Loyd, CEO
pH Sciences, Inc.
17230 12th Avenue, NE
Seattle, Washington 98155

Dear Mr. Loyd:

This is to inform you that the notification, dated April 10, 2006, that you submitted pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on April 12, 2006. Your notification concerned the substance that you called "Alka-Plex®". You identified "Alka-Plex®" as a new dietary ingredient that you intend to market in a dietary supplement product called "pH Balance™".

According to your notification, "[t]he new dietary supplement contains 1000mg of Alka-Plex® pressed into a tablet.... A single serving size of pH Balance™ is one tablet. The suggested use is two to four tablets per day, not to exceed six tablets per day. The label suggests that the user consult with a physician prior to using the supplement. The label suggests that the user consult a physician prior to use if the user is presently taking any medications or is under a physician's care. Precautions listed on the supplement label are: 'CAUTION: If you are pregnant or nursing, or taking any medications, consult your health care provider before using this product.'

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21 U.S.C. 350b (a) (2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. 342(f) (1) (B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

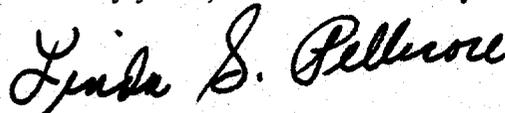
In accordance with 21 CFR 190.6(c), FDA must acknowledge its receipt of a notification for a new dietary ingredient. For 75 days after the filing date, your firm must not introduce or deliver for introduction into interstate commerce any dietary supplement that contains the dietary ingredient that is the subject of this notification.

Please note that acceptance of this notification for filing is a procedural matter, and thus, does not constitute a finding by FDA that the new dietary ingredient or supplement that contains the new dietary ingredient is safe or is not adulterated under 21 U.S.C. 342. FDA is not precluded from taking action in the future against any dietary supplement containing your new dietary ingredient if it is found to be unsafe, adulterated or misbranded.

Your notification will be kept confidential for 90 days after the filing date of April 12, 2006. After the 90-day date, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

If you have any questions concerning this matter please contact Victoria Lutwak at (301) 436-1775.

Sincerely yours,



Linda S. Pellicore, Ph.D.
Supervisory Team Leader, Senior Toxicologist
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety and Applied Nutrition



FACSIMILE COVER SHEET

Reed VL
JUN 12 2006

Date: June 10, 2006

To: Dr. Linda Pellicore
Division of Dietary Supplement Programs via FAX (301) 436-2636
Office of Nutritional Products
Center for Food Safety and Applied Nutrition
Food and Drug Administration (FDA)

Fr: Steve Loyd, CEO
pH Sciences, Inc. 

Re: Additional Information for the Alka-Plex® New Dietary Ingredient Notification

pH Sciences submitted a New Dietary Ingredient (NDI) notification for Alka-Plex® dated April 10, 2006. The purpose of this communication is to offer 24-hour response from this office to any questions that may arise during review of our NDI notification.

We have previously clarified that:

1. Alka-Plex is a physical mixture of GRAS ingredients;
2. No chemical (i.e. covalent) bonding occurs between the ingredients so no new compounds are formed;
3. The ingredients held in the Alka-Plex physical structure are also protected from reacting with the air so no new compounds are formed during its shelf life;
4. Alka-Plex has a long history of safety including animal tests and human tests;
5. The ingredients in Alka-Plex have a long history of safe consumption by humans (all are recognized as GRAS ingredients);
6. Prior NDI notifications contained confusing information that is easily misinterpreted and should not be relied upon to analyze the April 10 NDI notification; and
7. Patents referenced in prior NDI notifications describe a range of alkalizing formulas, not the precise Alka-Plex composition, and should not be used to analyze the NDI notification.

Based on all the facts available to this Company, Alka-Plex is safe and is not adulterated.

I recognize the tremendous resource and organizational constraints on your office. We do not wish to add a burden by leaving questions or concerns unanswered. Please be assured we will respond quickly to any questions that may arise during your review. My direct line is (206) 364-6761 ext 206 and my cell phone number is (206) 683-5080.

