Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004
T +1 202 637 5600
F +1 202 637 5910
www.hoganlovells.com

#696

By FedEx

March 23, 2017

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 respectfully submit the enclosed GRAS notice for the dolomite for use as a substitute for GRAS calcium and magnesium salts to enhance the mineral content of purified bottle water. In accordance with the Agency's guidelines, we have enclosed Form 3667, one original copy of the GRAS notice and one complete electronic copy of the GRAS notice on a compact disk (CD).

We are committed to cooperating with the Agency and believe an open dialog is one of the most effective ways to accomplish that objective. We trust that you will find the information provided in the enclosed GRAS notice supports the safety of the requested use of the dolomite. 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.

If you have any questions, please contact us.

Sincerely,

(b) (6)

Martin J. Hahn
Partner
martin.hahn@hoganlovells.com
202 637 5926

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

GENERALLY RECOGNIZED AS SAFE *(GRAS)* NOTICE (Subpart E of Part 170)

Form Approved: OMB No. 0910-0342; Expiration Date: 09/30/2019
(See last page for OMB Statement)

FDA USE ONLY

GRN NUMBER	DATE OF RECEIPT
000646	
ESTIMATED DAILY INTAKE	INTENDED USE FOR INTERNET
NAME FOR INTERNET	
KEYWORDS	

RECEIVED
MAR 28 2017
OFFICE OF FOOD ADDITIVE SAFETY

Transmit completed form and attachments electronically via the Electronic Submission Gateway *(see Instructions)*; OR Transmit completed form and attachments in paper format or on physical media to: 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.

SECTION A – INTRODUCTORY INFORMATION ABOUT THE SUBMISSION

1. Type of Submission *(Check one)*
   ☒ New ☐ Amendment to GRN No. _____ ☐ Supplement to GRN No. _____

2. ☒ All electronic files included in this submission have been checked and found to be virus free. *(Check box to verify)*

3 Most recent presubmission meeting *(if any)* with FDA on the subject substance *(yyyy/mm/dd)*: _____

4 For Amendments or Supplements: Is your amendment or supplement submitted in response to a communication from FDA? *(Check one)* ☐ Yes ☐ No If yes, enter the date of communication *(yyyy/mm/dd)*: _____

SECTION B – INFORMATION ABOUT THE NOTIFIER

1a. Notifier

Name of Contact Person	Position or Title
Martin J. Hahn	Partner

Organization *(if applicable)*: Hogan Lovells US LLP

Mailing Address *(number and street)*: 555 Thirteenth Street, NW

City	State or Province	Zip Code/Postal Code	Country
Washington	DC	20004	

Telephone Number	Fax Number	E-Mail Address
2026375926	2026375910	martin.hahn@hoganlovells.com

1b. Agent or Attorney *(if applicable)*

Name of Contact Person	Position or Title

Organization *(if applicable)*:

Mailing Address *(number and street)*:

City	State or Province	Zip Code/Postal Code	Country

Telephone Number	Fax Number	E-Mail Address

SECTION C – GENERAL ADMINISTRATIVE INFORMATION

1. Name of notified substance, using an appropriately descriptive term

Dolomite

2. Submission Format: *(Check appropriate box(es))*

☐ Electronic Submission Gateway

☒ Paper

☒ Electronic files on physical media

If applicable give number and type of physical media

3. For paper submissions only:

Number of volumes _____

Total number of pages _____

4. Does this submission incorporate any information in CFSAN's files? *(Check one)*

☐ Yes *(Proceed to Item 5)* ☒ No *(Proceed to Item 6)*

5. The submission incorporates information from a previous submission to FDA as indicated below *(Check all that apply)*

☐ a) GRAS Notice No. GRN _____

☐ b) GRAS Affirmation Petition No. GRP _____

☐ c) Food Additive Petition No. FAP _____

☐ d) Food Master File No. FMF _____

☐ e) Other or Additional *(describe or enter information as above)* _____

6. Statutory basis for conclusions of GRAS status *(Check one)*

☒ Scientific procedures *(21 CFR 170.30(a) and (b))* ☐ Experience based on common use in food *(21 CFR 170.30(a) and (c))*

7. Does the submission (including information that you are incorporating) contain information that you view as trade secret or as confidential commercial or financial information? (see 21 CFR 170.225(c)(8))

☐ Yes *(Proceed to Item 8*

☒ No *(Proceed to Section D)*

8. Have you designated information in your submission that you view as trade secret or as confidential commercial or financial information *(Check all that apply)*

☐ Yes, information is designated at the place where it occurs in the submission

☐ No

9. Have you attached a redacted copy of some or all of the submission? *(Check one)*

☐ Yes, a redacted copy of the complete submission

☐ Yes, a redacted copy of part(s) of the submission

☐ No

SECTION D – INTENDED USE

1. Describe the intended conditions of use of the notified substance, including the foods in which the substance will be used, the levels of use in such foods, and the purposes for which the substance will be used, including, when appropriate, a description of a subpopulation expected to consume the notified substance.

