ORIGINAL SUBMISSION

Arent Fox

March 10, 2011

COPY

Brian P. Waldman
Attorney
202.857.8971 DIRECT
202.857.6395 FAX
waldman.brian@arentfox.com

VIA HAND DELIVERY

Paulette Gaynor, Ph.D.
Division of Biotechnology and GRAS Notice Review (HFS-255)
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: GRAS Notification for Milk Mineral Concentrate

Dear Dr. Gaynor:

On behalf of Armor Proteines, and in accordance with proposed 21 C.F.R. § 170.36 [62 FR 18938 (17 April 1997)], I am submitting four (4) paper copies and an electronic copy of a notice of the determination that, on the basis of scientific procedures, milk mineral concentrate, produced by Armor Proteines and described in the notice, is GRAS under specific conditions of use as a salt substitute in various foods, and therefore, is exempt from the premarket approval requirements of the Federal Food, Drug and Cosmetic Act.

While we believe that the enclosed notice is acceptable and supports the lawful marketing of milk mineral concentrate, should you have any questions regarding this submission, please do not hesitate to contact me.

Sincerely,

(b) (6)

Brian P. Waldman
Counsel to Armor Proteines

Enclosures

cc: Emmanuel Treuil (Food Law Director, Armor Proteines)

Arent Fox

March 10, 2011

Brian P. Waldman
Attorney
202.857.8971 DIRECT
202.857.6395 FAX
waldman.brian@arentfox.com

VIA HAND DELIVERY

Paulette Gaynor, Ph.D.
Division of Biotechnology and GRAS Notice Review (HFS-255)
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: <u>GRAS Notification for Milk Mineral Concentrate</u>

Dear Dr. Gaynor:

On behalf of Armor Proteines, and in accordance with proposed 21 C.F.R. § 170.36 [62 FR 18938 (17 April 1997)], I am submitting four (4) paper copies and an electronic copy of a notice of the determination that, on the basis of scientific procedures, milk mineral concentrate, produced by Armor Proteines and described in the notice, is GRAS under specific conditions of use as a salt substitute in various foods, and therefore, is exempt from the premarket approval requirements of the Federal Food, Drug and Cosmetic Act.

While we believe that the enclosed notice is acceptable and supports the lawful marketing of milk mineral concentrate, should you have any questions regarding this submission, please do not hesitate to contact me.

Sincerely,

(b) (6)

Brian P. Waldman
Counsel to Armor Proteines

Enclosures

RECEIVED
MAR 10 2011
Division of
Biotechnology and
GRAS Notice Review

cc: Emmanuel Treuil (Food Law Director, Armor Proteines)

COPY

GRAS EXEMPTION CLAIM FOR

THE MILK MINERAL CONCENTRATE

LACTOSALT OPTITASTE

Table of Contents

1. GRAS Exemption Claim for Milk Mineral Concentrate Lactosalt Optitaste 3
1.1) Name and Address of Notifier: 3
1.2) Common or usual name of the notified substance: 3
1.3) Applicable conditions of use: 3
1.4) Basis for GRAS determination: 4
1.5) Statement of availability of data: 4
2. Identity and Specifications of the Notified Substance 6
2.1) Quantitative Composition: 6
2.2) Method of Manufacture: 6
2.3) Characteristic Properties: 8
2.4) Food-Grade Specifications: 8
3. Information on Self-Limiting Levels of Use: 9
4. Summary of Basis for GRAS Determination 11
4.1) Technical evidence and general availability of information relied on to support safety 11
4.1.1) Similarity to Other GRAS substances 11
4.1.2) Intended use and exposure 12
4.1.2.1) Estimation of current sodium chloride consumption 12
4.1.2.2) Estimate of the Potential Milk Mineral Concentrate intake from food 14
4.1.2.3) Estimate of the potential intake of the different constituents of Milk Mineral Concentrate 16
4.2) Information unfavorable to the GRAS determination 20
4.3) Basis for concluding that the notified use of Milk Mineral Concentrate is GRAS 21
References 24
Appendix A. 25

1. GRAS Exemption Claim for Milk Mineral Concentrate Lactosalt Optitaste

1.1) Name and Address of Notifier:

ARMOR PROTEINES
Z.I. Le Pont
35460 Saint-Brice en Coglès
France

All communications on this matter please should be sent in care of

ARENT FOX LLP
1050 Connecticut Avenue, N.W.
Washington, DC 20036-5339
Attention: Brian Waldman

Ph: (202) 857-8971

email: waldman.brian@arentfox.com

1.2) Common or usual name of the notified substance:

"Milk Mineral Concentrate" is the proposed common or usual name of the substance. It will be marketed under the tradename LACTOSALT OPTITASTE. To ensure that its customers as well as consumers understand the composition of Milk Mineral Concentrate, Armor Proteines will provide compositional information on its website.

1.3) Applicable conditions of use:

Milk Mineral Concentrate is intended to be used as a salt substitute to reduce the sodium content in a wide variety of foods, including meat and poultry products, by replacing some

or all of their salt content (NaCl). In the products in which it is used as salt substitute, Milk Mineral Concentrate also can serve as a flavor enhancer.