-end-

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WD1391

FACSIMILE COVER SHEET

Redd VL
MAY 15 2006

Date: May 10, 2006

To: Dr. Linda Pellicore
Division of Dietary Supplement Programs
Office of Nutritional Products
Center for Food Safety and Applied Nutrition
Food and Drug Administration (FDA)

via FAX (301) 436-2636

cc: WD1
Daw
Jeanne

Fr: Steve Loyd, CEO
pH Sciences, Inc.

Re: Additional Information for the Alka-Plex[®] New Dietary Ingredient Notification

pH Sciences submitted a New Dietary Ingredient (NDI) notification for Alka-Plex[®] dated April 10, 2006. On April 26 I submitted a clarification that Alka-Plex is a physical mixture of GRAS ingredients. I also clarified that no chemical bonding occurs and the ingredients are protected from reacting with the air. Alka-Plex[®], and its ingredients, has a long history of safety.

In a conversation you referred to the patent that protects the Alka-Plex[®] composition. This facsimile offers additional information regarding the patent. Please recognize the patent is not referenced in the NDI. However, I should address the patent lest it add any confusion about the exact ingredients in Alka-Plex[®].

Patent 6,066,342 describes a range of alkalizing products. The ingredients identified in the patent are described in ranges so the number of possible products is very large. Alka-Plex[®] is only one of those products. The ingredients in Alka-Plex[®] are precisely described in the April 10 NDI notification. The ingredient proportions are confirmed by the certificate of analysis attached to the notification.

The patent does not describe the precise composition of Alka-Plex[®]. Instead, it describes a many products of which Alka-Plex[®] is one. Alka-Plex[®] is precisely described in the April 10 NDI notification so the patent should not be relied upon to describe Alka-Plex[®].

Thank you for agreeing to review the Alka-Plex[®] NDI notification as a priority.

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FACSIMILE COVER SHEET

Rec'd VL
APR 27 2006

Date: April 26, 2006

To: Dr. Linda Pellicore
Division of Dietary Supplement Programs via FAX (301) 436-2636
Office of Nutritional Products
Center for Food Safety and Applied Nutrition
Food and Drug Administration (FDA)

Fr: Steve Loyd, CEO
pH Sciences, Inc.

Re: April 10 New Dietary Ingredient (NDI) Notification for Alka-Plex®

pH Sciences submitted an NDI notification for Alka-Plex® dated April 10, 2006. That NDI notification states, "Alka-Plex® granules are made by using microscopic calcium carbonate carrier particles to hold magnesium hydroxide, potassium chloride and potassium hydroxide (i.e. magnesium and potassium salts)."

As further clarification, Alka-Plex® is a physical mixture whereby the magnesium and potassium salts are held in fissures within the microscopic calcium carbonate crystals. The microscopic calcium carbonate crystals are coated and agglomerated into larger granules. The granule protects the magnesium and potassium salts from reacting with the air and holds them securely in the calcium carbonate fissures. Please recognize no chemical bonding occurs between the various ingredients in Alka-Plex®.

The certificate of analysis of Alka-Plex® attached to the April 10 notification confirms the ingredients in Alka-Plex® are the same as the formulation described in the NDI notification.

Based on the information in the April 10 NDI notification, the ingredients in Alka-Plex have been present in the food supply as generally recognized as safe ingredients and are being presented in a form that is not chemically altered. The April 10 NDI notification also provides history of Alka-Plex® use and evidence that Alka-Plex® is safe.

Thank you for reviewing this question with me on Friday, April 21. I trust this accurately portrays our understanding.

-end-

CONFIDENTIALITY NOTICE: The information transmitted with this facsimile cover sheet is legally privileged and confidential, intended solely for the addressee. If the reader of this message is not the addressee or intended recipient, you are notified that any dissemination, distribution or copying of the information is prohibited. If you have received this transmission in error, please destroy it and notify us by facsimile transmittal at (206) 364-5369.

2006-3217



April 10, 2006

Dr. Susan Walker, M.D.
Office of Nutritional Products, Labeling and Dietary Supplements (HFS-800)
Center for Food Safety and Applied Nutrition (CFSAN)
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

RECEIVED
APR 12 2006
BY:

Re: New Dietary Ingredient Notification for Alka-Plex[®]

Dear Dr. Walker:

Pursuant to 21 CFR § 190.6, pH Sciences is hereby notifying the Food and Drug Administration (FDA) of our intent to market dietary supplements containing a new dietary ingredient.

