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Via Federal Express

August 3, 2018

Office of Food Additive Safety (HFS–200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835

Re: GRAS Notice for Dolomite

Dear Sir or Madam:

We hereby submit the enclosed GRAS notice for the dolomite to enhance the taste of purified bottled water beverages by serving as a source of minerals that are solubilized into the beverage when the water passes through a bed of dolomite. The maximum target composition of the remineralized water is 40 mg/L (ppm) of calcium ions and 25 mg/L (ppm) of magnesium ions. Dolomite is not intended for use in infant formula, products under the jurisdiction of the U.S. Department of Agriculture (USDA) or any products that would require additional regulatory review by FDA. The GRAS notice does not contain any designated confidential business information. In accordance with the Agency's guidelines, we have enclosed one original copy of the GRAS notice, and one complete electronic copy of the GRAS notice on a compact disk (CD).

The notified substance was also the subject of GRAS Notice No. 696, which we requested the agency to cease its review on September 6, 2017. We appreciate the recommendations the Agency provided during our GRAS notice pre-submission meetings. We are committed to cooperating with the Agency and believe an open dialog is one of the most effective ways to accomplish that objective. If any questions arise in the course of your review, please contact us, preferably by telephone or e-mail, so that we can provide a prompt response.

Sincerely,

(b) (6)

Martin J. Hahn
Partner
Hogan Lovells US LLP
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GRAS Notice for Dolomite

August 3, 2018

Hogan Lovells US LLP

Table of Contents

1.0 GRAS Statements and Certification

1.1 Claim of Exemption

Hogan Lovells US LLP is submitting this GRAS notice for its conclusion that dolomite is generally recognized as safe (GRAS) when used as a source of calcium and magnesium salts to enhance the mineral content of purified bottle water and, therefore, exempt from the requirement of premarket approval.

1.2 Name and Address of the Notifier

Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004

1.3 Name of the Substance

Dolomite

1.4 Conditions of Use

Dolomite is intended to be used as a substitute for GRAS calcium and magnesium salts to enhance the mineral content of purified bottled water beverages. The maximum target composition of the remineralized water is 40 mg/L (ppm) of calcium ions and 25 mg/L (ppm) of magnesium ions. The bottled water beverage manufacturing process will include controls to address any microorganisms that could be present in the dolomite.

1.5 Statutory Basis of GRAS Determination

Dolomite's intended use is GRAS through scientific procedures in accordance with 21 CFR §170.30 (a) and (b).

1.6 GRAS Statement

The notified substance is not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act (FFDCA) based on our conclusion that the notified substance is GRAS under the conditions of the intended use.

1.7 Availability of Information

A complete copy of the data and information that was used as a basis for this GRAS conclusion can be provided to the FDA upon request, and is also available for FDA's copying and reviewing during customary business hours at:

Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004

1.8 Trade Secret and Confidential Information

This GRAS notice does not contain data or information that is exempt from disclosure under the Freedom of Information Act, 5 U.S.C. 552.

1.9 GRAS Certification

To the best of our knowledge, the GRAS notice is a complete, representative, and balanced submission that includes unfavorable information, as well as favorable information, known to us and pertinent to the evaluation of the safety and GRAS status of the use of the substance.

1.10 Signature

(b) (6)

_____

Martin J. Hahn
Partner
Hogan Lovells US LLP
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2.0 Identity, Method of Manufacture, Specifications, and Physical or Technical Effect

2.1 Identity

Dolomite is an anhydrous carbonate mineral composed of calcium magnesium carbonate. Raw dolomite material will be used to replace the mineral salts that are added today to purified water beverages to enhance the taste of the water. The dolomite is not used as a direct-add ingredient to the water. The treated water will pass through a bed of crushed dolomite and the calcium and mineral salts in the dolomite will dissolve into the water.

Chemical name: Calcium magnesium carbonate; $CaMg(CO_3)_2$

Common name: Dolomite

Empirical formula: $CaCO_3\,MgCO_3$

CAS No.: 16389-88-1

Molecular weight: 184.39

EINECS reference: 240-440-2

2.2 Characteristic Properties

Appearance: White or grey to brownish material in crushed and granular form

Density: 2.2 g/cm^3 to 2.9 g/cm^3 at 20 °C (bulk density: 1.2 g/cm^3 to1.6 g/cm^3)

Solubility in water: 0.032 g/L at 10°C

2.3 Quantitative Composition

Table 1. Typical Quantitative Composition of Dolomite

Constituents		Levels
Calcium	Ca, as $CaCO_3$	⩾54%
	Ca, as CaO*	⩾30%
	Ca, as Ca	⩾21%
Magnesium	Mg, as $MgCO_3$	⩾44%
	Mg, as MgO*	⩾21%
	Mg, as Mg	⩾12%
SO_3		0.04 – 0.06%
Na_2O		0.03 – 0.04%
Fe_2O_3		0.02 – 0.03%

Table 1. Typical Quantitative Composition of Dolomite	
Constituents	**Levels**
Al_2O_3	<0.01%
Mn_2O_3	<0.01%
K_2O	<0.01%
SiO_2	<0.01%

In addition to the above constituents, the notified substance may also contain very low levels of heavy metals, which are discussed in the specification section 2.5, below.

2.4 Manufacturing Process

Dolomite is an anhydrous carbonate mineral that is mined from the earth. The dolomite will be mined from the earth using a vein that has not been shown to be contaminated with heavy metals. The dolomite is crushed to meet the proper size, screened, and then dried. The testing provides assurance the dolomite is mined from a vein that meets the specifications. The dolomite will be packaged and stored under dry/ambient conditions. Dolomite is prepared under current Good Manufacturing Practices (cGMP). The dolomite will be used in manufacturing conditions that will control any microorganisms that could be present in the mined dolomite.

2.5 Specifications

Dolomite can be mined from various sites across the world and impurities levels for dolomite from different sources may vary. Specifications of dolomite subject to the GRAS notice and analysis results of three non-consecutive batches of dolomite are summarized in the table below. The specifications are set to provide assurance the vein of dolomite is of suitable purity for food use. Only dolomite that can comply with the following specifications will be used for enhancing the mineral content of bottled water beverages to improve the taste of the beverage.

Table 2. Specification and Batch Analysis of Dolomite					
Item	**Specification**	**Lot 1731672**	**Lot 1743842**	**Lot 1750282**	**Method**
CaO	⩾ 30%	Complies (30.68%)	Complies (30.50%)	Complies (30.54%)	EN 12485 (Complexometric titration)
MgO	⩾ 21%	Complies (21.72%)	Complies (21.77%)	Complies (21.76%)	EN 12485 (Complexometric titration)
$CaCO_3$	⩾ 54%	Complies (54.8%)	Complies (54.4%)	Complies (54.5%)	Calculated from CaO
$MgCO_3$	⩾ 44%	Complies (45.4%)	Complies (45.5%)	Complies (45.5%)	Calculated from MgO

Table 2. Specification and Batch Analysis of Dolomite					
Item	**Specification**	**Lot 1731672**	**Lot 1743842**	**Lot 1750282**	**Method**
Antimony (Sb)	< 3 mg/kg	Complies (Non-detected, ND*)	Complies (ND*)	Complies (ND*)	EN 12485 (AAS hydride)
Arsenic (As)	< 1 mg/kg	Complies (ND†)	Complies (ND†)	Complies (ND†)	EN 12485 (ICP-OES)
Cadmium (Cd)	< 2 mg/kg	0.1 mg/kg	Complies (ND‡)	Complies (ND‡)	EN 12485 (ICP-OES)
Chromium (Cr)	< 10 mg/kg	1.2 mg/kg	1.2 mg/kg	1 mg/kg	EN 12485 (ICP-OES)
Lead (Pb)	< 1 mg/kg	Complies (ND§)	Complies (ND§)	Complies (ND§)	EN 12485 (ICP-OES)
Mercury (Hg)	< 0.5 mg/kg	Complies (ND‖)	Complies (ND‖)	Complies (ND‖)	EN 12485 (cold vapor)
Nickel (Ni)	< 10 mg/kg	Complies (ND¶)	Complies (ND¶)	Complies (ND¶)	EN 12485 (ICP-OES)
Selenium (Se)	< 3 mg/kg	Complies (ND*)	Complies (ND*)	Complies (ND*)	EN 12485 (AAS hydride)
* LOD = 2.5 mg/kg; † LOD = 1.0 mg/kg; ‡ LOD = 0.1 mg/kg; § LOD = 0.2 mg/kg; ‖ LOD = 0.02 mg/kg; ¶ LOD = 0.5 mg/kg.					

Dolomite is mined from the earth and environmental microorganisms have the potential to be present in the raw dolomite. Microorganisms, if present, are controlled by the bottled water manufacturing process. The dolomite will be treated with hot water (>85 °C) for 30 minutes to one hour until the outlet temperature of the water exiting the filter reaches 85 °C. For purposes of comparison, the FDA regulation at 21 CFR §1240.61 provides that treating milk and milk products with 72 °C for 15 seconds meets the mandatory pasteurization requirements that kill microorganisms of public health concern. In addition, the dolomite-infused water will be treated after the addition of dolomite with processes that will kill pathogens or other microorganisms that could adversely impact the quality of the water such as thermal processing or the use of UV light or ozone. The manufacturers of bottled water beverages that use dolomite as a mineral source for taste must comply with the microbiological quality standards listed in 21 CFR § 165.110 (“Bottled water”). Because the process under which dolomite will be used involves microbiological controls, it is unnecessary to establish microbiological specifications for the dolomite.

2.6 Detailed Information on Intended Use

Dolomite is intended to be used as a substitute for the GRAS mineral salts such as the calcium and magnesium salts that are currently added to purified waters to enhance the taste of the water beverage.

Today, manufacturers add a mixture of salts after purifying water to enhance the taste of the beverage. These products are labeled with a statement of identity such as "purified water, enhanced with minerals for taste." By passing the purified water through a bed of dolomite, the manufacturer can dissolve the minerals found in the dolomite into the water. Dolomite dissolves readily in aqueous media to the same individual ions (i.e., calcium, magnesium, bicarbonate) as other common salts such as calcium carbonate (affirmed as GRAS in 21 CFR §184.1191), calcium oxide (affirmed as GRAS in 21 CFR §184.1210), magnesium carbonate (affirmed as GRAS in 21 CFR §184.1425), and magnesium oxide (affirmed as GRAS in 21 CFR §184.1431).

Dolomite will be used to enhance the levels of calcium, magnesium, and carbonate in the water that improves the taste of the purified water beverages.