1.4) Basis for GRAS determination:

The uses of Milk Mineral Concentrate described herein are Generally Recognized as Safe (GRAS) based on scientific procedures, in accordance with 21 C.F.R. § 170.30. The basis for the GRAS determination is set forth in the summary below.

1.5) Statement of availability of data:

The data and information upon which this GRAS determination rely are available for FDA's review and will be provided upon request.

* * *

Milk Mineral Concentrate LACTOSALT OPTITASTE has been determined to be Generally Recognized as Safe (GRAS) for the proposed uses described herein and, therefore, is exempt from the requirement of premarket approval under the Federal Food, Drug and Cosmetic Act. A summary of the basis for this GRAS determination is set forth herein.

Respectfully submitted,

ARMOR PROTEINES

By : (b) (6)

Emmanuel TREUIL

Food Law Director

2. Identity and Specifications of the Notified Substance

2.1) Quantitative Composition:

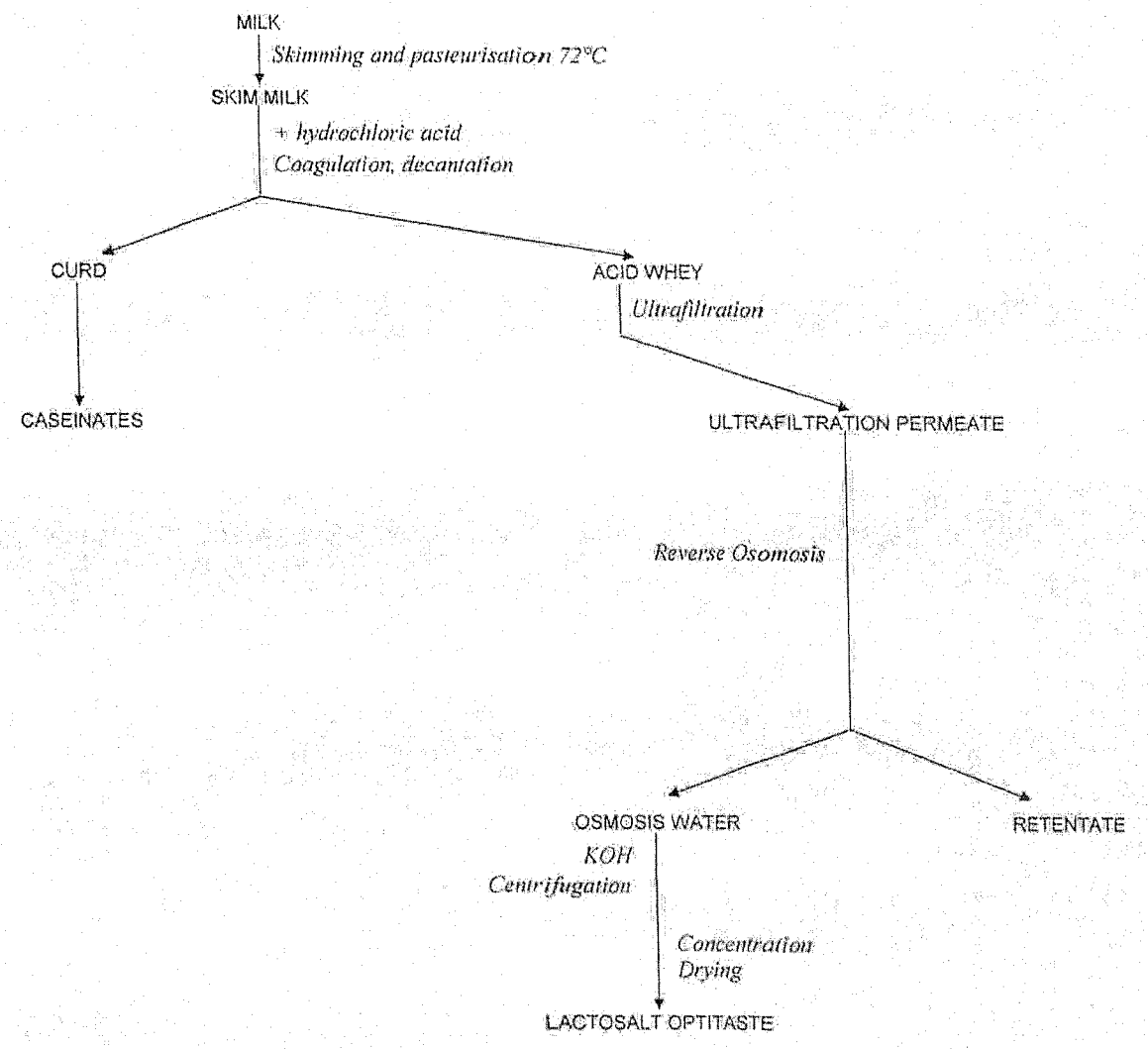
Typical Composition of the Milk Mineral Concentrate Lactosalt Optitaste	
Total minerals [1]	78-88 %
. Sodium	8-10 %
. Potassium	28-30 %
. Chlorides	40-45 %
. Calcium	2.5-3 %
Lactose	5-9 %
Protein	1 %
Free Moisture	2-5 %
Fat	< 0.5%

2.2) Method of Manufacture:

Milk Mineral Concentrate is produced by subjecting pasteurized whey, issued from skim milk, to a proprietary precipitation and membrane separation process followed by purification and drying steps, as illustrated below.