Dolomite is intended to be used as a substitute for GRAS calcium and magnesium salts to enhance the mineral content of purified bottle water. The maximum target composition of the remineralized water is 90.16 mg/L (ppm) of calcium ions and 55 mg/L (ppm) of magnesium ions.

2. Does the intended use of the notified substance include any use in product(s) subject to regulation by the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☒ No

3. If your submission contains trade secrets, do you authorize FDA to provide this information to the Food Safety and Inspection Service of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☐ No , you ask us to exclude trade secrets from the information FDA will send to FSIS.

SECTION E – PARTS 2 -7 OF YOUR GRAS NOTICE

(check list to help ensure your submission is complete – PART 1 is addressed in other sections of this form)

☒ PART 2 of a GRAS notice: Identity, method of manufacture, specifications, and physical or technical effect (170.230).

☒ PART 3 of a GRAS notice: Dietary exposure (170.235).

☒ PART 4 of a GRAS notice: Self-limiting levels of use (170.240).

☒ PART 5 of a GRAS notice: Experience based on common use in foods before 1958 (170.245).

☒ PART 6 of a GRAS notice: Narrative (170.250).

☒ PART 7 of a GRAS notice: List of supporting data and information in your GRAS notice (170.255)

Other Information

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

☐ Yes ☒ No

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

☐ Yes ☐ No

SECTION F – SIGNATURE AND CERTIFICATION STATEMENTS

1. The undersigned is informing FDA that Hogan Lovells US LLP

(name of notifier)

has concluded that the intended use(s) of Dolomite

(name of notified substance)

described on this form, as discussed in the attached notice, is (are) not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on your conclusion that the substance is generally recognized as safe recognized as safe under the conditions of its intended use in accordance with § 170.30.

2. Hogan Lovells US LLP *(name of notifier)* agrees to make the data and information that are the basis for the conclusion of GRAS status available to FDA if FDA asks to see them; agrees to allow FDA to review and copy these data and information during customary business hours at the following location if FDA asks to do so; agrees to send these data and information to FDA if FDA asks to do so.

555 Thirteenth Street, NW Washington, DC 20004

(address of notifier or other location)

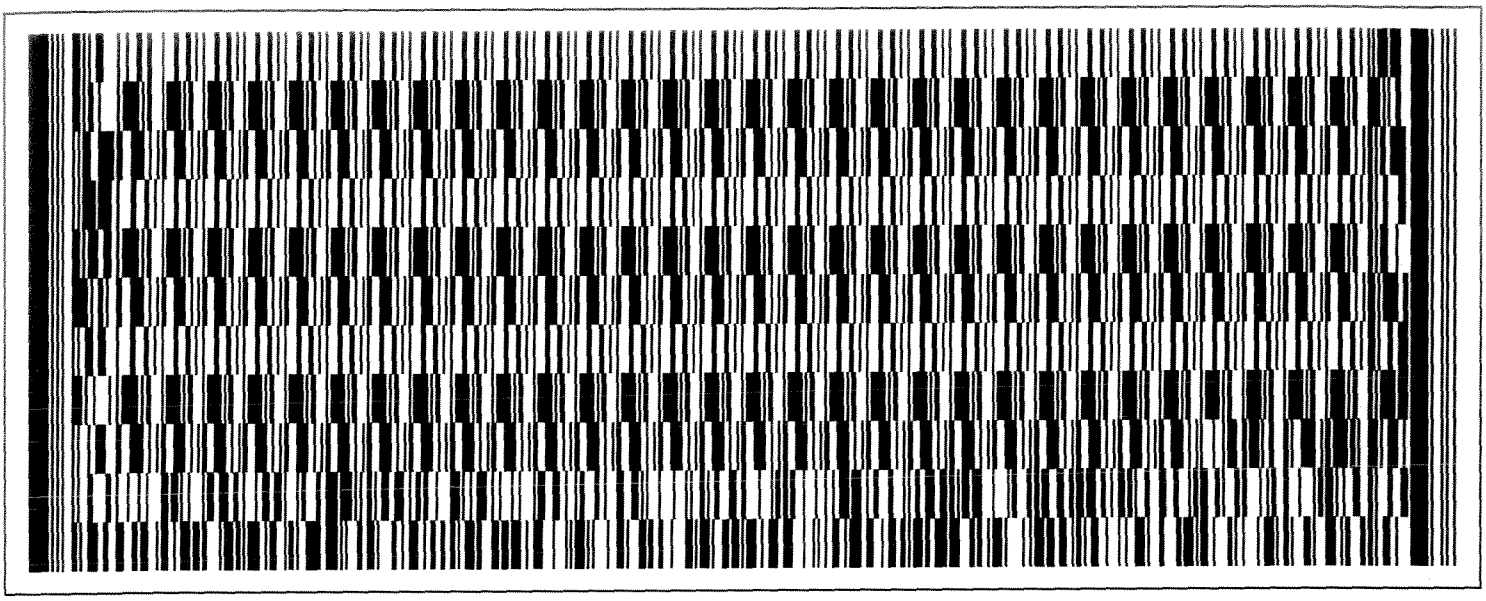
The notifying party certifies that this GRAS notice is a complete, representative, and balanced submission that includes unfavorable, as well as favorable information, pertinent to the evaluation of the safety and GRAS status of the use of the substance.The notifying party certifies that the information provided herein is accurate and complete to the best or his/her knowledge. Any knowing and willful misinterpretation is subject to criminal penalty pursuant to 18 U.S.C. 1001.