The remineralization process can be described with the following steps:

- Production of purified water by demineralization, for example with Reverse Osmosis membranes or Distillation;
- Optional addition of carbon dioxide (CO_2) to the purified water; pH value of the water with CO_2 added typically ranges from 4 to 6;
- After loading dolomite inside a filter, 1/ the manufacturer must subject the dolomite to a hot water or other treatment that would control for pathogens. The specific parameters will vary depending on the design of the filter. One approach involves the treatment of the dolomite with hot water at a temperature > 85°C. The hot water can be circulated through the filter for 30 minutes to one hour until the temperature at the water exiting the filter has reached a minimum of 85°C for at least 30 minutes.
- Once the dolomite has been heat treated in the filter, the dolomite and the filter is allowed to return to ambient temperature. The purified water passes through the filter at room temperature and solubilizes some mineral salts (the flow rate is controlled to reach the desired concentration of magnesium and calcium salts in the water); the contact time typically ranges from 15 to 30 minutes.

1/ We will only use filters that are approved under the food additive regulations, listed in FDA's Food Contact Notification (FCN) inventory, or can be considered GRAS. There are numerous filters that have the appropriate functionality that could be used in the manufacturing process. Examples of filters that could be incorporated into the process include sand filters, manganese dioxide filters, and activated carbon filters.

- The dolomite enhanced water is filtered to remove fine particles.
- The dolomite-containing water beverage will go through several further processing steps such as the use of UV light and ozonation after the dolomite is added to the water.
- The dolomite-containing water beverage will comply with the good manufacturing practice requirements for bottled water beverages found at 21 CFR Part 129 and the water quality standards found at 21 CFR 165.110(b), including those requirements for microbiological and chemical quality.

The chemical reaction happening in the dolomite filter:

$$CaMg(CO_3)_2 + 2\ CO_2 + 2\ H_2O \rightarrow Ca^{2+} + Mg^{2+} + 4\ HCO_3^-$$

As the above chemical reaction indicates, calcium, magnesium, and bicarbonate ions are dissolved into the purified water. The molar ratio and mass ratio between calcium, magnesium and bicarbonate ions dissolved in water are fixed:

Molar ratio:

$Ca : Mg : HCO_3 = 1 : 1 : 4$

Mass ratio:

$Ca : Mg : HCO_3 = 1 : 0.61 : 6.1$

The maximum calcium and magnesium composition of remineralized water is 40 mg/L of calcium and 25 mg/L magnesium.

As part of our safety assessment we considered the possibility that heavy metals found in the dolomite could dissolve into the water along with the calcium and magnesium ions. We conclude the presence of the heavy metals in the dolomite will not present a safety issue. The specifications have been established to limit the use of those sources of dolomite that meet the heavy metal levels in the specifications. The batch analysis results in Table 2 demonstrate it is possible to source dolomite that meets the established specifications. Data from two pilot studies evaluating the composition of purified water that is treated with dolomite demonstrates the finished water will comply with the specifications established by FDA for bottled water. We conducted two pilot studies using dolomite with a composition similar to those reported in Table 2. The first study, Pilot A, involved the use of dolomite to produce a finished product with a target of 20 mg/L calcium and 12 mg/L magnesium while Pilot B had a target of 112 mg/L of calcium and 68 mg/L, the latter study involving a use level about three times the level covered by this notification.

Specifically, Pilot A had a target of 20 mg/L of calcium and 12 mg/L magnesium with the pH of the CO_2-added water reported as 5.5. The calcium, magnesium, bicarbonate and other ion levels added to the purified water and the level of impurities are reported in Table 3, below.

Table 3. Analysis of Purified Water by Dissolution of Dolomite
Pilot Test A

Constituents	Levels Added by Dolomite	Unit
Calcium	18	mg/L
Magnesium	10.6	mg/L
Sodium	0.07	mg/L
Potassium	0.01	mg/L
Manganese	0.001	mg/L
Bicarbonate	108	mg/L
Silicon	0.1	mg/L
Antimony	ND (LOD = 1.0)	µg/L
Arsenic	ND (LOD = 0.5)	µg/L
Cadmium	ND (LOD = 0.25)	µg/L
Chromium	ND (LOD =1.0)	µg/L
Lead	ND (LOD =1.0)	µg/L
Nickel	ND (LOD =1.0)	µg/L
Selenium	ND (LOD =0.25)	µg/L

Data in the above table show the mass ratio of calcium, magnesium, and bicarbonate ions in the pilot study is Ca : Mg : HCO_3 = 1 : 0.59 : 6.0. This ratio is very close to the projected mass ratio of 1 : 0.61 : 6.1. Accordingly, the resulting Ca and Mg ions in bottled water beverages reflect the dolomite composition. The data also demonstrate the dissolution does not favor the extraction of a specific component of the dolomite. The analysis also found very low levels of other minerals such as sodium, potassium, and manganese that are added by dolomite but are present at insignificant levels. For example, potassium was detected at 0.01 mg/L (10 ppb). Importantly, none of the heavy metals were detected in the finished purified waters with limits of detection ranging from <0.25 µg/L (ppb) to <1 ppb.

Pilot Test B involved a higher concentration with a target of 112 mg/L of calcium, 68 mg/L of magnesium; the pH of the CO_2-added water in Pilot B is reported as 4.3. The results from Pilot B are summarized in Table 4, below. No heavy metals were detected in the finished purified water.

Table 4. Analysis of Purified Water by Dissolution of Dolomite Pilot Test B		
Constituents	**Levels Added by Dolomite**	**Unit**
Calcium	112	mg/L
Magnesium	65.5	mg/L
Sodium	1.9	mg/L
Potassium	0.55	mg/L
Manganese	0.008	mg/L
Bicarbonate	672	mg/L
Silicon	2.0	mg/L
Antimony	ND (LOD = 1.0)	µg/L
Arsenic	ND (LOD = 0.5)	µg/L
Cadmium	ND (LOD = 0.25)	µg/L
Chromium	ND (LOD =1.0)	µg/L
Lead	ND (LOD =1.0)	µg/L
Nickel	ND (LOD =1.0)	µg/L
Selenium	ND (LOD =0.25)	µg/L

The data in Tables 3 and 4 reveal non-detectable levels of the above-analyzed heavy metals in purified water treated with dolomite. We also note the manufacturers of purified bottled water beverages must comply with the allowable levels for inorganic substances listed in 21 CFR§ 165.110 (“Bottled water.”) The standard of quality for bottled water sets limits on the levels of microorganisms as well as impurities such as heavy metals that may be present in bottled water.

Finally, we are aware of reports in the literature regarding the use of dolomite as an effective treatment to remove heavy metals from waste water. A 2017 study investigated the adsorption of Cd, Zn, and Pb from waste water using dolomite powder, the authors found that dolomite adsorbed almost 100% of the Cd, Pb, and Zn ions being present in a solution with concentrations of 500, 1,000, and 2,000 mg/L under a pH value of 3 and a minimum contact time of 45 minutes. 2/ While we recognize the pH value, contact time, and heavy metal concentrations in the study differ markedly from the proposed intended use of dolomite as a mineral source for purified bottled waters, the study demonstrates dolomite can actually be used to absorb heavy metals from water.

In conclusion, the data from the two pilot studies demonstrate the use of dolomite with a composition similar to the three samples reported in Table 2 do not result in detectable levels of heavy metals in the purified water beverage, including when the dolomite is used at a level three

2/ Gruszecka-Kosowska, Agnieszka, et al. "Waste dolomite powder as an adsorbent of Cd, Pb (II), and Zn from aqueous solutions." *Environmental Earth Sciences* 76.15 (2017): 521.

times of that covered by this notification. Moreover, at least one study suggests dolomite has the potential to absorb rather than release heavy metals. And in the event detectable levels of dolomite could be dissolved in the water, the FDA regulations for bottled provide set restrictions on the level of heavy metals that may be present in bottled waters and thus provide further assurance the dolomite will not contribute heavy metals to the bottled water that present a safety issue.

3.0 Dietary Exposure

The average and 90th percentile intake for bottled water can be determined from a database called the National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS). NHANES is a national food survey of non-institutionalized youth and adult civilians in the United States. The NHANES consumption data ("consumer exposure" data that only include those who reported consuming bottled water) can be summarized in Table 5, below.

Table 5. Bottled Water Consumption (NHANES 2013-2014)

Age Group	Average Consumption	90th Percentile
Total Population	841.46 g/person	1,775 g/person
Children 1 Through 3 Years of Age	255.21 g/person	540 g/person
Children 4 Through 8 Years of Age	408.9 g/person	805.31 g/person
Adolescents and Adults > 8 Years	888.52 g/person	1,920 g/person

The average and 90th percentile dietary exposures for the main constituents after dolomite dissolves into water (i.e., calcium ions and magnesium ions) can be calculated using the following conservative assumptions:

- A maximum level of 40 mg/L calcium ions and 25 mg/L magnesium ions to all the purified water products it markets, which corresponds to 184 mg/L dolomite.
- Purified water beverages remineralized by dolomite have a 100% market share of the bottled water market in the U.S.
- An average consumer drinks 841.46 g bottled water per day, and the 90th percentile consumers drink 1,775 g bottled water per day.
- Bottled water has a density of 1 g/mL.