Prior new dietary ingredient notifications regarding Alka-Plex[®] contained a typographical error and a "proportionality assay" that is subject to misinterpretation. Please be aware that Alka-Plex[®] is a precisely formulated composition as described in this notification. Also, Alka-Plex[®] is protected by U.S. patents and patents pending. The patents refer to a broad range of products and potential applications. The patents do not have the level of specificity required for a new dietary ingredient notification and should not be considered when reviewing this notification. Please review this notification on its merits without reference to patents or prior notifications which may contain errors or be subject to misinterpretation.

1. NAME AND ADDRESS OF MANUFACTURER OF DIETARY SUPPLEMENT THAT CONTAINS THE DIETARY INGREDIENT.

pH SCIENCES, INC.
17230 12th Ave NE
Seattle, WA 98155
206-850-5987
206-364-5369 (FAX)

2. NAME OF THE NEW DIETARY INGREDIENT THAT IS THE SUBJECT OF THE PRE-MARKET NOTIFICATION:

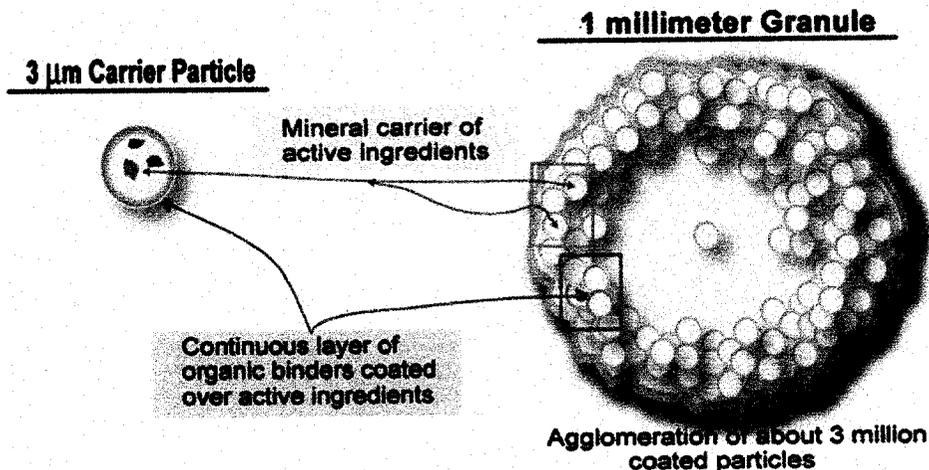
Alka-Plex[®]

The New Dietary Ingredient is Alka-Plex[®], a combination of dietary minerals delivered in the form of generally recognized as safe (GRAS) ingredients. The GRAS ingredients are mixed and held in their unaltered composition in a precisely formed granule using a patented

New Dietary Ingredient Notification – Alka-Plex®

process.^{1, 2} The granule is designed to help the user maintain a healthy pH level by providing a mild alkalizing effect. Alka-Plex® granules are made by using microscopic calcium carbonate carrier particles to hold magnesium hydroxide, potassium chloride and potassium hydroxide (i.e. magnesium and potassium salts). Calcium carbonate is chosen because it does not react with the magnesium and potassium salts and is a stable carrier for those components. The microscopic carrier particles are coated with micro-crystalline cellulose and croscarmellose sodium. Then they are assembled (agglomerated) into granules in order to protect and maintain the integrity of the magnesium and potassium salts.

The following diagram provides a graphic representation of the microscopic calcium carbonate carrier particle; impregnated with unaltered, stable magnesium and potassium salts; coated with micro-crystalline cellulose and croscarmellose sodium; and then assembled (i.e. agglomerated) into an Alka-Plex® granule for use as a new dietary ingredient.



The component dietary minerals are not modified in any way nor do they create new compounds during the patented agglomeration process. The new dietary ingredient is a carefully constructed granule that protects the integrity of the magnesium and potassium salts.

3. DESCRIPTION OF THE DIETARY SUPPLEMENT THAT WILL CONTAIN THE NEW DIETARY INGREDIENT.

PH BALANCE™

A new dietary supplement, labeled pH Balance™, will contain the new dietary ingredient. pH Balance™ contains Alka-Plex® granules in a tablet form. The supplement will be packaged in opaque white plastic bottles containing 90 tablets each, or approximately one month's supply for supplementation.

