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January 17, 2006

**Dr. Susan Walker**  
**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**

## **New Dietary Ingredient Notification**

**Dear Dr. Walker:**

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

- 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:**

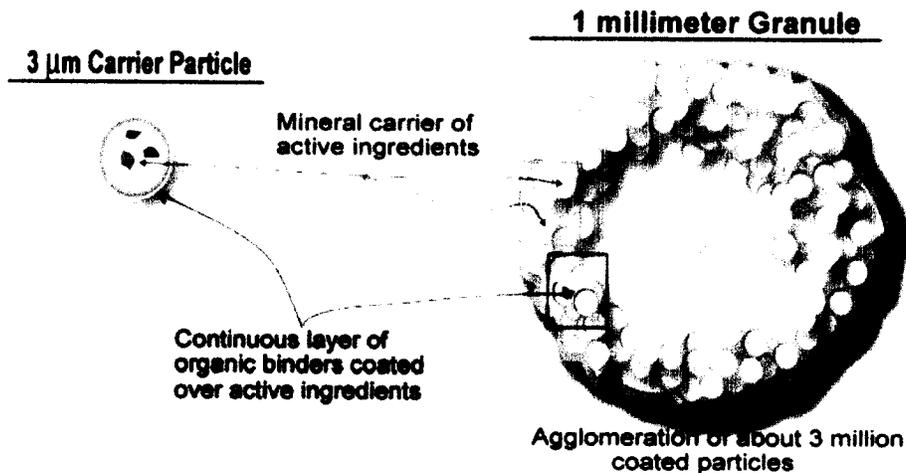
### **Alka-Plex®**

The New Dietary Ingredient is Alka-Plex®, a proprietary combination of dietary minerals designed to help the user maintain a healthy pH level by providing a mild alkalizing effect. Alka-Plex® granules are made by using calcium carbonate powder as the carrier particle for magnesium hydroxide, potassium hydroxide and potassium chloride. The calcium carbonate carrier particle, impregnated with magnesium hydroxide, potassium chloride and potassium hydroxide, is coated with micro-crystalline cellulose and croscarmellose sodium. The carrier particles are formed into granules to maintain a very controlled release rate of the ingredients in the

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digestive system. The carrier particles are precisely agglomerated into granules using a patented process<sup>1, 2</sup> whereby the resulting granules are in a form that provides protection for the integrity of the magnesium hydroxide and potassium hydroxide.

The following diagram provides a graphic representation of the calcium carbonate carrier particle; impregnated with magnesium hydroxide, potassium chloride and potassium hydroxide; 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.



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

#### PH BALANCE™

The new dietary supplement that will contain the new dietary ingredient is labeled as pH Balance™. This product contains Alka-Plex® granules in a tableted 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:

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

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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<sup>3,4,5</sup> 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<sup>6</sup> and various health concerns. Using Alka-Plex® granules as the single ingredient, pH Balance™ is being introduced to provide the user with a mild alkalizing effect to neutralize the acids consumed on a daily basis.

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 are listed on the supplement label are as follow: Contraindicated for women who are pregnant or nursing and contraindicated for individuals with impaired kidney function, kidney disease.

Claims made on the label state that "pH Balance™ is designed to promote a healthy body pH and to reduce body acidity. This statement is accompanied by the FDA disclaimer as required by Law and stated as: "These statements have not been approved 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 primary 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:

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

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

Magnesium stearate - 21CFR 184.1400

As indicated by the September 2, 2005, report from Analytical Chemistry, Inc. (Attachment A) the proportions of calcium, magnesium and potassium do not change as a result of the proprietary agglomeration process. The report indicates the proportions of calcium, magnesium and potassium in the mix before agglomeration (containing 26% water) and after agglomeration (containing 8% water). The test has a +/- 2% variability of proportions.

Please note this test is not a good measure the absolute calcium, magnesium and potassium concentrations due to the significant dilutions of the product required by the test. Absolute concentrations can vary as much as +/- 20% using this test and is not appropriate for measuring absolute concentrations.

### 4.2 History of Use

- 4.2.1 Alka-Plex® granules, as described above, have been used in food and beverage products as an ingredient to reduce acidity since 1997. In 1997, Tamer Laboratories, Inc. ("Tamer"), the holder of all intellectual property rights related to the formulation and manufacturing of Alka-Plex® granules, introduced Coffee Tamer® to reduce coffee acidity in the form of a 160mg packet for one cup of coffee. Since 1997, over 270,000 boxes of Coffee Tamer® have been sold in 50-count packet boxes. The typical consumer uses 150 packets per month and consumes about .8 grams of Alka-Plex® per day using Coffee Tamer®.
- 4.2.2 In 1997, Tamer Laboratories, Inc. ("Tamer"), the holder of all intellectual property rights related to the formulation and manufacturing of Alka-Plex® granules, introduced Food Tamer® to reduce food acidity in the form of 1.5 ounce and 4.0 ounce shaker bottles. The formulation for Food Tamer® is the same as Alka-Plex®. Since 1997, over 75,000 bottles of Food Tamer® have been sold. The typical consumer uses 1.5 ounces of Food Tamer® per month and consumes about 1.4 grams of Alka-Plex® per day using Food Tamer®.
- 4.2.3 In 1995, prior to marketing the ingredient, Tamer (then named Tamer International, Ltd.) requested GRAS approval for the Alka-Plex® granules for use in foods. 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 "TAMER' products" were GRAS. The basic formulation of Alka-Plex® has not changed since 1995 but it has been marketed under the name Coffee Tamer® and Food Tamer®.
- 4.2.4 There have been no adverse events reported for Alka-Plex® use under the trade name Coffee Tamer® or Food Tamer®. There has been no

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change to the ingredient formulation for Alka-Plex® since 1995 and has been in continuous use as Coffee Tamer® and Food Tamer® since that time.

### 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.

- 4.3.2 MEM Endpoint Dilution Using L-929 Mouse Fibroblast Cells. Experimental work done at the American Institute for Biosocial and Medical Research in Puyallup, WA evaluated the response of cultured mouse fibroblast cells being introduced to Alka-Plex®. The test introduced 4.2g of Alka-Plex® to 21.0g of cell solution. Researchers evaluated the cytotoxic response in cultured mouse fibroblast cells under microscopic examination. The results concluded that Alka-Plex® granules are considered non-toxic under the test conditions employed.

### 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

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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 for breakfast, lunch, dinner and 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 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®.

**We trust that the New Dietary Ingredient application and related documents contained herein provide your office with information as required by the FDA. If there are any questions regarding this submission, please contact me at (802) 223-2271 or by mail.**

**Respectfully submitted,**



**Dierdre Allen,  
Consultant to pH Sciences**

## References

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- <sup>1</sup> United States Patent 6,270,708. Gurol August 7, 2001. Agglomerating and drying apparatus.
- <sup>2</sup> United States Patent 6,143,221 Gurol November 7, 2000 Agglomerating and drying apparatus.
- <sup>3</sup> 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.
- <sup>4</sup> 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.
- <sup>5</sup> 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.
- <sup>6</sup> 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.