3. Signature of Responsible Official, Agent, or Attorney	Printed Name and Title	Date (mm/dd/yyyy)
[redacted]	Martin J. Hahn; Partner	03/23/2017

SECTION G – LIST OF ATTACHMENTS

List your attached files or documents containing your submission, forms, amendments or supplements, and other pertinent information. Clearly identify the attachment with appropriate descriptive file names (or titles for paper documents), preferably as suggested in the guidance associated with this form. Number your attachments consecutively. When submitting paper documents, enter the inclusive page numbers of each portion of the document below.

Attachment Number	Attachment Name	Folder Location (select from menu) (Page Number(s) for paper Copy Only)



#696

GRAS Notice for Dolomite

March 23rd, 2017

Table of Contents

1.0 GRAS Statements and Certification

1.1 Claim of Exemption

Hogan Lovells US LLP (Hogan) is submitting this GRAS notice for its conclusion that dolomite is generally recognized as safe (GRAS) when used as a source of calcium and mineral 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 bottle water. The maximum target composition of the remineralized water is 90.16 mg/L (ppm) of calcium ions and 55 mg/L (ppm) of magnesium ions.

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
martin.hahn@hoganlovells.com
202 637 5926
(b) (6)

_____

Xin Tao
Associate
Hogan Lovells US LLP
xin.tao@hoganlovells.com
202 637 6986

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. Dolomite is also known as, dolomitic limestone, magnesian limestone, or dolostone. Raw dolomite material will be used for the remineralization of bottled purified 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. Quantitative Composition of Dolomite				
$CaMg(CO_3)_2$		% weight on dry solid	min.	98.50%
Calcium	Ca, as $CaCO_3$	% weight on dry solid	min.	54.50%
	Ca, as CaO*	% weight on dry solid	min.	30.50%
	Ca, as Ca	% weight on dry solid	min.	21.82%
Magnesium	Mg, as $MgCO_3$	% weight on dry solid	min.	44.00%
	Mg, as MgO*	% weight on dry solid	min.	21.00%
	Mg, as Mg	% weight on dry solid	min.	12.68%
*Calcium and magnesium oxide levels are also measured in dolomite to more accurately quantify the mineral levels through analytical procedures.				

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 raw material is tested to make certain it complies with the specifications for heavy metals. The dolomite will be packaged and stored under dry/ambient conditions.

Dolomite is prepared under current Good Manufacturing Practices (cGMP) using food-grade raw materials where available or otherwise using materials of suitable purity and quality for their intended use.

2.5 Specifications

Table 2. Heavy Metal Impurities Specifications				
Antimony	Sb	mg/kg of commercial product	max.	3
Arsenic	As	mg/kg of commercial product	max.	3
Cadmium	Cd	mg/kg of commercial product	max.	2
Chromium	Cr	mg/kg of commercial product	max.	10
Lead	Pb	mg/kg of commercial product	max.	10
Mercury	Hg	mg/kg of commercial product	max.	0.5
Nickel	Ni	mg/kg of commercial product	max.	10
Selenium	Se	mg/kg of commercial product	max.	3

2.6 Detailed Information on Intended Use

Dolomite is intended to be used as a substitute for GRAS calcium and magnesium salts. Dolomite provides a source of calcium carbonate, which has been affirmed as GRAS by FDA with no limitation other than good manufacturing practices (21 CFR 184.1191) and magnesium carbonate, which is affirmed as GRAS as a nutrient supplement with no limitation other than GMPs (21 CFR 184.1425), dolomite will be used as a source of these magnesium and calcium salts to enhance the levels of calcium, magnesium, and carbonate in the water as a nutrient supplement that improves the taste of the purified water.