---

[1] *The minerals found in Milk Mineral Concentrate are those found naturally in milk and milk products. See Appendix A for a list of the minerals in milk. As noted in the description of the manufacturing process, the processing aides used to produce the finished Milk Mineral Concentrate product (hydrochloric acid and potassium hydroxide, each Generally Recognized as Safe: see 21 CFR §§ 182.1057, 184.1631) also contribute potassium and chloride.*


MILK
Skimming and pasteurisation 72°C
SKIM MILK
+ hydrochloric acid
Coagulation, decantation
CURD
ACID WHEY
Ultrafiltration
CASEINATES
ULTRAFILTRATION PERMEATE
Reverse Osomosis
OSMOSIS WATER
RETENTATE
KOH
Centrifugation
Concentration
Drying
LACTOSALT OPTITASTE

2.3) Characteristic Properties:

Milk Mineral Concentrate occurs as a free-flowing, bland white powder. Its taste is salty, and it is quite soluble in water (360 g/L of water).

2.4) Food-Grade Specifications:

Milk Mineral Concentrate has a heavy metals content (as Pb) of not more than 10 ppm (10 parts per million (0.001%)), in accordance with European regulation (EC 1881/2006 and its amendments) regarding the undesirable contents of certain substances, and as determined by the method described in the Food Chemicals Codex, 7th edition, 2010.

Details of the Metals

Heavy metals	Content in ppm
	Average
Arsenic	< 0.5
Cadmium	< 0.01
Copper	0.36
Mercury	< 0.1
Lead	< 0.05

Analysis ICP-AES

Microbiological Limits

Standard plate count 30°C: ≤ 10 000 CFU/g

Enterobacteriacae: ≤ 10 CFU /g

Salmonella: Negative /125g

Staphylococcus coagulase + : Negative /0.1g

Yeasts and molds: ≤ 100 CFU /g

Listeria: Negative/25g

3. Information on Self-Limiting Levels of Use:

Milk Mineral Concentrate is intended for use as a substitute for the addition of sodium chloride (salt).

Milk Mineral Concentrate is recommended for use in foods containing salt, at levels that are consistent with current levels of salt use[2]. That is, to the extent sodium chloride is added to a product, the added sodium chloride can be replaced by almost an equal amount of Milk Mineral Concentrate (a 1:0.8 to 1:1 substitution).

In countries in which Milk Mineral Concentrate Lactosalt Optitaste is currently marketed, it is used by companies generally to reduce the content of sodium by 20% to 25%. Sometimes, when a company seeks to make a nutrient content claim for the reduction of sodium, the percent substitution may be higher.

Examples of Sodium Reduction Associated with Partial Substitution of Lactosalt Optitaste for Sodium Chloride in Representative[3]:

□ **Example One: 26 % sodium reduction in cooked ham.**

Before	**After**
Ham cooked with 1.8g of nitrite salt/100g + 0.2g of salt/100g ➔ **0.68 g of Na**	1.27g of nitrite salt/100 g + 0.73g of Lactosalt Optitaste /100g ➔ **0.50 of Na**

(Salt : 39.3% Na - Lactosalt Optitaste: 10% Na)

---

[2] Milk Mineral Concentrate is not intended for use as a table-top salt replacement.

[3] In the three examples provide, the amount of substitution of salt with Lactosalt Optitaste was guided by the desire to achieve a sodium reduction of at least 25%.

□ **Example Two: 27 % sodium reduction in soft cheese.**

Before	After
Soft cheese with 1.5g of salt/100g ➔ **0.59 g of Na**	1.0 g of salt + 0.4g of Lactosalt Optitaste /100g ➔ **0.43 g of Na**

(Salt : 39.3% Na - LactoSalt OPTITASTE: 10% Na)

□ **Example Three: 30 % sodium reduction in flour.**

Before	After
1.6g of salt/100g of flour ➔ **0.63 g of Na**	1.0 g of salt + 0.5g of Lactosalt Optitaste /100g flour ➔ **0.44 g of Na**

(Salt : 39.3% Na - LactoSalt OPTITASTE: 10% Na)

For technological reasons, it is highly unlikely that Milk Mineral Concentrate would replace one hundred percent of the salt used in all foods. Indeed, salt has an important role as a preservative in many foods, due to its bacteriostatic properties. Further, salt can contribute to a food's physical properties, which may facilitate processing or help achieve desired final product qualities. For example, salt can help the development of texture expected by consumers. Salt also enhances the positive sensory attributes of foods, even some otherwise unpalatable foods (Institute of Medicine (IOM), Food and Nutrition Board, consensus report on the strategies to reduce sodium intake in the United States, April 2010). Because salt substitutes like Milk Mineral Concentrate Lactosalt Optitaste cannot reproduce all of the technical effects of pure salt, it may be undesirable, if not impossible, to remove all salt from all foods. As noted above, in countries in which Milk Mineral Concentrate is marketed currently, manufacturers typically substitute 20-25% of the salt content with the product. Even if Milk Mineral Concentrate is widely accepted in the U.S. marketplace, the Company would expect no more than a 1% substitution for sodium chloride across all food categories.