Average EDI of calcium = 40 mg/L x (841.46 g ÷ 1 g/mL) ÷ 1,000 mL/L = 33.7 mg/day

90th percentile EDI of calcium = 40 mg/L x (1,775 g ÷ 1 g/mL) ÷ 1,000 mL/L = 71 mg/day

Average EDI of magnesium = 25 mg/L x (841.46 g ÷ 1 g/mL) ÷ 1,000 mL/L = 21 mg/day

90th percentile EDI of magnesium = 25 mg/L x (1,775 g ÷ 1 g/mL) ÷ 1,000 mL/L = 44.4 mg/day

Average EDI of solubilized dolomite = 184 mg/L x (841.46 g ÷ 1 g/mL) ÷ 1,000 mL/L = 154.8 mg/day

90th percentile EDI of solubilized dolomite = 184 mg/L x (1775 g ÷ 1 g/mL) ÷ 1,000 mL/L = 326.6 mg/day

The EDIs for calcium ions, magnesium ions, and dolomite can be summarized in the table below:

Table 6. EDIs of Dolomite, Calcium Ions, Magnesium Ions, and Bicarbonate Ions

Constituents	Average EDI	90th Percentile EDI
Calcium	33.7 mg/day	71 mg/day
Magnesium	21 mg/day	44.4 mg/day
Solubilized Dolomite	154.8 mg/day	326.6 mg/day

The EDIs for calcium ions, magnesium ions, and dolomite for different subpopulation can be calculated and summarized with the table below:

Table 7. EDIs of Dolomite, Calcium Ions, Magnesium Ions, and Bicarbonate Ions in Subpopulations

Age Group	Constituents	Average EDI	90th Percentile EDI
Children 1 Through 3 Years of Age	Calcium	10.2 mg/day	21.6 mg/day
	Magnesium	6.3 mg/day	13.4 mg/day
	Solubilized Dolomite	47 mg/day	99.4 mg/day
Children 4 Through 8 Years of Age	Calcium	16.4 mg/day	32.2 mg/day
	Magnesium	10.2mg/day	20mg/day
	Solubilized Dolomite	75.2 mg/day	148.2 mg/day
Adolescents and Adults > 8 Years	Calcium	35.5 mg/day	76.8 mg/day
	Magnesium	22.1mg/day	47.8mg/day
	Solubilized Dolomite	163.5 mg/day	353.3 mg/day

We would like to note the above dietary intake assessment is very conservative as it is based on the assumption that dolomite is going to be added to all the purified water beverages in the U.S. Not all bottled waters will have minerals added. Further, it would be reasonable to assume that most consumers would have at most one or two bottles of purified water beverages with dolomite added (i.e., up to 24 fl. Oz.). An intake of about 30 mg/day intake of calcium ions and about 18 mg/day of magnesium ions from two bottles of purified water is a more accurate estimate of the typical daily intake.

4.0 Self-limiting Levels of Use

The use of dolomite in purified water is not self-limiting and will be controlled closely through formulation.

5.0 Experience Based on Common Use in Food before 1958

Dolomite is a mineral formation that is frequently exposed to ground water and spring water. When the ground water or spring water comes in contact with the dolomite, it will contribute calcium, magnesium, and carbonate ions when the ground water contains minor amounts of carbon dioxide. Dolomite, therefore, has been contributing mineral salts to ground water and spring water for over millennia. The GRAS notification involves a novel use of the dolomite that was not in existence prior to 1958. The information in this notification demonstrates the GRAS status on the basis of scientific procedures.

6.0 GRAS Narrative

6.1 Overview

Dolomite is an anhydrous carbonate mineral composed of calcium magnesium carbonate. According to the Scientific Report of the 2015 Dietary Guidelines Advisory Committee, both calcium and magnesium are shortfall nutrients that are considered underconsumed in the United States. Dolomite dissolves readily in aqueous media to the same individual ions (i.e., calcium, magnesium, bicarbonate) as other common salts such as calcium carbonate (affirmed as GRAS in 21 CFR §184.1191), calcium oxide (affirmed as GRAS in 21 CFR §184.1210), magnesium carbonate (affirmed as GRAS in 21 CFR §184.1425), and magnesium oxide (affirmed as GRAS in 21 CFR §184.1431). The regulatory status of these salts can be further summarized with the table below.

Table 8. Regulatory Status of Salts Formed through the Use of Dolomite

Salt	Regulatory Citation	Limitations
Calcium Carbonate	21 CFR §184.1191	None other than GMPs
Calcium Oxide	21 CFR §184.1210	No limitations other than GMPs
Magnesium Carbonate	21 CFR §184.1425	No limitations other than GMPs (regulation identifies the conditions of use at the time, including as a nutrient supplement)
Magnesium Oxide	21 CFR §184.1431	No limitations other than GMPs (regulation identifies the conditions of use at the time, including as a nutrient supplement)

As shown in **Table 8,** each of the salts contributed by dolomite is authorized for use in food. Moreover, we have identified the reported levels of calcium and magnesium in bottled waters currently on the U.S. market in a peer-reviewed public literature. In particular, Azoulay et al. (2001) reported on the maximum level of calcium ions in North American bottled waters ("Mineral Waters") to be 310 mg/L and the maximum level of magnesium ions to be 130 mg/L. 3/ In contrast, the maximum levels of calcium ions and magnesium ions from the intended use of dolomite in bottled water are 40 mg/L and 25 mg/L, respectively. Our intended

3/ Azoulay, Arik, Philippe Garzon, and Mark J. Eisenberg. "Comparison of the mineral content of tap water and bottled waters." *Journal of General Internal Medicine* 16.3 (2001): 168-175.

use of dolomite would result in bottled water beverages with calcium and magnesium levels in line with those currently on the market.

In addition, the proposed use of dolomite is supported by the many scientific reviews that have concluded calcium carbonate, magnesium carbonate, and other salts of these minerals are safe. Several groups of recognized experts have evaluated the safety of the calcium and magnesium components of the dolomite. These include assessments by the Select Committee on GRAS Substances (SCOGS), the European Commission Scientific Committee on Food (SCF), and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Institute of Medicine (IOM). We also calculated the EDI of dolomite using the NHANES database, 2013-2014. Based on the findings of these experts, as well as the dietary exposure levels of dolomite, the intended use can be reasonably expected to be safe.

6.2 Safety Assessment

Because dolomite is dissolved into calcium ions and magnesium ions once in contact with purified water, we consider the safety of calcium ions, magnesium ions, and dolomite below separately. We also briefly addressed the heavy metal levels in the remineralized water.

6.2.1 Calcium

Calcium is one of the major mineral components of the human skeletal system and is also an essential nutrient required for nerve conduction, muscle contraction, hormone and enzyme secretion, and blood clotting. 4/ Adequate calcium is needed for adequate mineralization and maintenance of growing bones. 5/ The 2015 Dietary Guidelines Advisory Committee (DGAC) found that calcium is under consumed relative to the Estimated Average Requirement or Adequate Intake levels set by the IOM. 6/ As such, DGAC characterized calcium as a shortfall nutrient and also as a nutrient of public health concern because its under-consumption has been linked in the scientific literature to adverse health outcomes. 7/

Milk, yogurt, cheese and other dairy foods are rich sources of calcium and are the major food contributors of this nutrient to people in the United States. Nondairy foods such as Chinese cabbage, kale, and broccoli also contain calcium. While excess calcium intake from foods alone is difficult if not impossible to achieve, high levels of calcium in the blood known as

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4/ Bailey, Regan L., et al. "Estimation of total usual calcium and vitamin D intakes in the United States." *The Journal of nutrition* 140.4 (2010): 817-822.
5/ SarDesai, Vishwanath. *Introduction to clinical nutrition*. CRC Press, 2011.
6/ 2015 Dietary Guidelines Advisory Committee (DGAC) Scientific Report.
7/ *See id*.

hypercalcemia can cause renal insufficiency, vascular and soft tissue calcification, hypercalciuria (high levels of calcium in the urine) and kidney stones. 8/ Below, we summarized various expert panels opinions on the safe levels of calcium.

- **The Select Committee on GRAS Substances (SCOGS) Opinion**

In 1975, while reviewing the GRAS status of calcium salts including calcium acetate, calcium chloride, calcium gluconate, and calcium phytate, SCOGS found that "[e]xtensive studies have been made to determine the nutritional significance of calcium and its salts. … ***A review of the concentrations of calcium compounds normally present in or added to foods provides no evidence that suggests possible untoward effects at these level***s…" (emphasis added.)9 The SCOGS then concluded "[t]here is no evidence in the available information on calcium acetate, calcium chloride… that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current or that might reasonably be expected in the future."

In addition to reviewing the safety of calcium salts generally, SCOGS also specifically addressed the GRAS status of calcium carbonate, potassium bicarbonate, potassium carbonate, sodium bicarbonate, sodium carbonate, and sodium sesquicarbonate SCOGS concluded that "[t]here is no evidence in the available information on calcium carbonate, potassium carbonate, potassium bicarbonate, sodium carbonate, sodium bicarbonate, or sodium sesquicarbonate that demonstrates or suggests reasonable grounds to suspect a hazard to the public when used at levels that are now current or that might reasonably be expected in the future."10

- **The European Commission Scientific Committee on Food (SCF) Opinion**

In 2003, the SCF conducted an extensive safety review of calcium before setting the safety level or tolerable upper intake level for calcium at 2,500 mg/day for adults. 11/ The Committee based its decision on the evidence of different interventional studies of long duration in adults, some of which were placebo-controlled and the total daily calcium intake of 2,500 mg/day were tolerated

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8/ Del Valle, Heather B., Ann L. Yaktine, Christine L. Taylor, and A. Catharine Ross, eds. *Dietary reference intakes for calcium and vitamin D*. National Academies Press, 2011.

9 *See* Select Committee on GRAS Substances (SCOGS) Opinion: Calcium acetate, calcium chloride, calcium gluconate, and calcium phytate, *available at*: http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm260876.htm.

10 *See* Select Committee on GRAS Substances (SCOGS) Opinion: Carbonate Salts, *available at*: http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm260878.htm.

11/ Scientific Committee on Food of European Commission. "Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Calcium." *European Commission* (2003).

without any adverse effects. 12/ The Committee also noted that an excessive accumulation of calcium in blood or tissue through excessive calcium intake should not occur in the absence of diseases such as bone cancer, hyperthyroidism, and hyperparathyroidism or in the absence of excessive vitamin D intake. 13/

- **The Institute of Medicine (IOM) Review**

In 2011, the committee to review dietary reference intakes of vitamin D and calcium of the IOM conducted a review of the safety studies associated with calcium intake. We highlight below the key safety findings.

Calcium Intake and Kidney Stone

High intake level of calcium from supplements, but not foods, has been associated with increased risk of kidney stones. For example, a recent study using data from the Women's Health Initiative (WHI) trial, which recruited more than 36,000 post-menopausal women ages 50 to 79 years, reported findings on the incidence of kidney stones associated with higher level of calcium supplemental intake. 14/ In particular, the subjects were randomly assigned to receive a placebo or 1,000 mg of elemental calcium. 15/ Because the baseline intake of calcium was approximately 1,100 mg/day for the subjects, and the supplemental intake added another 1,000 mg/day, the total average calcium intake for the test subjects is about 2,100 mg/day. 16/ The authors found that among the healthy postmenopausal women in the WHI study, the higher doses of calcium and vitamin D resulted in an increased risk (i.e., 17%) of kidney stone. 17/ The IOM concluded that based on its review, the data indicate the calcium content of foods does not cause stone formation.