3.1. LEVEL OF THE NEW DIETARY INGREDIENT IN THE DIETARY SUPPLEMENT.

The new dietary supplement contains 1000mg of Alka-Plex® pressed into a tablet. Each tablet consisting of the following key nutritional ingredients:

New Dietary Ingredient Notification – Alka-Plex®

Calcium (as calcium carbonate)	225mg	or	22%DV
Magnesium (as magnesium hydroxide)	1mg	or <	1%DV
Potassium (as potassium hydroxide and potassium chloride)	35mg	or	1%DV

Inert ingredients are identified as water, micro-crystalline cellulose, croscarmellose sodium and magnesium stearate. Magnesium stearate is added during the tableting process and is not part of the Alka-Plex® formulation.

3.2. CONDITIONS OF USE RECOMMENDED OR SUGGESTED IN LABELING OF THE DIETARY SUPPLEMENT.

It is well known that the average western diet is acidic in nature^{3,4,5} especially when considering the amount of highly acidic beverages such as coffee and soft drinks consumed on a daily basis. However, few individuals understand the nature of the body's pH level and the related influence on both health and wellness.⁶ Alka-Plex® granules are being introduced to provide the user with a mild alkalizing effect to neutralize the acids consumed on a daily basis. Pilot studies and clinical trials are underway to document specific health benefits and structure-function claims.

A single serving size of pH Balance™ is one tablet. The suggested use is two to four tablets per day, not to exceed six tablets per day. The label suggests that the user consult with a physician prior to using the supplement. The label suggests that the user consult a physician prior to use if the user is presently taking any medications or is under a physician's care. Precautions listed on the supplement label are: "CAUTION: If you are pregnant or nursing, or taking any medications, consult your health care provider before using this product."

Claims made on the label state that "pH Balance™ promotes a healthy body pH and helps maintain a balanced body pH." This statement is accompanied by the FDA disclaimer as required by Law and stated as: "These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease."

4. HISTORY OF USE OR OTHER EVIDENCE OF SAFETY ESTABLISHING THAT THE DIETARY INGREDIENT, WHEN USED UNDER THE CONDITIONS RECOMMENDED, WILL REASONABLY BE EXPECTED TO BE SAFE.

4.1. ALKA-PLEX® GRANULES ARE MADE OF 100% GRAS INGREDIENTS

The GRAS ingredients are listed below:

Calcium carbonate	-	21CFR 184.1191
Magnesium hydroxide	-	21CFR 184.1428
Potassium hydroxide	-	21CFR 184.1631
Potassium chloride	-	21CFR 184.1622

All excipients used in processing the ingredients are GRAS or approved Food Additives, as listed below:

New Dietary Ingredient Notification – Alka-Plex®

Micro-crystalline cellulose	-	REGNUM - 977005-28-9
Croscarmellose sodium	-	21CFR 175.105 (Listed as Carboxymethylcellulose)

In addition, the tablet manufacturer adds a GRAS ingredient to assist with tablet formation, as listed below:

Magnesium stearate	-	21CFR 184.1400
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As indicated in the March 28, 2006 certificate of analysis from TAMER Laboratories, Inc., (see Attachment A) the calcium, magnesium and potassium content of Alka-Plex® conform to label indications and are held in the granule in their unaltered state.

The certificate of analysis also has a microbiological assay of Alka-Plex® which indicates the dietary ingredient is free from microbiological contaminants.