4. Summary of Basis for GRAS Determination

4.1) Technical evidence and general availability of information relied on to support safety

General recognition of safety for Milk Mineral Concentrate is based on scientific procedures, in accordance with 21 C.F.R. §170.30(b), as described in detail below.

4.1.1) Similarity to Other GRAS substances

Milk Mineral Concentrate is produced from skim milk. The product is manufactured by the physical removal – via well-understood precipitation and membrane separation processes – of certain constituents of the whey obtained after coagulation of milk.

Whey has been affirmed as GRAS by FDA (21 CFR § 184.179).

Moreover, Milk Mineral Concentrate is closely related to a number of whey-derived permeates, including reduced lactose whey, reduced mineral whey, and whey protein concentrate, all of which FDA has affirmed as GRAS. 21 C.F.R. §§ 184.1979a - 184.1979c.

Finally, Milk Mineral Concentrate also is similar to the whey mineral concentrate for which Glanbia Ingredients, Inc. (Glanbia) submitted a GRAS Notice (GRN No. 000052) in 2000, and to which the FDA did not object. Although the mineral content of the two products differ, the products are derived from the same source material and rely on similar manufacturing processes. [Precipitation and membrane separation processes are widely used in the dairy industry in order to prepare dairy ingredients, such as whey protein concentrate and whey protein isolate. Glanbia uses such processes to produce whey mineral concentrates, which it has marketed around the world for many years.] Neither product presents safety concerns with respect to human consumption.

4.1.2) Intended use and exposure

As explained above, Milk Mineral Concentrate is intended to be used as a salt substitute to reduce the sodium content in a wide variety of food (e.g., dairy products, meat products, bread, soup), by replacing some or all of their salt content (NaCl).

The substitution of salt with Milk Mineral Concentrate can help to reduce the consumption of sodium, which individuals (especially Americans) tend to consume at levels higher than advised by most recommendations[4].

Potential exposure to Milk Mineral Concentrate and its components may be estimated using current data on sodium chloride consumption by the US population.

4.1.2.1) Estimation of current sodium chloride consumption

Data from the 2007-2008 NHANES, a continuous survey of the health and nutritional status of the U.S. civilian, non-institutionalized population, were used to estimate the daily sodium chloride intake of adults aged ≥2 years[5].

Considering only adults (males and females) aged ≥2 years, data from NHANES 2007-2008 showed that daily intakes of sodium from foods were the following :

[4] According to a recent report from the Institute of Medicine (IOM, Food and Nutrition Board, report brief, consensus report on The Strategies to Reduce Sodium Intake in the United States, April 2010), *«Americans consume unhealthy amounts of sodium in their food, far exceeding public health recommendations. Consuming too much sodium increases the risk for high blood pressure, a serious health condition that is avoidable and can lead to a variety of diseases. Analysts estimate that population-wide reductions in sodium could prevent more than 100,000 deaths annually. While numerous stakeholders have initiated voluntary efforts to reduce sodium consumption in the United States during the past 40 years, they have not succeeded. Without major change, hypertension and cardiovascular disease rates will continue to rise, and consumers will pay the price for inaction. »*

[5] There are no more recent data concerning sodium intakes in the USA. Data from the 2009-2010 NHANES have not been yet published.

Table 1 - Sodium intake from food (including table salt)[1]

Mean (mg/day)	90th percentile (mg/day)
3330	5574

1° Aged 2 and over

These values include sodium from sodium chloride (NaCl) added to food during the manufacturing process, at the table and during cooking, and sodium naturally present in foods. As Milk Mineral Concentrate is intended to be added to food only during the food manufacturing process, it is inappropriate to base an estimate of potential intake using estimates that include sodium consumption based on the addition of salt at the table or during cooking, or sodium naturally present in food. Consequently, we must exclude from the calculation of sodium exposure:

- At least the salt added at the table[6]. According to the Institute of Medicine (IOM, 2010), *"use of table salt continues to be relatively minor contributor to overall sodium intake"*. Data from NHANES 2003-2006 suggest that table salt contributes on average, 5 % of total sodium. We use this percentage as reference.
- The amount of sodium naturally occurring in foods. According to the Institute of Medicine (IOM, Food and nutrition board, Dietary Reference Intakes for water, potassium, sodium, chloride and sulfate, 2005), 12% of total sodium comes from sodium naturally present in foods.