Calcium Intake and Prostate Cancer

Excessive calcium intake has also been associated with prostate cancer, although the vast majority of the data are derived from observational studies. For example, in Raimondi S et al., (2010), the authors assessed the association of dairy products and dietary calcium on prostate

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12/ *See id*.
13/ *See id*.
14/ Jackson, Rebecca D., et al. "Calcium plus vitamin D supplementation and the risk of fractures." *New England Journal of Medicine* 354.7 (2006): 669-683.
15/ *See id*.
16/ *See id*.
17/ *See id*.

cancer risk in a case-control study of 197 cases. 18/ The authors found a twofold increased risk of prostate cancer associated with an increased intake of dairy products. 19/ The authors also found the calcium showed a borderline association with prostate cancer risk, with slightly higher risk for higher calcium intake. 20/ It would be challenging to sort the effect of dairy products on prostate cancer from that of calcium.

In a randomized controlled clinical trial based on 672 men, however, the authors found no increase in cancer risk associated with calcium supplementation and some suggestion of a protective effect. 21/ In particular, Baron JA et al., (2005) randomly assigned the study subjects to receive either 3 g of calcium carbonate (1,200 mg of calcium), or placebo, daily for 4 years. 22/ The subjects were followed for up to 12 years and asked periodically to report new cancer diagnoses. 23/ After a mean follow-up of 10.3 years, there were 33 prostate cancer cases in the calcium-treated group and 37 in the placebo-treated group. 24/ Overall, the IOM concluded that data in this area are at best emerging and cannot be relied upon for the development of a safety level or UL level.

IOM UL Levels for Calcium Intake

After carefully reviewing the various potential indicators for calcium intake toxicity, the IOM established the UL levels for various age groups as follows:

Table 9. Calcium IOM ULs for All Age Groups

Age Group	ULs
Children 1 Through 3 Years of Age	2,500 mg/day
Children 4 Through 8 Years of Age	
Children 9 Through 13 Years of Age	3,000 mg/day
Adolescents 14 Through 18 Years of Age	
Adults 19 Through 30 Years of Age	2,500 mg/day
Adults 31 Through 50 Years of Age	

18/ Raimondi, Sara, et al. "Diet and prostate cancer risk with specific focus on dairy products and dietary calcium: a case–control study." *The Prostate* 70.10 (2010): 1054-1065.
19/ *See id*.
20/ *See id*.
21/ Baron, John A., et al. "Risk of prostate cancer in a randomized clinical trial of calcium supplementation." *Cancer Epidemiology Biomarkers & Prevention*14.3 (2005): 586-589.
22/ *See id*.
23/ *See id*.
24/ *See id*.

Table 9. Calcium IOM ULs for All Age Groups	
Age Group	**ULs**
Adults 51 Through 70 Years of Age	2,000 mg/day
Adults > 70 Years of Age	

IOM Recommended Dietary Allowance (RDA) for Calcium Intake

The IOM also established the calcium RDA levels, which are intended to serve as a guide for good nutrition, for various age groups as follows:

Table 10. Calcium IOM RDAs for All Age Groups	
Age Group	**RDAs**
Children 1 Through 3 Years of Age	700 mg/day
Children 4 Through 8 Years of Age	1,000 mg/day
Adults 9 Through 13 Years of Age	1,300 mg/day
Adults 14 Through 18 Years of Age	
Adults 19 Through 30 Years of Age	1,000 mg/day
Adults 31 Through 50 Years of Age	
Adults 51 Through 70 Years of Age	1,000 mg/day (male); 1,200 mg/day (female)
Adults > 70 Years of Age	1,200 mg/day

Calcium Safety Conclusion

While excessive calcium intake might lead to adverse health effects including kidney stones, the intended use of dolomite can be considered reasonably safe. The intended use of dolomite in the remineralization of purified water beverages is a substitutional use and would replace calcium salts that are currently authorized for use in food with no limitations other than cGMPs. Further, as summarized in the table below, even the highest calcium EDI for the 90th percentile consumers from the consumption of beverages fortified with dolomite among various subpopulations (i.e., 76.8 mg/day) is far below the ULs and RDAs of calcium among all age groups and, thus, is unlikely to produce any adverse effects.

Table 11. Calcium IOM RDAs, ULs, and EDIs Comparison for All Age Groups				
Age Group	**Average EDIs**	**90% EDIs**	**RDAs**	**ULs**
Children 1 Through 3 Years of Age	10.2 mg/day	21.6 mg/day	700 mg/day	2,500 mg/day
Children 4 Through 8 Years of Age	16.4 mg/day	32.2 mg/day	1,000 mg/day	2,500 mg/day
Adolescents and Adults > 8 Years	35.5 mg/day	76.8 mg/day	1,000 mg/day*	2,000 mg/day*
*The lowest RDA and UL values among >8 years re used for comparison.				

6.2.2 Magnesium

Like calcium, magnesium is an essential element that plays many crucial roles in the human body. Among other things, magnesium is critical in energy-requiring metabolic processes, in protein synthesis, membrane integrity, nervous tissue conduction, and muscle contraction. 25/ Magnesium is present in fruits, vegetables, grains, milk, meat, and fish. The 2015 DGAC characterized magnesium as a shortfall nutrient. As discussed in more detail below, excessive magnesium intake from the intended use of dolomite is difficult if not impossible to achieve. Further, too much magnesium from food does not pose a safety risk in healthy individuals because the kidneys eliminate excess amounts in the urine. 26/

However, it was reported that high doses of magnesium from dietary supplements or medications often result in diarrhea that can be accompanied by nausea and abdominal cramping. 27/ The diarrhea and laxative effects of magnesium salts are due to the osmotic activity of unabsorbed salts in the intestine and colon and the stimulation of gastric motility. Below, we summarized various expert panels' opinions on the safe levels of magnesium.

- **The SCOGS Opinion**

While reviewing the GRAS status of magnesium carbonate, magnesium chloride, magnesium hydroxide, magnesium oxide, dibasic magnesium phosphate, tribasic magnesium phosphate, magnesium stearate, and magnesium sulfate in 1975, the Select Committee found that while chronic toxicity data are lacking, the status of magnesium as a ubiquitous and essential dietary

25/ Laires, Maria José, Cristina Paula Monteiro, and Manuel Bicho. "Role of cellular magnesium in health and human disease." *Front Biosci* 9.262 (2004): 76.
26/ Musso, Carlos G. "Magnesium metabolism in health and disease."*International urology and nephrology* 41.2 (2009): 357-362.
27/ Institute of Medicine (IOM). Food and Nutrition Board. Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride external link disclaimer. Washington, DC: National Academy Press, 1997.

ingredient for the maintenance of homeostatic and bioenergetics mechanisms leads to the opinion that none of the available evidence suggests any probable hazard when any of the GRAS compounds of magnesium is used as a food ingredient. 28 The Select Committee concluded that" [t]here is no evidence in the available information on magnesium carbonate, magnesium chloride, magnesium sulfate, magnesium hydroxide, magnesium oxide, magnesium stearate, dibasic magnesium phosphate and tribasic magnesium phosphate that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current and in the manner now practiced, or which might reasonably be expected in the future."

- **The SCF Opinion**

In 2001, the SCF conducted a review of safety studies associated with excessive magnesium intake. 29/ The SCF found that mild diarrhea is the most sensitive non-desirable effect of orally administered easily dissociable magnesium salts. The SCF concluded that based on the data it has reviewed, mild diarrhea occurred in a small percentage of adult subjects at oral doses of about 360 to 365 mg magnesium per day. Moreover, no laxative effects have been observed in adult men and women at doses up to 250 mg magnesium per day. Therefore, the 250 mg is considered as being the no-observed-adverse-effect level (NOAEL) for magnesium.

- **The IOM Review**

In 1997, the IOM conducted an extensive review of the safety studies associated with magnesium. We highlighted below the IOM key safety findings.

Magnesium Intake and Gastrointestinal Symptoms

The IOM reviewed the few studies that report mild diarrhea and other gastrointestinal symptoms from uses of magnesium salts. In particular, in Bashir et al., (1993), gastrointestinal symptoms, including diarrhea, developed in 6 of 21 patients receiving long-term magnesium chloride therapy at levels of 360 mg of magnesium. 30/ The findings are also supported by other studies.

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28 *See* Select Committee on GRAS Substances (SCOGS) Opinion: Magnesium salts, *available at*: http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm261275.htm.

29/ Scientific Committee on Food of European Commission. "Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Magnesium." European Commission (2001).

30/ Bashir, Yaver, et al. "Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease." *The American journal of cardiology* 72.15 (1993): 1156-1162.

For example, in Ricci et al., (1991), gastrointestinal manifestations developed in 5 of 25 pregnant women being giving 384 mg of daily magnesium as magnesium chloride supplements for the prevention of preterm delivery. 31/ The IOM concluded that the studies it reviewed supported a lowest observed adverse effect level (LOAEL) for magnesium-induced diarrhea in adults at 360 mg.

IOM UL Levels for Magnesium Intake

Based on the studies it reviewed, the IOM concluded that osmotic diarrhea has not been reported with normal dietary intake of magnesium and magnesium ingested as a component of food. Thus, a UL could not be based on magnesium obtained from foods. Rather, because some individuals may be at risk of a mild, reversible adverse effect (i.e., diarrhea) from non-food sources, the IOM developed a UL for magnesium as summarized in the table below for magnesium intake from pharmacological uses:

Table 12. Magnesium IOM ULs for All Age Groups

Age Group	ULs
Children 1 Through 3 Years of Age	65 mg of supplementary magnesium
Children 4 Through 8 Years of Age	110 mg of supplementary magnesium
Adolescents and Adults > 8 Years	350 mg of supplementary magnesium

IOM RDA for Magnesium Intake

The IOM also established the magnesium RDA levels for various age groups as follows:

Table 13. Magnesium IOM RDAs for All Age Groups

Age Group	RDAs
Children 1 Through 3 Years of Age	80 mg/day
Children 4 Through 8 Years of Age	130 mg/day
Adults 9 Through 13 Years of Age	240 mg/day
Adults 14 Through 18 Years of Age	410 mg/day (male); 360 mg/day (female)
Adults 19 Through 30 Years of Age	400 mg/day (male); 310 mg/day (female)
Adults 31 Through 50 Years of Age	420 mg/day (male); 320 mg/day (female)
Adults 51 Through 70 Years of Age	420 mg/day (male); 320 mg/day (female)
Adults > 70 Years of Age	420 mg/day (male); 320 mg/day (female)

31/ Ricci, Jean M., et al. "Oral tocolysis with magnesium chloride: a randomized controlled prospective clinical trial." *American journal of obstetrics and gynecology* 165.3 (1991): 603-610.