4.2 History of Use

- 4.2.1 Alka-Plex® granules, in the composition described above, have been used in food and beverage products as an ingredient to reduce acidity since 1997. In 1997, the product was introduced as a food additive to reduce coffee acidity in the form of a 160mg packet. One 160mg packet of Alka-Plex® reduces coffee acids by 90% in a cup of coffee. Since 1997, over 270,000 boxes of Alka-Plex® have been sold in 50-count packet boxes to reduce coffee acidity. The typical consumer uses 150 packets per month and consumes about 0.8 grams of Alka-Plex® per day using the product to reduce the acidity of coffee.
- 4.2.2 In 1997, Alka-Plex® was introduced as a food additive to reduce acidity in a wide range of foods. Alka-Plex® was sold as granules in a 1.5 ounce and 4.0 ounce shaker bottle. Since 1997, over 75,000 bottles of Alka-Plex® have been sold to reduce acidity in foods. The typical consumer uses 1.5 ounces of Alka-Plex® per month to reduce acidity in foods and consumes about 1.4 grams of Alka-Plex® per day.
- 4.2.3 In 1995, prior to marketing the Alka-Plex® as a food additive, the FDA was asked to review the ingredients and weigh in on the GRAS status of the ingredients. On July 7, 1995, the CFSAN confirmed the ingredients of the product were acceptable for use in foods (Attachment B). Again, on March 25, 1998, CFSAN confirmed the ingredients in the product were GRAS (Attachment B). The basic formulation of Alka-Plex® has not changed since 1995. It has been marketed under various names.
- 4.2.4 There have been *no* adverse events reported for Alka-Plex® use as a coffee acid neutralizer or a food acid neutralizer. However, consumers have reported general and specific improvements in their health after continuous use of the product. Consumer initiated reports on health improvements prompted pH Sciences to introduce the product as a dietary supplement and begin clinical research on the product.

4.3 Safety/Toxicity/Cytotoxicity

- 4.3.1 Acute Oral Toxicity of a Nutraceutical (Alka-Plex Granules) in Male and Female Sprague-Dawley Rats. SRI Study No.M384-05. Experimental work performed between June 8, 2005 (start date) and June 22, 2005 (completion date) at Stanford Research Institute, BioSciences Division, (Attachment C) attempted to determine the maximum tolerated dose of Alka-Plex® granules in male and female Sprague-Dawley rats after a single oral dose administration. Clinical observations were recorded 2-5 hours post dose and once daily thereafter. Individual animal body weights were measured for each treatment group on Day 1 prior to dosing, Day 8 and Day 15 prior to necropsy of the animals. Gross necropsy was performed on all animals on Day 15.

Three dose levels were administered to determine the maximum tolerated dose -- 0.5g/Kg; 2.0g/Kg; and 5.0g/Kg of body weight. All animals survived until the end of the study and had no adverse clinical signs or effects on body weight at any time during the study. Necropsy of all animals at the end of the study revealed gross pathologic findings in four females and in the 2.0g/Kg treatment group, which were considered unrelated to treatment with the test article. No grossly observable abnormalities occurred in any of the other animals in the study including those in the highest dose group (5.0g/Kg).

In conclusion, the No Observable Adverse Effect Level (NOAEL) of Alka-Plex® granules administered in a single oral dose was 5.0g/Kg, based on the parameters evaluated, and the maximum tolerated single oral dose is greater than 5.0g/Kg. NOAEL is 340 times the suggested single oral dose, 85 times the suggested daily dose and 57 times the recommended maximum dose for a 150 pound person.

4.4 Human Clinical Data

- 4.4.1 A Novel Therapy for Interstitial Cystitis: A Two Year Follow-Up Study. In early 2003, representatives from the Nutrition Education and Consulting Service in East Syracuse, New York, interviewed fifteen persons who participated in a three-month trial use of Alka-Plex® granules. The three-month trial was conducted by Tamer Laboratories in 2001 with eighteen (18) subjects. The objective of the follow up study was to identify, locate and survey the subjects in the three-month trial to measure the effectiveness, possible continued use and side-effects, if any, of Alka-Plex® granules included in the diet to reduce nutritional acid intake. During the initial three-month study, the average daily dosage of Alka-Plex® granules was at least 1gram with breakfast, 1gram with lunch, 1gram with dinner and 1gram at bedtime. Typically, the subjects consumed in excess of 4grams of Alka-Plex® per day – the suggested use on the pH Balance™ label.