Thus, considering only adults (males and females) aged ≥2 years and considering data from NHANES 2007-2008, we must reduce the exposure estimates by removing daily intake of sodium from foods with natural sodium (12%) and from table salt (5%), yielding a total reduction of 17%:

---

6 We do not have any estimate of the salt added during cooking, thus this source of sodium exposure is not excluded from our estimates.

Table 2 - Sodium intake from food excluding table salt and sodium naturally present in food [1]

Mean (mg/day)	90th percentile (mg/day)
2764	4626.4

1° Aged 2 and over

If one makes the conservative assumption that all the sodium added in food during the manufacturing process comes from sodium chloride (i.e., salt), the following salt intake estimates are obtained :

Table 3 - Sodium chloride (salt) intake from food excluding table salt and salt naturally present in food [1],[2]

Mean (mg/day)	90th percentile (mg/day)
7020.6	11751.1

1° Aged 2 and over

2° Calculated from sodium intake : sodium intake x [m.w. sodium chloride/m.w.sodium] : sodium intake mg/day x 2,54.

4.1.2.2) Estimate of the Potential Milk Mineral Concentrate intake from food

As indicated hereabove, only a very small portion of sodium chloride added to foods is expected to be replaced by Milk Mineral Concentrate. Indeed, salt is an essential component of many foods because it provides beneficial effects in addition to flavor enhancement[7]. In meat products, for example, one of the main products in which Milk Mineral Concentrate would be added, salt is necessary for food safety reasons (shelf life,

[7] Marjorie Ellin Doyle and Kathleen A. Glass. Sodium Reduction and its Effect on Food Safety, Food Quality, and Human Health. Comprehensive Reviews in Food Science and Food Safety. Vol. 9, Issue 1, pp. 44-56, Jan. 2010.

microbiological safety) and to regulate the water activity (a_w). Chlorure sodium affects also the texture of foods. In meat for example, added salt increases tenderness ans decrease fluid loss in heat-processed products. Chloride sodium is necessary to produce yeast bread, controlling growth of yeast and developing an extensible gluten network. Salt also is essential for establishing the texture of cheese (firmness of soft, semi hard and hard cheeses) and therefore has direct impact on the cutting and slicing properties of cheeses. In addition, it contributes to the draining of whey and the formation of rind.
Milk Mineral Concentrate is not able to precisely reproduce each of these technical effects produced by sodium chloride. Further, it is unlikely that use of this ingredient will be economically feasible for many food manufacturers.

The hypothesis of 20%, or even 10% or 5%, replacement of all added salt (consumed by Americans through the diet) by Milk Mineral Concentrate is thus highly unlikely. However, for the demonstration of the total safety of Milk Mineral Concentrate, we will use a very conservative hypothesis, assuming that up to 30% of the sodium chloride consumed by Americans through their diets can be replaced by the ingredient.

The table below sets three different simulations, in order to estimate the corresponding Milk Mineral Concentrate intake by American consumers in the event that part of the sodium chloride added in the manufacturing process has been replaced by Milk Mineral Concentrate.

Table 4 - Potential Milk Mineral Concentrate From food assuming 10%, 20%, 30% Replacement of All Added Sodium Chloride (excluding table salt and naturally occurring salt in food)[1/]

	Milk Mineral Concentrate intake in mg/day	
	Mean	**90th percentile**
Milk Mineral Concentrate intake with replacement of 10% sodium chloride	702.1	1175.1
Milk Mineral Concentrate intake with replacement of 20% sodium chloride	1404.1	2350.2
Milk Mineral Concentrate intake with replacement of 30% sodium chloride	2106.2	3525.3

1 Estimates based on sodium exposure calculations set forth in Table 3

4.1.2.3) Estimate of the potential intake of the different constituents of Milk Mineral Concentrate

The mineral content of sodium chloride and Milk Mineral Concentrate are not the same.

Table 5 – Mineral content of both Sodium Chloride and Milk Mineral Concentrate

	Mineral content of sodium chloride in %	Mineral content of Milk Mineral Concentrate in %
Sodium	39%	10%
Potassium	-	30%
Chlorides	61%	45%
Calcium	-	3%

Consequently, as we can assume, on the basis of the respective composition of sodium chloride and Milk Mineral Concentrate, as described in Table 5, the replacement of added sodium chloride by Milk Mineral Concentrate will lead to :

- a decrease in the consumption of sodium

- a decrease in the consumption of chlorides
- an increase in the consumption of calcium
- an increase in the consumption of potassium

Sodium and Chlorides

As the content of sodium (10%) and chloride (45%) in Milk Mineral Concentrate is less than that in sodium chloride (39% of sodium, 61% of chlorides), the replacement of sodium chloride by Milk Mineral Concentrate would reduce, not increase, the total consumption of sodium and chlorides.

Calcium

As Milk Mineral Concentrate contains 3% calcium, consumer exposure to calcium would increase slightly with the replacement of sodium chloride by Milk Mineral Concentrate.