Magnesium Safety Conclusion

While excessive magnesium intake might lead to adverse health effects, the intended use of dolomite can be considered reasonably safe. The intended use of dolomite in the remineralization of purified water beverages is a substitutional use and would replace magnesium salts that are currently authorized for use in food with no limitations other than cGMPs. The proposed use of dolomite, therefore, would not increase dietary exposure to its main component magnesium. Further, as summarized in the table below, even the highest magnesium EDI for the 90th percentile consumers from the consumption of beverages fortified with dolomite among various subpopulations (i.e., 47.8 mg/day) is below the ULs and RDAs of magnesium among all age groups and is unlikely to produce any adverse effects.

Table 14. Magnesium IOM RDAs, ULs, and EDIs Comparison for All Age Groups

Age Group	Average EDIs	90% EDIs	RDAs	ULs
Children 1 Through 3 Years of Age	6.3 mg/day	13.4 mg/day	80 mg/day	65 mg/day
Children 4 Through 8 Years of Age	10.2mg/day	20 mg/day	130 mg/day	110 mg/day
Adolescents and Adults > 8 Years	22.1mg/day	47.8mg/day	240 mg/day*	350 mg/day
*The lowest RDA value among >8 years is used for comparison.				

6.2.3 Dolomite

Dolomite dissolves into calcium and magnesium ions when in contact with purified water injected with CO_2 and are not added directly as an ingredient to the purified water. Nonetheless, out of an abundance of caution, we conducted a safety review of dolomite. Dolomite is not mutagenic, and there are no indications of carcinogenicity. 32/ A natural mixture of dolomite, magnesite, and magnesium-phyllosilicates (talc and chlorite) was tested for mutagenicity in a bacterial reverses mutation test. 33/ The study used concentrations of the mixture of up to 5,000 µg/plate in two independent experiments, using strains TA 1537, TA1535, TA98, TA100 and TA102 of *Salmonella Typhimurium*. 34/ The authors reported that none of the strains showed any evidence of mutagenesis in either the presence or absence of metabolic activation. 35/ The mixture that contains dolomite was also tested in an *in vitro* chromosome

32/ Safety and efficacy of a natural mixture of dolomite plus magnesite and magnesium-phyllosilicates (Fluidol) as feed additive for all animal species. *EFSA Journal* 2016;14(1):4341.
33/ *See id*.
34/ *See id*.
35/ *See id*.

aberration test in human lymphocytes. 36/ Up to 1,500 µg/mL was used, and there is not any statistically significant increase in the number of cells with chromosome aberrations. 37/

The potential of oral exposure to dolomite was also analyzed using Wistar rats. 38/ In particular, animals received dolomite oral dosages of 500 and 1,500 mg/kg during the period of gestation. 39/ Maternal, embryo and fetal toxicity were evaluated. 40/ Dolomite exposure did not produce maternal toxicity assessed by clinical observations, body weight gain, hematology parameters and relative organs weight. 41/ While the slight increase was observed in fetal body weight in the dolomite-treated group, the authors concluded that the oral exposure to rats of up to 1,500 mg/kg of dolomite during organogenesis did not induce significant maternal and embryo-fetal toxicity. 42/ We consider these studies of limited relevance for assessing the safety of the proposed use because the dolomite is not consumed per se but used as a source of calcium carbonate and magnesium carbonate. Nonetheless, the studies demonstrate the levels of dolomite that would be needed to produce the calcium carbonate and magnesium carbonate, if consumed orally as dolomite, would not pose any human safety concern at a level of 353.3 mg/day (or 5.89 mg/kg bw/day).

6.2.4 Heavy Metals

Table 15. Heavy Metal Levels In the Remineralized Water Comparison

Constituents	Levels (Pilot A)	Levels (Pilot B)	21 CFR 165.110 Limits
Antimony	<1.0 µg/L	<1.0 µg/L	6 µg/L
Arsenic	<0.5 µg/L	<0.5 µg/L	10 µg/L
Cadmium	<0.25 µg/L	<0.25 µg/L	5 µg/L
Chromium	<1.0 µg/L	<1.0 µg/L	100 µg/L
Lead	<1.0 µg/L	<1.0 µg/L	5 µg/L
Nickel	<1.0 µg/L	<1.0 µg/L	100 µg/L
Selenium	<0.25 µg/L	<0.25 µg/L	50 µg/L

As the above table demonstrates, the heavy metal levels in the remineralized water in both pilot studies are much lower than the allowable levels under FDA's regulation 21 CFR 165.110(b)(4)(iii)(A). Also, all the purified water beverages manufactured comply with the heavy

36/ *See id*.
37/ *See id*.
38/ Lagarto, Alicia, et al. "Effect of dolomite oral exposure in Wistar rats during organogenesis period of pregnancy." *Experimental and Toxicologic Pathology* 60.6 (2008): 499-504.
39/ *See id*.
40/ *See id*.
41/ *See id*.
42/ *See id*.

metal levels in 21 CFR 165.110. As such, the heavy metal impurities in the bottled water beverages do not present any human safety concern.

6.2.5 Background Calcium and Magnesium Intake from Foods and Beverages

Below, we provide the background intake of these two shortfall nutrients and compare them to the IOM ULs and the dietary exposure from the intended use.

The Scientific Report of the 2015 Dietary Guidelines Advisory Committee provides information on the average and 90th percentile intake for calcium and magnesium from foods and beverages, which we summarize in Table 16, below.

Table 16: Calcium and Magnesium Intake from Foods and Beverages (mg/day)

Age Group	Constituents	Average	90th Percentile	UL
Children 1 Through 3 Years of Age	Calcium	1067	1536	2500
	Magnesium	198	266	65
Children 4 Through 8 Years of Age	Calcium	1011	1393	2500
	Magnesium	216	277	110
Children/Teens 9 Through 13 Years of Age	Calcium	1129	1558	3000
	Magnesium	251	334	350
General Population (1 and Over)	Calcium	988	1474	2500
	Magnesium	282	410	350

With regard to dietary supplement and food intake specifically, Bailey et. al (2011), reported on the impact of including foods and supplements in intake assessments for the adult population (≥ 19 years of age). 43/ Bailey et. al (2011) reported average total intakes from foods and supplements of magnesium to be 449 mg for men and 387 mg for women, and average total intakes of calcium reported to be 1319 mg for men and 1331 mg for women. Unfortunately, Bailey did not provide intake for the 90th percentile. In the table below we list the mean intake

43/ Bailey, Regan L., et al. "Dietary supplement use is associated with higher intakes of minerals from food sources." *The American journal of clinical nutrition* 94.5 (2011): 1376-1381.

levels of calcium and magnesium from food, beverage and supplement use, the mean and 90th percentile intake, along with intake from the intended use, as well as the ULs.

Table 17. Calcium and Magnesium Background Intake and Intended Use Comparison					
Constituents	**Food & Supplement Users 44/**	**Nonusers of Supplements**	**Average EDI from Intended Use**	**90% EDI from Intended Use**	**ULs**
Calcium	1331 mg/day (women)	727 mg (women)	33.7 mg/day	71 mg/day	2,500 mg/day
Magnesium	449 mg/day (men)	268 mg (men)	21mg/day	44.4mg/day	350 mg/day

We recognize the intake for magnesium currently exceeds the UL of 350 mg of supplementary magnesium on the basis of current exposures. We do not view the proposed use as presenting an issue with regard to magnesium intake for several reasons. The Dietary Guidelines list magnesium as a short fall nutrient in the diet even though the 90th percentile intake of magnesium exceeds the UL. Magnesium remains a shortfall nutrient for which consumers are encouraged to increase total dietary intake. The use of dolomite will help accomplish those public health objectives by providing a convenient food source for magnesium intake. The safety is further supported by the GRAS regulations for each of the mineral salts contributed by the dolomite. Calcium carbonate, calcium oxide, magnesium carbonate, and magnesium oxide are authorized for addition to bottled water with no limits other than GMPs. We also question whether it is appropriate to apply the UL for magnesium in a safety assessment. The IOM has set the UL at 350 mg on the basis of adverse events noticed with pharmacological uses of magnesium and osmotic diarrhea has not been reported with normal dietary intake of magnesium as a component of food. Moreover, the reference daily intake (RDI) for adults and children over 4 for magnesium is set at 420 mg/day.45/ It is inconsistent to set the acceptable daily intake for magnesium at a level that is substantially lower than the RDI for nutrition labeling purposes. Finally, as discussed above, an intake of 18 mg/day of magnesium ions based on the consumption of one or two bottled of purified water beverage with added dolomite is a more accurate estimate of the actual intake. This level is not expected to increase the magnesium intake in any appreciable manner.

44/ When different mineral intakes are reported for men and women, we use the higher one in the table.

45/ *See,* 21 CFR §101.9(c)(8)(iv).

6.3 Conclusion

Several expert panels organized by reputable scientific and regulatory agencies including SCOGS, SCF, and IOM have reviewed the available safety data on the component ions of dolomite including calcium and magnesium and established safety levels for various age groups. All these reports are publicly available. The calculated EDIs from the proposed use are far below these safety levels. Further, based on the available data and information we have reviewed, we are not aware of any data and information that are, or may appear to be, inconsistent with our conclusion of GRAS status. We, therefore, are of the view that there is a consensus among experts qualified by scientific training and experience to evaluate the safety that there is reasonable certainty the intended use of dolomite is not harmful under the intended conditions of use.

In summary, due to the demonstrated safe history of use of various calcium and magnesium salts, the desirability of increased calcium and magnesium in people's diets, as well as the expert panels opinions, we concluded that the intended use of dolomite in purified water beverages at levels not to exceed 40 mg/L calcium and 25 mg/L magnesium can be considered GRAS through scientific procedures.

7.0 List of Supporting Data and Information

All of the following data and information are publicly available.

- Gruszecka-Kosowska, Agnieszka, et al. "Waste dolomite powder as an adsorbent of Cd, Pb (II), and Zn from aqueous solutions." *Environmental Earth Sciences* 76.15 (2017): 521.

- Azoulay, Arik, Philippe Garzon, and Mark J. Eisenberg. "Comparison of the mineral content of tap water and bottled waters." *Journal of General Internal Medicine* 16.3 (2001): 168-175.

- Bailey, Regan L., et al. "Estimation of total usual calcium and vitamin D intakes in the United States." *The Journal of nutrition* 140.4 (2010): 817-822.

- SarDesai, Vishwanath. *Introduction to clinical nutrition*. CRC Press, 2011.