Follow-up on the original participants began two years after the three-month trial. Fifteen (15) of the original eighteen (18) participants were located and interviewed. Of those, ten (10) had continued to use Alka-Plex® granules for the entire two-year period. Specific data on daily use was not collected but anecdotal

New Dietary Ingredient Notification – Alka-Plex®

evidence indicates between 2grams and 3grams of Alka-Plex® granules were used daily for two years by ten (10) individuals. Most used Alka-Plex® granules to reduce acidity in coffee and foods during the day and with water at bedtime. All were satisfied with their results and none identified any adverse events associated with use of Alka-Plex®. (See Attachment D)

Conclusion

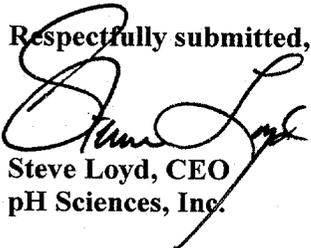
The information provided above is true and accurate. Based on that information, pH Sciences management concludes that the new dietary ingredient, Alka-Plex®, and a dietary supplement made from Alka-Plex®, pH Balance™, is reasonably expected to be safe based on the following facts:

1. All the component ingredients in the new dietary ingredient are generally recognized as safe by the FDA;
2. The new dietary ingredient has been tested by hundreds of people as a food additive for continuous use over long periods of time without adverse effects;
3. An independent third party confirms that there are no adverse effects associated with long term use of Alka-Plex®; and
4. An independent laboratory giving massive doses of Alka-Plex® to laboratory animals have shown no toxicity in any of the animals.

We believe our conclusion that Alka-Plex®, when used under the conditions recommended, will reasonably be expected to be safe is a reasonable and logical conclusion based on the facts known to pH Sciences at this time. We trust this New Dietary Ingredient Notification letter and related documents contained herein provide your office with information as required by the FDA and statute.

If you have questions regarding this notification, please contact Dierdre Allen at (802) 223-2271 or me at (206) 364-6761 ext 206.

Respectfully submitted,



Steve Loyd, CEO
pH Sciences, Inc.

Cc: Dierdre Allen,
Consultant to pH Sciences, Inc.

References

- ¹ United States Patent 6,270,708. GuroI August 7, 2001. Agglomerating and drying apparatus. (See Attachment E)
- ² United States Patent 6,143,221 GuroI November 7, 2000 Agglomerating and drying apparatus. (See Attachment D)
- ³ Sebastian A, Frassetto LA, Sellmeyer DE, Merriam RL, Morris RC Jr. Estimation of the net acid load of the diet of ancestral preagricultural Homo sapiens and their hominid ancestors. **Am J Clin Nutr.** 2002 Dec;76(6):1308-16.
- ⁴ Maurer M, Riesen W, Muser J, Hulter HN, Krapf R. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. **Am J Physiol Renal Physiol.** 2003 Jan;284(1):F32-40. Epub 2002 Sep 24.
- ⁵ Frassetto L, Morris RC Jr, Sellmeyer DE, Todd K, Sebastian A. Diet, evolution and aging--the pathophysiologic effects of the post-agricultural inversion of the potassium-to-sodium and base-to-chloride ratios in the human diet. **Eur J Nutr.** 2001 Oct;40(5):200-13.
- ⁶ Frassetto L, Sebastian A Age and systemic acid-base equilibrium: analysis of published data. **J Gerontol A Biol Sci Med Sci.** 1996 Jan;51(1):B91-9.

LIST OF ATTACHMENTS

Attachment A – March 28, 2005 Certificate of Analysis from Macit Gurol, CSO, Tamer Laboratories, Inc.

Attachment B – A July 7, 1995 letter signed by Mitchell Cheeseman, Ph.D., and a March 25, 1998 letter signed by Lawrence J. Linn, Ph.D., both from the Center for Food Safety and Applied Nutrition.

Attachment C – A July 19, 2005 report entitled “Acute Oral Toxicity of a Nutraceutical (Alka-Plex Granules) in Male and Female Sprague-Dawley Rats” prepared by Janice Schindler-Horvat, B.S. from Stanford Research Institute International.

Attachment D – May 5, 2003 report entitled “A Novel Therapy for Interstitial Cystitis: A Two Year Follow-Up Study” prepared by Susan E. Brown, Ph.D., from The Nutrition Education and Consulting Service.