Considering data from NHANES 2007-2008, and continuing to rely on the conservative hypothesis, assuming that 30% of the sodium chloride consumed by Americans through their diets would be replaced by Milk Mineral Concentrate, the calcium intake would be :

Table 6 – Potential calcium intake assuming a Maximum 30% Replacement of Added Sodium Chloride by Milk Mineral Concentrate[1]

	Mean (mg/day)	**90th percentile (mg/day)**
Calcium intake from food (NHANES 2007-2008)	946	1651
Calcium intake from food, assuming a Maximum 30% Replacement of Added Sodium Chloride by Milk Mineral Concentrate[2]	1009	1736

1° Aged 2 and over

2° Calculated by adding to the daily intakes of calcium from foods (NHANES 2007-2008), the quantity of calcium contributed by Milk Mineral Concentrate, assuming a 30% replacement of sodium chloride by this ingredient.

This increase is trivial, representing roughly a 5% increase to the total daily calcium intake, but still well within safe levels[8].

Potassium

As Milk Mineral Concentrate contains 30% potassium, which is not present in salt, it is important to estimate the potential intake of potassium resulting from the Milk Mineral Concentrate, adding it to the potassium consumed from other sources.

Considering individuals (males and females) aged ≥2 years, data from NHANES 2007-2008 showed that mean daily intake of potassium from foods is 2509 mg/day, with 90th percentile intake of 4104 mg/day.

In the case of a 30% replacement of Sodium Chloride by Milk Mineral Concentrate, potassium intake would therefore be :

Table 7 – Potential Potassium Intake from food, assuming a Maximum 30% Replacement of Added Sodium Chloride by Milk Mineral Concentrate[1],[2]

	Mean (mg/day)	90th percentile (mg/day)
Potassium intake from food (NHANES 2007-2008)	2509	4104
Potassium intake from food, assuming a Maximum 30% Remplacement of Added Sodium Chloride by Milk Mineral Concentrate[2]	3142	5069

1° Aged 2 and over

2° Calculated adding the daily intakes of potassium from foods (NHANES 2007-2008) to the quantity of potassium contributed by the Milk Mineral Concentrate, assuming a 30% replacement of sodium chloride by this ingredient.

8 The Tolerable upper intake levels for calcium are 2,500 milligrams per day from age 1 through 8; 3,000 milligrams daily from age 9 through 18; 2,500 milligrams daily from age 19 through 50; and 2,000 milligrams per day for all other age groups. (IOM report, Reference Intake for calcium and vitamine D, November 30, 2010)

Even with such additional intake of potassium from Milk Mineral Concentrate, the mean is far below the current level of Adequate Intake (AI) set by the IOM (4,700 mg/day for both men and women; IOM 2005). According to the report on Dietary Reference Intakes (IOM, 2005)), *« this level of dietary intake (i.e., from foods) should maintain lower blood pressure levels, reduce the adverse effects of sodium chloride intake on blood pressure, reduce the risk of recurrent kidney stones, and possibly decrease bone loss ».*

Even for the 90th percentile (worst case estimate), the potassium intake would be only slightly more than the IOM's Adequate Intake, and still within safe levels. Indeed, the additional potassium associated with Milk Mineral Concentrate would not be expected to be associated with any toxicity.

In the 2005 IOM report, it is indicated that *« in the generally healthy population with normal kidney function, a potassium intake from foods above the Adequate Intake poses no potential for increased risk because excess potassium is readily excreted in the urine. Therefore, a Tolerable Upper Intake Level (UL) was not set ».* The potassium content of the blood is highly regulated (even in the face of multi-gram doses of potassium; IOM 2005b).

Moreover, in the original Select Committee on GRAS Substances (SCOGS) Report #102 on potassium chloride, ID Code 7447-40-7 (potassium chloride was affirmed to be GRAS by the FDA; 21 C.F.R. §184.1622), the Committee considered the potential health effects of substituting potassium chloride for sodium chloride in the diet and concluded that the importance of reducing sodium intake in the diet would be greater than the risks of increased consumption of potassium (FASEB 1979). When administered as a supplement to the diet, adverse gastrointestinal effects were observed only following bolus doses many-fold higher than that provided by the worst case estimate (IOM 2004; SCF 20). Regarding potential concern about the development of hyperkalemia among individuals with chronic renal failure or on potassium-sparing diuretics, the IOM report on hypertension observed, *"this severity of kidney disease is uncommon in the general population (about*

0.1 percent of the population), and awareness is higher among these individuals (Coresh et al., 2005)." (IOM, Committee on Public Health, A population–based policy and systems change approach to prevent and control hypertension, 2010) Further, such individuals are typically under medical supervision.

Finally, according to the same IOM report on hypertension (IOM, 2010), dietary intake of potassium in all groups in the United States is considerably lower than the Adequate Intake. The report notes that only approximately 2 percent of U.S. adults met the current guidelines for dietary potassium intake, according to a report from the CDC (NCHS, 2008). The IOM report on hypertension adds that *"there is evidence that increasing the potassium intake of the general U.S population would have favorable effects on blood pressure"* and notes that one strategy to increase potassium intake *"is by the use of "modified salt" in food preparation in which part of the sodium chloride is replaced by potassium chloride. This has the double advantage of decreasing sodium and increasing potassium intake, and the likelihood of excessive potassium is limited by its effect on flavor. The more widespread use of these substitutes, accompanied by clear labeling for those whose intake of potassium should be limited for medical reasons, deserves further consideration."*

In sum, the increased intake of potassium due to the replacement of sodium chloride with Milk Mineral Concentrate would not be expected to have any adverse health consequences, even using these conservative, worst-case estimates above.