- 2015 Dietary Guidelines Advisory Committee (DGAC) Scientific Report.

- Del Valle, Heather B., Ann L. Yaktine, Christine L. Taylor, and A. Catharine Ross, eds. *Dietary reference intakes for calcium and vitamin D*. National Academies Press, 2011.

- Scientific Committee on Food of European Commission. "Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Calcium." *European Commission* (2003).

- Jackson, Rebecca D., et al. "Calcium plus vitamin D supplementation and the risk of fractures." *New England Journal of Medicine* 354.7 (2006): 669-683.

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- Baron, John A., et al. "Risk of prostate cancer in a randomized clinical trial of calcium supplementation." *Cancer Epidemiology Biomarkers & Prevention*14.3 (2005): 586-589.

- Laires, Maria José, Cristina Paula Monteiro, and Manuel Bicho. "Role of cellular magnesium in health and human disease." *Front Biosci* 9.262 (2004): 76.

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- Institute of Medicine (IOM). Food and Nutrition Board. Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride external link disclaimer. Washington, DC: National Academy Press, 1997.

- Scientific Committee on Food of European Commission. "Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Magnesium." European Commission (2001).

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- Safety and efficacy of a natural mixture of dolomite plus magnesite and magnesium-phyllosilicates (Fluidol) as feed additive for all animal species. *EFSA Journal* 2016;14(1):4341.

- Lagarto, Alicia, et al. "Effect of dolomite oral exposure in Wistar rats during organogenesis period of pregnancy." *Experimental and Toxicologic Pathology*60.6 (2008): 499-504.

- Bailey, Regan L., et al. "Dietary supplement use is associated with higher intakes of minerals from food sources." *The American journal of clinical nutrition* 94.5 (2011): 1376-1381.

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December 11, 2018

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Re: Response to FDA's Questions for GRN 000806

Dear Mr. Wafula,

We hereby submit our responses to FDA's questions for GRN 000806, which covers the intended use of dolomite to enhance the taste of bottled water beverages by serving as a source of minerals that are solubilized into the beverage when the water passes through a bed of dolomite.

For your ease of reference, we first copied FDA's question below, followed by each of our response:

- ***FDA Question #1****: The notice includes results obtained from pilot studies that use dolomite to add calcium (Ca) and magnesium (Mg) ions to water. Please clarify whether the water used in these studies was carbonated or non-carbonated. It is well known that the dissolution of minerals by water is affected by pH. Please clarify the conditions of pH in the pilot study, including a brief discussion of how the pilot study relates to both conditions of use (carbonated and non-carbonated).*

Response to Question 1: We provided data and information on two pilot studies in GRN 000806, both of which involved carbonated waters. Specifically, for Pilot A, the pH of the CO_2-added water is 5.5. For Pilot B, the pH of the CO_2-added water is 4.3. The pilot studies demonstrate that dolomite can be used to produce remineralized water with mineral levels in line with the levels targeted. As discussed in Section 1.4 "Conditions of Use" of the GRN 000806, the maximum target composition of the remineralized water with dolomite added is 40 mg/L of calcium ions and 25 mg/ml of magnesium ions.

We agree with the agency the dissolution of minerals by water is affected by pH, as well as other conditions including temperature and flow rate of the water. The data we submitted from the trials demonstrate that dolomite is effective at remineralizing water with different pH values.

We also recognize the pH values of natural drinking water from different geological locations may vary. Carbonation is an optional step that may or may not be used in adjusting the pH. Ultimately, the entity that is using the dolomite for remineralization will need to assess whether carbonation is appropriate and if carbonation is not used, the company will need to assess the processing parameters that are necessary to achieve the desired degree of remineralization such as changing the temperature or flow of the water through the dolomite.

- ***FDA Question #2a****: Minerals – a. Please clarify methodology used to determine levels of sulfur, silicon, potassium, manganese, and aluminum in the dolomite (Table 1). Also, please clarify the form of sulfur present in dolomite, which is listed as SO_3 in Table 1.*

Response to Question 2a: In Table 2 of the GRN 000806, Hogan Lovells provided all the analytical test methods used in establishing specifications for dolomite. The specifications are set in accordance with the European Standard NF EN 16003 ("Chemicals used for treatment of water intended for human consumption – Calcium magnesium carbonate") 1/

Table 1 of the GRN 000806 provides a typical composition of the dolomite, based on information provided by the supplier of the dolomite. The supplier conducted the testing for sulfur, silicon, potassium, manganese, and aluminum following the European Standard NF EN 12485 ("Chemicals used for treatment of water intended for human consumption – Calcium carbonate, high-calcium lime, half-burn dolomite, magnesium oxide and calcium magnesium carbonate"). In particular, the testing methods are listed below:

- Sulfur: ICP-OES
- Manganese: ICP-OES
- Silicon: AAS flame technique
- Aluminum: AAS flame technique
- Potassium: AAS flame technique

- ***FDA Question #2b****: We note that phosphorous is present in all standard dolomite materials identified by OFAS. How much phosphorous is in the GRN 000806 dolomite?*

Response to Question 2b: Based on the information provided by the supplier, the phosphorous level in dolomite is no more than 0.01% (weight %).

- ***FDA Question #2c***: *We note the availability of reference standards from different regions worldwide. What reference standard did you use to identify dolomite?*

Response to Question 2c: European Standard NF EN 16003 ("Chemicals used for treatment of water intended for human consumption – Calcium magnesium carbonate").

- ***FDA Question #3****: Please clarify the intended use of dolomite: Is it to enhance the mineral content of bottled water (per statement in section 1.4 Conditions of use) or is it to*

1/ See Tables 1, 2, and 3 of the NF EN 16003 (Attachment A).

enhance taste (per statement in section 2.6 Detailed information on intended use)? If it is to enhance the mineral content of bottled water, please comment on the increase of Ca and Mg over background intakes following use of this product. If it is to enhance taste as indicated on p. 7, please clarify intended use statement at the beginning of the notice. Additionally, if it is also used to alter water pH (as it has been used in some municipal water systems), please note this use.

Response to Question 3: As stated under Section 1.4 ("Conditions of Use") in GRN 000806, dolomite is intended to be used as a substitute for GRAS calcium and magnesium salts to enhance the mineral content of bottled water beverages. For example, FDA has a standard of identity for purified water that restricts the total dissolved solids that may be present in products labeled as "purified water." See, 21 CFR 165.110(a)(iv). When FDA issued the standard of identity, the agency recognized that many companies would add minerals to a purified water to enhance the taste of the water. The agency recognized in the preamble to the final regulation that such products should bear a statement of identity such as "purified water with minerals added for taste."

> The agency agrees with the comments that pointed out that if minerals are added to a bottled water or drinking water, an appropriate statement of identity must appear on the principal display panel of the label of the product to inform consumers of this fact (e.g., "drinking water with minerals added for taste").

60 Fed. Reg. 57076, 57081 (Nov. 13, 1995). The GRAS notification uses the terms "to enhance the mineral content" because the dolomite is being used to increase the mineral content of the water "to enhance the taste." In other words, dolomite helps improve the taste of the bottled water beverages by enhancing the mineral content of the water.

The dolomite is not being used to enhance calcium and magnesium intake over background levels. As discussed in the GRN 000806 the use of dolomite would be substitutional for other calcium and magnesium salts that today can be added to bottled water beverages for taste. As discussed in Section 6.1 of GRN 000806, many calcium and magnesium salts are already permitted for addition to bottled water beverages and other beverages. In particular, calcium carbonate, calcium oxide, magnesium carbonate, and magnesium oxide are currently authorized for addition to bottled water beverages with no limits other than GMPs. Further, some bottled water beverages on the market currently, particularly mineral waters, have much higher calcium and magnesium levels than the intended maximum levels of calcium (40 mg/L) and magnesium (25 mg/L) from the use of dolomite. Therefore, the intended use of dolomite would result in bottled water beverages with calcium and magnesium levels in line with those currently on the market and would not increase the background levels of the mineral intake.

With regard to your question about the use of dolomite to alter pH, the GRAS notification is not being submitted to cover these uses of dolomite. GRN 000806 is limited to the use of dolomite to enhance the mineral content of bottled water beverages such as purified waters to enhance the taste of the product.

- ***FDA Question #4****: In the notice, you discuss multiple food sources of calcium and magnesium and cite published estimates of total calcium and magnesium intakes from food and supplements in the U.S. You also note that ground waters and spring waters are frequently exposed to mineral formations of dolomite. However, your estimate of exposure to dolomite does not specifically address known current sources of dolomite in the diet, including dolomite dietary supplements and certain bottled waters sourced from regions where dolomite is present. We note that any existing uses of dolomite should be discussed in the context of total estimated exposure to dolomite for consumers in the US. This discussion might include a summary of current uses of dolomite and whether the intended uses are additive or substitutional for these uses of dolomite. If additive, the notice should include a statement that the total intake was considered in concluding that the ingredient is GRAS for its intended use.*

Response to Question 4: Dolomite can be found in dietary supplements in today's marketplace. According to the Dietary Supplement Label Database, which is maintained by the National Institutes of Health, there is one dolomite product listed – "Nature's Plus Natural Dolomite 44 Grain." On the "Supplement Facts" of the product label, it declares 633 mg calcium or 63% of the daily value and 360 mg magnesium or 90% of the daily value. We are not aware of other dietary supplements of dolomite or the use of dolomite in water treatment in the United States. As the agency noted, however, ground water or spring water that moves through dolomite layers would be expected to contain calcium or magnesium from dolomite.

We should have been more specific in the notification with regard to existing uses of dolomite and the fact that we considered these uses in our assessment. We recognize it is possible consumers could ingest dolomite via its use as a dietary supplement or through drinking ground water or spring water that comes in contact with dolomite. We intended to capture these background uses of dolomite in the discussion about consumer exposure to dietary sources of calcium and magnesium in Section 6.2.5. Specifically, we provided a reference to Bailey et. al (2011) that reported average total intakes from foods and supplements for all dietary sources of calcium and magnesium. Bailey et. al reported average magnesium intake to be 449 mg for men and 387 mg for women and average total intakes of calcium to be 1319 mg for men and 1331 mg for women. 2/ Because Bailey et. al reported total calcium and magnesium intake from all dietary sources, including dietary supplements of calcium and magnesium (regardless of source) and calcium and magnesium that could be found in foods and beverages, we considered this report to encompass any of the existing dietary exposures from dolomite as a dietary supplement or from water that came in contact with dolomite formations.