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;
- The water passes through a bed of dolomite and solubilizes some mineral salts (the flow rate is controlled to reach the desired concentration of magnesium and calcium salts in the water); and
- The dolomite enhanced water is filtered to remove fine particles.

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 added to 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 composition of remineralized water is 90.16 mg/L of calcium and 55 mg/L magnesium. A pilot test with a target of 20 mg/L of calcium and 12.2 mg/L magnesium was conducted with dolomite and the calcium, magnesium, bicarbonate and other ion levels added to the purified water are reported as follows:

Table 3. Constituents Added to Purified Water by Dissolution of Dolomite

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

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. The analysis also found very low levels of other mineral 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).

The heavy metal levels in the remineralized water are reported as follows:

Table 4. Heavy Metal Levels In Remineralized Water

Constituents	Levels	Unit
Antimony	<1.0	µg/L
Arsenic	<0.5	µg/L

Cadmium	<0.25	µg/L
Chromium	<1.0	µg/L
Lead	<1.0	µg/L
Nickel	<1.0	µg/L
Selenium	<0.25	µg/L

3.0 Dietary Exposure

The average and 90th percentile intake for bottled water can be determined from a database maintained by the U.S. Environmental Protection Agency (EPA). EPA's What We Eat in America - Food Commodity Intake Database, 2005-2010 (WWEIA-FCID 2005-10) reports intake for bottled water in the food category, "water, direct bottled." Specifically, EPA reports consumption by the general population in the U.S. of 992.28 g/person by average and 2073.75 g/person at the 90th percentile. The consumption of bottled water in different age groups can be further summarized in the table below.

Table 5. Bottled Water Consumption

Age Group	Average Consumption	90th Percentile
Children 1 Through 3 Years of Age	325.65 g/person	681.38 g/person
Children 4 Through 8 Years of Age	472.76 g/person	1,000 g/person
Adolescents and Adults > 8 Years	1054 g/person	2,133 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 90.16 mg/L calcium ions and 55 mg/L magnesium ions to all the purified water products it markets, which corresponds to 422.56 mg/L dolomite
- Purified water beverages remineralized by dolomite have a 100% market share in the U.S.
- An average consumer drinks 992.27 g bottled water per day, and the 90th percentile consumers drink 2073.75 g bottled water per day
- Bottled water has a density of 1 g/mL

Average EDI of calcium = 90.16 mg/L x (992.27 g ÷ 1 g/mL) ÷ 1,000 mL/L = 89.5 mg/day

90th percentile EDI of calcium = 90.16 mg/L x (2073.75 g ÷ 1 g/mL) ÷ 1,000 mL/L = 187 mg/day

Average EDI of magnesium = 55 mg/L x (992.27 g ÷ 1 g/mL) ÷ 1,000 mL/L = 54.6 mg/day

90th percentile EDI of magnesium = 55 mg/L x (2073.75 g ÷ 1 g/mL) ÷ 1,000 mL/L = 114.1 mg/day

Average EDI of dolomite = 422.56 mg/L x (992.27 g ÷ 1 g/mL) ÷ 1,000 mL/L = 419.3 mg/day

90^{th} percentile EDI of dolomite = 422.56 mg/L x (2073.75 g ÷ 1 g/mL) ÷ 1,000 mL/L = 876.3 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	90^{th} Percentile EDI	Reference Daily Intake (Adults and Children ⩾4 years)
Calcium	89.5 mg/day	187 mg/day	1,300 mg
Magnesium	54.6 mg/day	114.1 mg/day	420 mg
Dolomite	419.3 mg/day	876.3 mg/day	N/A

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	90^{th} Percentile EDI
Children 1 Through 3 Years of Age	Calcium	29.36 mg/day	61.43 mg/day
	Magnesium	17.91 mg/day	37.45 mg/day
	Dolomite	137.61 mg/day	287.92 mg/day
Children 4 Through 8 Years of Age	Calcium	42.62 mg/day	90.16 mg/day
	Magnesium	26 mg/day	55 mg/day
	Dolomite	199.77 mg/day	422.56 mg/day
Adolescents and	Calcium	95.03 mg/day	192.31 mg/day