4.2) Information unfavorable to the GRAS determination

We are not aware of any information on or related to Milk Mineral Concentrate that demonstrates or suggests reasonable grounds to suspect a risk to consumers from the proposed use. In countries where Milk Mineral Concentrate currently is marketed[9], we have never received any reports of adverse effects associated with consumption of the

[9] The product has been marketed since 2007, in the United Kingdom first, then in France, Germany, Spain, Japan, the Czech Republic, and Switzerland.

product.

As noted above, FDA has recognized the GRAS status of whey and modified whey products. To our knowledge, the only safety issue about which FDA has raised concern is the possibility that production of certain whey-derived ingredients might result in the concentration of potentially harmful constituents (e.g.,lead or heavy metals) beyond what might typically be expected in whey itself. To address this potential concern, we have established a specification for heavy metals [<10 ppm (as pb)], which is consistent with heavy metal limits set for other modified whey products. Moreover, the ingredient's manufacturing process does not result in such potentially harmful concentrations.

4.3) Basis for concluding that the notified use of Milk Mineral Concentrate is GRAS

In this document, we demonstrate that Milk Mineral Concentrate intake resulting from its intended use is safe, and is also Generally Recognized As Safe ("GRAS") under the Federal Food, Drug, and Cosmetic Act.

The safety of Milk Mineral Concentrate has been determined to be safe through scientific procedure as set forth under 21 CFR § 170.30 (b), based on the following:

1) Milk Mineral Concentrate is well-characterized and complies with limits on contaminants appropriate for food-grade ingredients.
2) Milk Mineral Concentrate is produced with techniques commonly used in the dairy industry. It is manufactured from whey -- derived from skim milk -- through well-understood precipitation and membrane processes. Whey (21 CFR 184.1979) and certain modified whey products using similar processing methods[10] (reduced

[10] The physical separation techniques of these whey products are not exactly the same as the manufacturing process used for Milk Mineral Concentrate. But, in the preamble to the final rule affirming these whey products as GRAS, the FDA stated that : *"The agency does not intend to limit the processing*

lactose whey, reduced minerals whey, whey protein concentrate), were determined as GRAS by FDA, after a review of all available information on whey and whey products and extensive public comment on the subject. 46 Fed. Reg.44434 (Sep. 4, 1981). It is widely accepted that methods used for physically separating whey constituents from the whey source do not alter the chemical identity and characteristic properties of the resulting whey-derived permeate. *See, e.g.,* 46 Fed. Reg. at 44437. Milk Mineral Concentrate also is similar to the whey mineral concentrate for which Glanbia Ingredients, Inc. submitted a GRAS Notice (GRN 52) in 2000 and to which the FDA did not object.

3) The estimated daily intakes of Milk Mineral Concentrate, based on a very conservative hypothesis (assuming that 30% of the sodium chloride consumed by Americans through their diets could be replaced by Milk Mineral Concentrate, which is quite unlikely to occur), is not anticipated to produce adverse effects. In particular, the estimated exposure to Milk Mineral Concentrate provides modest increases in the daily human exposure through the diet to calcium and potassium.

4) In France, where Milk Mineral Concentrate is manufactured and was used for the first time in a wide range of foods, the ingredient was approved by authorities, without any limits concerning potential uses. The "General Directorate for Competition, Consumer Affairs and the Prevention of Fraud" (D.G.C.C.R.F.)[11], again based on the ingredient's safety profile, did not require the ingredient to undergo a premarket assessment. Now, the Milk Mineral Concentrate is legally marketed in several countries (the United Kingdom, France, Germany, Spain, Japan, the Czech Republic, and Switzerland). In these countries, we have never received any reports of adverse effects associated with consumption of the product. Although not marketed in New Zealand, Milk Mineral Concentrate is also authorized for use in this country. Given the ingredient's safety profile, authorities there did not require a

---

methods that may be used. Furthermore, the agency has no objection to the use of newly developed physical separation techniques, if there are no new toxicants introduced as a result of these techniques, and if these techniques do not result in a concentration of natural toxicants in whey products. FDA believes that such results can be avoided by the use of good manufacturing practices and by the establishment of specifications for heavy metals." (46 FR 44434 at 44437 (Sept. 4, 1981))."

[11] The D.G.C.C.R.F. is the legal authority in France responsible for monitoring foodstuffs, especially regarding their conditions of marketing and labeling.

formal assessment of public health and safety considerations.

* * *

Considering the foregoing, we respectfully submit that all criteria for General Recognition of Safety based on scientific procedures are met and, thus, that Milk Mineral Concentrate LACTOSALT OPTITASTE is generally recognized as safe for the use as a salt replacement in recipes for all foods.