We recognize the intended use of dolomite to enhance bottled water beverages for calcium and magnesium intake could result in an increase in exposure to dolomite over exposures today for dolomite. We do not anticipate the use, however, would result in an increase in calcium or magnesium. We focused on the calcium and magnesium contributed by the dolomite because those are the minerals that are being dissolved into the bottled water beverages. Companies

2/ See Attachment B.

have the ability today to add other calcium and magnesium sources to bottled water beverages. We considered dolomite to be substitutional to the other calcium and mineral salts that are currently authorized for use. We did consider the total intake from dolomite, the calcium and magnesium levels that would be contributed to bottled water beverages from dolomite, and concluded the propose use of dolomite is GRAS.

- ***FDA Question #5****: Please provide FDA with a full reference for the 2011 review by IOM (page 19).*

Response to Question 5: A copy of the reference is attached as Attachment C.

- ***FDA Question #6****: On page 26 you state that that "…the studies demonstrate the levels of dolomite that would be needed to produce the calcium carbonate and magnesium carbonate, if consumed orally as dolomite, would not pose any human safety concern at a level of 353.3 mg/day (or 5.89 mg/kg bw/day)." Please explain how you arrived at the value of 353.3 mg/day. Please show calculations and provide reference for the study (or studies) based on which this value was calculated.*

Response to Question 6: We arrived at the values based on the maximum levels of calcium and magnesium that would be added to the bottled water beverages. The GRAS notification covers a maximum level of 40 mg/L calcium and 25 mg/L of magnesium ions that would be added to bottled water beverages. Based on the molecular weight of dolomite, 184 mg of dolomite/L is needed to produce 40 mg of calcium and 25 mg of magnesium. GRN 000806 covers the use of dolomite to bottled water beverages.

The average and 90th percentile intake for water is 841.46 and 1775 grams per day, respectively. The highest 90th percentile intake in subpopulation is among adolescences and adults > 8 years, we calculated the average and 90th percentile exposure to dolomite when added to water using the equations below in this subpopulation.

> Average EDI of solubilized dolomite = 184 mg/L x (888.52 g ÷ 1 g/mL) ÷ 1,000 mL/L = 163.5 mg/day
>
> 90th percentile EDI of solubilized dolomite = 184 mg/L x (1920 g ÷ 1 g/mL) ÷ 1,000 mL/L = 353.3 mg/day

These values and the calculations can be found prior to Table 6 in GRN 000860. We calculated the 5.89 mg/kg bw/day using 60 kg as the weight of an average adult in the U.S.

> 353.3 mg/day ÷ 60 kg = 5.89 mg/kg/day

GRN 000806 discussed a toxicity study in mice that found no significant toxicity in mouse with an oral dosage up to 1,500 mg/kg. The EDI of 5.89 mg/kg bw/day of dolomite is well below the 1,500 mg/kg bw in the mouse study. We, therefore, respectfully submit the intended use would not pose any human safety concern at the intended use level of 5.89 mg/kg bw/day.

- ***FDA Question #7****: This notice is a resubmission for GRN 000696. In GRN 000696 Hogan Lovells states "…the studies demonstrate the levels of dolomite that would be needed to produce the calcium carbonate and magnesium carbonate, if consumed orally as dolomite, would not pose any human safety concern at a level of 901.32 mg/day (or 15.02 mg/kg bw/day)." Please explain why this value changed from 901.32 mg/day to 353.3 mg/day even though you basically discuss the same studies in both notices.*

Response to Question 7: When we resubmitted GRN we decreased the maximum intended use of dolomite that would be added to bottled water beverages. GRN 000696 covered the use of 90.16 mg/L calcium and 55 mg/L magnesium while GRN 000806 covers a maximum level of calcium of 40 mg/L and magnesium of 25 mg/L. In addition, we used different sources when calculating the average and 90th percentile exposures to water. In GRN 000696 we relied on data published by EPA while in GRN 000806 we used NHANES data for calculating the average and 90th percentile exposures for water. The differences in the value are explained by the lower maximum intended use and the different sources for calculating the 90th percentile level for water.

- ***FDA Question #8****: To further support your safety conclusion, please briefly discuss the following study: 90-day oral toxicity study in rats by A. Lagarto, J. Tillán, V. Bueno, J. Rodríguez, M. Paz, Y. Cabrera, et al. Estudio toxicológico del Calcidol, un suplemento nutricional de calcio y magnesio. Rev Toxicol, 19 (2002), pp. 35-40. Additionally, please provide FDA with a certified translation of the above article.*

Response to Question 8: In this study, acute toxicity of dolomite was evaluated using the limit test at the dose of 2,000 mg/kg in Wistar rats of both sexes. Oral mucous irritation was determined by an acute test and after repeated doses in hamster males. Oral subchronic toxicity was evaluated in Wistar rats for 90 days with three doses: 1,280, 2,560, and 5,000 mg/kg/day. The study concluded that the acute administration of dolomite in rats was neither lethal, nor did it cause toxic manifestations. The highest dose of 5,000 mg/kg/day used in the chronic study showed no significant toxic effects, with a normal weight increase, food consumption, and the absence of toxic symptoms or mortality. The authors also noted an increase in urine pH, a physiological hyper-cellularity of thyroid cells, and histopathological disorders in the kidney, indicate the need for keeping special vigilance on these target organs in future studies. The findings are in line with the GRN 000806 and do not impact our conclusion that a consumption level of 5.89 mg/kg/day would not pose any human safety concern.

A certified translation of the article is provided as Attachment D.

- ***FDA Question #9****: EFSA recently reviewed the safety of dolomite (reference: Panel, E. F. (2016). Scientific opinion on the safety and efficacy of a natural mixture of dolomite plus magnesite and magnesium-phyllosilicates (Fluidol) as feed additive for all animal species. EFSA Journal, 14(1), 4341.).*
    a. *Please briefly discuss the findings of the 42-day piglet study found in this publication. Please calculate approximate dose levels in mg/kg bw/day and state what the no-observed-adverse-effect-level (NOAEL), if any exists.*

b. *Please briefly discuss the findings of the in vivo mouse micronucleus test found in this publication.*

Response to Question 9: We note the product evaluated in the 2016 EFSA review is a natural mixture of dolomite, magnesite, and magnesium-phyllosilicates (talc and chlorite), subsequently referred to as MDMM. According to the 2016 EFSA review, a total of 96 male piglets of about 26 days of age was fed pelleted diets supplemented with 0, 20,000 or 100,000 mg MDMM/kg for 42 days. At the end of the experiment, a blood sample was taken from two piglets per pen for haematology and clinical chemistry. No mortality occurred. Final body weight of the control was 30.7 kg and average daily weight gain was 511 g, both not being significantly different from the two MDMM treated groups. Among the blood biochemical parameters, differences between groups were seen for serum phosphorus, for AP, ALT and for β-globulins. They were not treatment related. Haematology did not show differences between the groups except the relative white blood cell differentials, which were considered minor and not treatment related differences. In total, there was evidence that 100,000 mg MDMM/kg feed was tolerated by piglets. The NOAEL from this study would be 100,000 mg/kg.

For the *in vivo* mouse micronucleus, five male and five female Swiss albino mice were used per experimental group. Animals were treated orally (by gavage) with the limit dose of 2,000 mg/kg body weight using two treatments separated by 24 hours. Toxicity to bone marrow (as indicated by the polychromatic to total erythrocytes ratio) was not seen in the group treated with the additive, therefore, there was no evidence of target exposure. There was no increase in the number of micronucleated polychromatic erythrocytes seen in the bone marrow of the additive-treated group. The positive control group responded as expected. The finding of this *in vivo* mouse micronucleus test is consistent with discussion in Section 6.2.3 of GRN 000806 and demonstrated the chemical is not mutagenic.

* * *

In addition to our above specific responses to each of the agency's questions, we also reviewed the agency's general comments for the GRN 000806. As the agency did not raise any specific questions in those general comments, in this letter, we focused on the FDA questions regarding GRN 000806. If any additional questions arise in the course of your review, please contact us, preferably by telephone or e-mail, so that we can provide a prompt response.

Sincerely,

(b) (6)

Martin J. Hahn
Partner
Hogan Lovells US LLP
martin.hahn@hoganlovells.com
202 637 5926

1165 pages have been removed in accordance with copyright laws. The removed reference citations can be found in Part 7.0 List of Supporting Data and Information.

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Via Electronic Mail

February 14, 2019

Denis N. Wafula
Denis.Wafula@fda.hhs.gov
Office of Food Additive Safety (HFS–200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835

Re: Response to FDA's Additional Questions for GRN 000806

Dear Mr. Wafula,

We hereby submit our responses to FDA's additional questions for GRN 000806 we received on February 7, 2019. For your ease of reference, we first copied FDA's question below, followed by each of our response:

> ***FDA Question #1****: The notifier missed answering the last section of Question 2a (in bold font below). The question stated; 'Please clarify methodology used to determine levels of sulfur, silicon, potassium, manganese, and aluminum in the dolomite (Table 1).* ***Also, please clarify the form of sulfur present in dolomite, which is listed as SO_3 in Table 1****.'*
>
> *In their response, the notifier states that the supplier of the dolomite conducted the testing for sulfur among other elements by following the European Standard NF EN 12485 ("Chemicals used for treatment of water intended for human consumption – Calcium carbonate, high-calcium lime, half-burn dolomite, magnesium oxide and calcium magnesium carbonate"). We note that in NF EN 12485, sulfur is analyzed as sulfate (SO_4^-) and not as sulfur trioxide (SO_3). Please comment on the discrepancy.*

Response to Question 1: We should have identified sulfate, which is the form of sulfur present in dolomite. We apologize for any confusion caused by the discrepancy between the actual form of sulfur in dolomite and the constituent form reported in Table 1. Modern and ancient sedimentary carbonate minerals (calcite, aragonite and dolomite) generally contain sulfate as a trace constituent. *See* Staudt, Wilfried J., and Martin AA Schoonen. "Sulfate incorporation into sedimentary carbonates." ACS Symposium Series. Vol. 612. Washington, DC: American Chemical Society,[1974]-, 1995. We hereby clarify that the form of sulfur present in the dolomite is sulfate, which is also tested under the method described in NF EN 12485.

In Table 1 of the GRAS notice, the typical quantitative composition of dolomite was provided and the sulfate levels (described as SO_3) is reported as 0.04-0.06%. SO_3, instead of sulfate (SO_4), was listed as the constituents for the ease of comparison when calcium was listed as "$CaCO_3$, CaO, Ca" and magnesium was listed as "$MgCO_3$, MgO, and Mg." Again, we apologize for any confusion caused by the discrepancy between the actual form of sulfur in dolomite and the constituent form reported in Table 1.