Attachment A

**March 28, 2005 Certificate of Analysis from Macit Gurol, CSO, Tamer
Laboratories, Inc.**

2 PAGES TOTAL

REDACTED IN ITS
ENTIRETY

CONTAINS

TRADE SECRET

CONFIDENTIAL

COMMERICAL

INFORMATION

Attachment B

**A July 7, 1995 letter signed by Mitchell Cheeseman, Ph.D., and a
March 25, 1998 letter signed by Lawrence J. Linn, Ph.D.,
both from the Center for Food Safety and Applied Nutrition.**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington DC 20204

July 7, 1995

Mr. Macit Gurol
President
12047-A 31st Ave. NE.
Seattle, WA 98125

Dear Mr. Gurol:

This is in response to your letter dated June 5, 1995, requesting approval for the use of your Coffee Tamer product containing calcium carbonate, magnesium hydroxide, potassium hydroxide, magnesium carbonate, potassium chloride, and gelatin as a pH control agent in brewed coffee. You state in your letter that all these active ingredients in your product are generally recognized as safe (GRAS) for use in food. In addition, you identify the inactive ingredients in your product as follows: methyl paraben, propyl paraben, micro crystalline cellulose, crosscarmelose sodium NF, FD&C Color Numbers 5,6, and 40, instant coffee, and beta carotene.

We agree that the active ingredients in your product are GRAS for use in food. In addition the inactive ingredients methyl paraben, propyl paraben, and beta carotene are also GRAS for use in food and micro crystalline cellulose may be considered GRAS for use in food. We assume that crosscarmelose sodium NF refers to caramel coloring produced using a sodium containing alkali and that the FD&C Color Numbers 5,6, and 40 identified in your letter are FD&C Yellow Nos. 5 and 6, and Red No. 40, respectively. If our assumptions are correct, the components of your product are acceptable for use in food.

If you have further questions, please do not hesitate to contact us.

Sincerely yours,



Mitchell Cheeseman, Ph.D.
Direct Additives Branch, HFS-217
Division of Petition Control
Center for Food Safety
and Applied Nutrition



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington DC 20204

March 25, 1998

Mr. Macit Gurol
President
Tamer International, Ltd.
17230 12th Avenue N.E.
P.O. Box 65260
Seattle, WA 98155

Dear Mr. Gurol:

This is in response to your letter of March 11, 1998, concerning your "TAMER" products, which are used to temper the acidic content of foods and beverages. You listed several active and inactive ingredients that you believe are generally recognized as safe (GRAS). You asked for FDA approval of these products.

Under the Federal Food, Drug, and Cosmetic Act, FDA does not approve food products. It is the responsibility of the manufacturer or distributor to make certain that the product being marketed is safe within the meaning of the Act and regulations promulgated thereunder. Ingredients that are used as components of food must be either generally recognized as safe (GRAS) or approved as food additives. Direct food additives that have been approved by FDA are codified in 21 CFR Part 172. GRAS substances, on the other hand, are listed in 21 CFR Parts 182 and 184.

The following ingredients that you listed are covered by the FDA regulations indicated below:

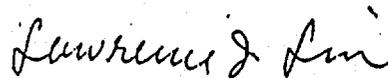
Calcium carbonate	----- 21 CFR 184.1191
Magnesium hydroxide	----- 21 CFR 184.1428
Potassium hydroxide	----- 21 CFR 184.1631
Potassium chloride	----- 21 CFR 184.1622
Sodium carboxymethylcellulose	----- 21 CFR 182.1745
Polyethylene glycol (mean molecular weight 200-9500)	----- 21 CFR 172.820

Page 2 - Mr. Macit Gurol

In addition, microcrystalline cellulose is considered to be GRAS, although it is not listed in FDA regulations. Sea salt can be GRAS if it is prepared under conditions of good manufacturing practice. Instant coffee and distilled water are of course acceptable drinks.

If you have further questions, please feel free to contact us.

Sincerely yours,



Lawrence J. Lin, Ph.D.
Division of Petition Control, HFS-215
Center for Food Safety
and Applied Nutrition

Attachment C

A July 19, 2005 report entitled "Acute Oral Toxicity of a Nutraceutical (Alka-Plex Granules) in Male and Female Sprague-Dawley Rats" prepared by Janice Schindler-Horvat, B.S. from Stanford Research Institute International.

10 PAGES TOTAL

REDACTED IN ITS
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Attachment D

May 5, 2003 report entitled "A Novel Therapy for Interstitial Cystitis: A Two Year Follow-Up Study" prepared by Susan E. Brown, Ph.D., from The Nutrition Education and Consulting Service.

13 PAGES TOTAL

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