References

Federation of American Societies for Experimental Biology, 1979. Evaluation of the health aspect of sodium chloride and potassium chloride as food ingredients. NTIS PB298139.

Institute of Medicine (IOM). 2005. Food and nutrition board, Dietary Reference Intakes for water, potassium, sodium, chloride and sulfate.

Institute of Medicine (IOM). April 2010. The strategies to Reduce Sodium Intake in the United States, April 2010, IOM Food and Nutrition Board, report brief.

Institute of Medicine (IOM) 2010. Committee on Public health, A population - Based policy and systems change approach to prevent and control hypertension.

Institute of Medicine (IOM) 2010, Reference Intake for calcium and Vitamin D.

Marjorie Ellin Doyle and Kathleen A. Glass. Sodium Reduction and its Effect on Food Safety, Food Quality, and Human Health. Comprehensive Reviews in Food Science and Food Safety, Vol. 9, Issue 1, pp. 44-56, Jan. 2010.

National Health and Nutrition Examination Survey (NHANES) data, 2007-2008.

National Health and Nutrition Examination Survey (NHANES) data, 2005-2006.

Appendix A.

GRAS NOTIFICATION

WHEY MINERAL CONCENTRATE

Mineral composition of fluid milk

The mineral content of fresh milk is given below. A wide range is shown, based on variability due to intrinsic (lactogenesis in the secretory cell of individual animals) and extrinsic factors (mainly feed and season/climate adaptation, but also contaminants).

Mineral	Content per litre
Sodium (mg)	**250-640**
Potassium (mg)	**1100-1500**
Chloride (mg)	**800-1200**
Calcium (mg)	**1100-1300**
Magnesium (mg)	70-140
Phosphorus (mg)	800-1000
Iron (ug)	100-700
Zinc (ug)	2500-7000
Copper (ug)	100-350
Manganese (ug)	10-50
Iodine (ug)	50-600
Fluoride (ug)	20-80
Selenium (ug)	20-40
Cobalt (ug)	0.5-1.3
Chromium (ug)	0.5-20
Molybdenum (ug)	20-100
Nickel (ug)	0-50
Arsenic (ug)	20-60
Aluminum (ug)	50-1600
Lead (ug)	tr-20

This information is consolidated from C. D. Hunt and F. H. Nielsen, Chap. 10.1 in McSweeney, P.L.H. and P.F. Fox, 2009. Advanced Dairy Chemistry, Vol. 3, Lactose, water, salts and minor constituents, 3rd edn., Springer, pp. 392-8; and from, Cristina Sola-Larranaga; Inigo Navarro-Blasco. 2009. Chemometric analysis of minerals and trace elements in raw cow milk from the community of Navarra, Spain . Food Chemistry, 112 (1), 189-196.

Arent Fox

March 22, 2011

Brian P. Waldman
Attorney
202.857.8971 DIRECT
202.857.6395 FAX
waldman.brian@arentfox.com

VIA FEDERAL EXPRESS

Paulette Gaynor, Ph.D.
Division of Biotechnology and GRAS Notice Review (HFS-255)
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

RECEIVED
MAR 23 2011
Division of Biotechnology and GRAS Notice Review

Re: <u>GRAS Notification for Milk Mineral Concentrate</u>

Dear Dr. Gaynor:

On behalf of Armor Proteines, I am following up on my telephone conversation of March 17, 2011 -- with Ms. Bianca Farias and Dr. Mary Ditto of your office – regarding the Company's GRAS Notification for Milk Mineral Concentrate submitted on March 10, 2011. At the agency's request, and in accordance with proposed 21 C.F.R. § 170.36 [62 FR 18938 (17 April 1997)], we have set forth below additional information regarding the availability of the data upon which Armor Proteines reached its GRAS determination, and a statement reiterating the Company's conclusion that its Milk Mineral Concentrate is exempt from premarket approval under the Federal Food, Drug and Cosmetic Act.

Statement of Availability of Data (Section 1.5 of the Company's GRAS Notification):

> The data and information that are the basis for Armor Proteines' GRAS determination are available for the Food and Drug Administration's review and copying at reasonable times at Armor Proteines' facility in Saint-Brice en Coglès, France (see Section 1.1 of the GRAS Notification for full address), or will be sent to the Food and Drug Administration upon request.

GRAS Exemption Claim:

> Armor Proteines has determined that Milk Mineral Concentrate LACTOSALT OPTITASTE is Generally Recognized as Safe (GRAS) for the proposed uses described in its GRAS Notification and, therefore, is exempt from the requirement for premarket approval under the Federal Food, Drug and Cosmetic Act. A summary of the basis for the Company's GRAS determination is set forth in its GRAS Notification.

Arent Fox

I am submitting four (4) paper copies of this letter.

Of course, if you have any questions regarding this submission, please do not hesitate to contact me.

Sincerely,

(b) (6)

Brian P. Waldman
Counsel to Armor Proteines

cc: Emmanuel Treuil (Food Law Director, Armor Proteines)

SUBMISSION END