> ***FDA Question #2****: Please specify what the NOAEL of 100,000 mg MDMM/kg feed is in units of mg/kg body weight/day in the piglet study.*

Response to Question 2: The initial body weight of the piglet was 8.3 kg with an average daily weight gain of 511 g to a 30.7 kg final body weight. The feed-to-gain of the groups receiving 100,000 mg MDMM/kg was 1.46. As such, the average feed amount consumed by piglet was 511 g x1.46 = 746.06 g. This translates to 74.61 g MDMM per day. Using the final body weight, which would give us a lower NOAEL than using the initial body weight, the conservative NOAEL on a body weight basis can be calculated as 74.61 g MDMM x 1,000 mg/kg / 30.7kg = 2430.3 mg/kg body weight/day.

* * *

We trust our answers are responsive. If any additional questions arise in the course of your review, please contact us, preferably by telephone or e-mail, so that we can provide a prompt response.

Sincerely,

(b) (6)

Martin J. Hahn
Partner
Hogan Lovells US LLP
martin.hahn@hoganlovells.com
202 637 5926

From: Hahn, Martin J.
To: Wafula, Denis
Cc: Tao, Xin
Subject: RE: Extension of Review timeframe for GRAS Notice GRN000806 (Dolomite)
Date: Monday, April 15, 2019 10:55:37 AM

Denis:

Thank you for the information. We look forward to receiving the agency response.

Martin Hahn
Partner

Hogan Lovells US LLP
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Direct: +1 202 637 5926
Fax: +1 202 637 5910
Email: martin.hahn@hoganlovells.com
www.hoganlovells.com

From: Wafula, Denis [mailto:Denis.Wafula@fda.hhs.gov]
Sent: Monday, April 15, 2019 10:32 AM
To: Hahn, Martin J.
Subject: Extension of Review timeframe for GRAS Notice GRN000806 (Dolomite)

Hello Mr. Hahn,
This email is to inform you that, in accordance with 21 CFR 170.265 (b)(2), FDA is extending the normal 180-day review timeframe by 90 days for GRN 000806 (Dolomite).
We are finalizing the response and I hope you will get it soon. Do not hesitate to call or email me if you have any questions.
Regards,
Denis

From: Wafula, Denis
Sent: Friday, February 15, 2019 9:27 AM
To: 'Tao, Xin' <xin.tao@hoganlovells.com>
Cc: Hahn, Martin J. <martin.hahn@hoganlovells.com>
Subject: RE: Reviewers comments and questions for GRAS Notice 000806 (Dolomite)

Hello Xin,
Thanks for the quick reply, I will pass them on to the reviewer. But, a cursory glance makes me think

the answers are ok.
Best Regards,
Denis

From: Tao, Xin <xin.tao@hoganlovells.com>
Sent: Thursday, February 14, 2019 4:28 PM
To: Wafula, Denis <Denis.Wafula@fda.hhs.gov>
Cc: Hahn, Martin J. <martin.hahn@hoganlovells.com>
Subject: RE: Reviewers comments and questions for GRAS Notice 000806 (Dolomite)

Denis,

Please find our response to the agency's additional questions attached.

Best regards,

Xin Tao
Senior Associate

Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004

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Direct: +1 202 637 6986
Mobile +1 979-422-7860
Fax: +1 202 637 5910
Email: xin.tao@hoganlovells.com
www.hoganlovells.com

From: Wafula, Denis [mailto:Denis.Wafula@fda.hhs.gov]
Sent: Thursday, February 07, 2019 10:21 AM
To: Tao, Xin
Cc: Hahn, Martin J.
Subject: Reviewers comments and questions for GRAS Notice 000806 (Dolomite)

Hello Martin and Xin,
Thanks for your response to our last batch of questions. Find attached 2 questions/comments from the reviewers that need your attention. Please provide responses to the questions within the next 10 business days. If it is not possible to do so or you need help with the questions, please feel free to contact me.
Best Regards,
Denis

From: Tao, Xin <xin.tao@hoganlovells.com>
Sent: Tuesday, December 11, 2018 10:47 AM
To: Wafula, Denis <Denis.Wafula@fda.hhs.gov>

Cc: Hahn, Martin J. <martin.hahn@hoganlovells.com>
Subject: RE: Reviewers comments and questions for GRAS Notice 000806 (Dolomite) Part 1/2

Denis,

Please attached our response to the agency reviewers' questions for GRN 000806. Due to the size limitations, we will send you the Attachment C in a separate e-mail.

If any additional questions arise in the course of the agency's review, please contact us, preferably by telephone or e-mail, so that we can provide a prompt response.

Best regards,
Martin & Xin

Xin Tao
Senior Associate

Hogan Lovells US LLP
Columbia Square
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Direct: +1 202 637 6986
Mobile +1 979-422-7860
Fax: +1 202 637 5910
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From: "Wafula, Denis" <Denis.Wafula@fda.hhs.gov>
Date: November 23, 2018 at 2:02:05 PM EST
To: "Hahn, Martin J." <martin.hahn@hoganlovells.com>
Subject: Reviewers comments and questions for GRAS Notice 000806 (Dolomite)

Dear Mr. Hahn,
Find attached the reviewers' questions and comments for GRAS Notice 000806 that you submitted to FDA. If you have any questions or you need any further clarification/information about the contents of the attachment please feel free to contact me and I will be glad to help.
Best Regards,
Denis

From: Hahn, Martin J. <martin.hahn@hoganlovells.com>
Sent: Tuesday, September 18, 2018 11:02 AM
To: Wafula, Denis <Denis.Wafula@fda.hhs.gov>
Subject: RE: GRAS Notice 000806 (Dolomite)

No problem. We will use this version of the document.

Martin Hahn
Partner

Hogan Lovells US LLP
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Washington, DC 20004

Tel: +1 202 637 5600
Direct: +1 202 637 5926
Fax: +1 202 637 5910
Email: martin.hahn@hoganlovells.com
www.hoganlovells.com

From: Wafula, Denis [mailto:Denis.Wafula@fda.hhs.gov]
Sent: Tuesday, September 18, 2018 11:01 AM
To: Hahn, Martin J.
Subject: RE: GRAS Notice 000806 (Dolomite)

Dear Mr. Hahn,
The document should have been titled 'GRN 806' instead of 'FCN 806'. Attached is correctly labelled document. The information contained in the documents does not change.
Best Regards,
Denis

From: Wafula, Denis
Sent: Tuesday, September 18, 2018 10:53 AM
To: 'martin.hahn@hoganlovells.com' <martin.hahn@hoganlovells.com>
Subject: GRAS Notice 000806 (Dolomite)

Dear Mr. Hahn,
Find attached the filing letter for GRAS Notice 000806 that you submitted to FDA. If you have any questions, do not hesitate to contact us.
Best Regards,

Denis

Denis Wafula, Ph.D.
Staff Fellow
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
U.S. Food and Drug Administration
Office: 2404021314
denis.wafula@fda.hhs.gov

From: Hahn, Martin J.
To: Wafula, Denis
Subject: RE: Response Letter for GRAS Notice 000806 (Dolomite)
Date: Friday, May 17, 2019 3:13:59 PM
Attachments: image003.png

Denis:

Many thanks for the letter. We appreciate the time and the attention the agency has given to this submission. We hope you have a great weekend.

Martin Hahn
Partner

Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004

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Direct: +1 202 637 5926
Fax: +1 202 637 5910
Email: martin.hahn@hoganlovells.com
www.hoganlovells.com

From: Wafula, Denis [mailto:Denis.Wafula@fda.hhs.gov]
Sent: Friday, May 17, 2019 2:38 PM
To: Hahn, Martin J.
Subject: Response Letter for GRAS Notice 000806 (Dolomite)

Hello Mr. Hahn,
Find attached the Response Letter to GRN 000806. Please review the letter and if you have any questions let me know.
Best Regards,
Denis

Denis Wafula, Ph.D.
Staff Fellow
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
U.S. Food and Drug Administration
Office: 2404021314
denis.wafula@fda.hhs.gov

From: Tao, Xin <xin.tao@hoganlovells.com>
Sent: Thursday, February 14, 2019 4:28 PM
To: Wafula, Denis <Denis.Wafula@fda.hhs.gov>
Cc: Hahn, Martin J. <martin.hahn@hoganlovells.com>
Subject: RE: Reviewers comments and questions for GRAS Notice 000806 (Dolomite)

Denis,

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Best regards,

Xin Tao
Senior Associate

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Best Regards,
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Sent: Tuesday, December 11, 2018 10:47 AM
To: Wafula, Denis <Denis.Wafula@fda.hhs.gov>
Cc: Hahn, Martin J. <martin.hahn@hoganlovells.com>
Subject: RE: Reviewers comments and questions for GRAS Notice 000806 (Dolomite) Part 1/2

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Best regards,
Martin & Xin

Xin Tao
Senior Associate

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From: "Wafula, Denis" <Denis.Wafula@fda.hhs.gov>
Date: November 23, 2018 at 2:02:05 PM EST
To: "Hahn, Martin J." <martin.hahn@hoganlovells.com>
Subject: Reviewers comments and questions for GRAS Notice 000806 (Dolomite)

Dear Mr. Hahn,
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Best Regards,
Denis

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Sent: Tuesday, September 18, 2018 11:02 AM

To: Wafula, Denis <Denis.Wafula@fda.hhs.gov>
Subject: RE: GRAS Notice 000806 (Dolomite)

No problem. We will use this version of the document.

Martin Hahn
Partner

Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004

Tel: +1 202 637 5600
Direct: +1 202 637 5926
Fax: +1 202 637 5910
Email: martin.hahn@hoganlovells.com
www.hoganlovells.com

From: Wafula, Denis [mailto:Denis.Wafula@fda.hhs.gov]
Sent: Tuesday, September 18, 2018 11:01 AM
To: Hahn, Martin J.
Subject: RE: GRAS Notice 000806 (Dolomite)

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Best Regards,
Denis

From: Wafula, Denis
Sent: Tuesday, September 18, 2018 10:53 AM
To: 'martin.hahn@hoganlovells.com' <martin.hahn@hoganlovells.com>
Subject: GRAS Notice 000806 (Dolomite)

Dear Mr. Hahn,
Find attached the filing letter for GRAS Notice 000806 that you submitted to FDA. If you have any questions, do not hesitate to contact us.
Best Regards,
Denis

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