Adults > 8 Years	Magnesium	57.97 mg/day	117.32 mg/day
	Dolomite	445.38 mg/day	901.32 mg/day

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 a 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. Because it 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 carbonate")) and magnesium carbonate (affirmed as GRAS in 21 CFR §184.1425 ("Magnesium carbonate")). Calcium carbonate is affirmed as GRAS with no limitations other than GMPs and magnesium carbonate is affirmed as a GRAS nutrient supplement (amongst other uses) with no limitations other than GMPs. Both calcium carbonate and magnesium carbonate could be used as a nutrient source of calcium and magnesium added to bottled waters today. The proposed use of dolomite would not increase dietary exposures over the current authorized uses for these mineral salts.

The individual salts are GRAS with no limitations other than GMPs so this proposed use will not drive up exposures — because the existing salts are approved for this use.

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 EPA's What We Eat in America - Food Commodity Intake Database, 2005-2010. 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 injected with minor amounts of carbon dioxide, 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. 1/ Adequate calcium is needed for adequate mineralization and maintenance of growing bones. 2/ 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. 3/ 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. 4/ Assuming that 192.31 mg/day calcium is provided by the intended use of dolomite, the highest amount of calcium ingested by 90th percentile consumers in different age groups through the consumption of purified water would be less than 20% of the daily value (DV) of 1,300 mg calcium. 5/

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 hypercalcemia can cause renal insufficiency, vascular and soft tissue calcification, hypercalciuria (high levels of calcium in the urine) and kidney stones. 6/ 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.)7 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."

1/ 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.
2/ SarDesai, Vishwanath. *Introduction to clinical nutrition*. CRC Press, 2011.
3/ 2015 Dietary Guidelines Advisory Committee (DGAC) Scientific Report.
4/ *See id*.
5/ 192.31 mg ÷ 1,300 mg x 100% = 14.79% < 20%.
6/ 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.
7 *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.

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."8

- **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. 9/ 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 without any adverse effects. 10/ 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. 11/

- **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. 12/ In particular, the subjects were randomly assigned to receive

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

9/ 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).

10/ *See id*.

11/ *See id*.

12/ 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.

a placebo or 1,000 mg of elemental calcium. 13/ 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. 14/ 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. 15/ 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 cancer risk in a case-control study of 197 cases. 16/ The authors found a twofold increased risk of prostate cancer associated with an increased intake of dairy products. 17/ The authors also found the calcium showed a borderline association with prostate cancer risk, with slightly higher risk for higher calcium intake. 18/ 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. 19/ 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. 20/ The subjects were followed for up to 12 years and asked periodically to report new cancer diagnoses. 21/ 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. 22/ 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.

13/ *See id*.
14/ *See id*.
15/ *See id*.
16/ 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.
17/ *See id*.
18/ *See id*.
19/ 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.
20/ *See id*.
21/ *See id*.
22/ *See id*.

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 8. 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	
Adults 51 Through 70 Years of Age	2,000 mg/day
Adults > 70 Years of Age	

Calcium Safety Conclusion

While excessive calcium intake above 2,500 mg/day 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 carbonate that is currently authorized for use in food with no limitations other than GMPs. The proposed use of dolomite, therefore, would not increase dietary exposure to its main component calcium. Further, the highest calcium EDI for the 90th percentile consumers from the consumption of beverages fortified with dolomite among various subpopulation (i.e., 192.31 mg/day) is far below the ULs of calcium among all age groups and is unlikely to produce any adverse effects.

6.2.2 Magnesium

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. 23/ Magnesium is present in fruits, vegetables, grains, milk, meat, and fish. The 2015 DGAC characterized magnesium as a shortfall nutrient. Assuming that 117.32 mg magnesium (highest 90th percentile consumption among different age groups) is provided by the intended use of dolomite, the amount of magnesium ingested by consumers through purified water would be only 27.9%

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

of the daily value (DV) of 420 mg magnesium. 24/ As such, 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. 25/

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. 26/ 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 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. 27 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."

24/ 27.9% = 117.32 mg/day ÷ 420 mg/day x 100%.

25/ Musso, Carlos G. "Magnesium metabolism in health and disease."*International urology and nephrology* 41.2 (2009): 357-362.

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

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

- **The SCF Opinion**

In 2001, the SCF conducted a review of safety studies associated with excessive magnesium intake. 28/ 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. 29/ The findings are also supported by other studies. 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. 30/ 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

The IOM established the following UL levels of magnesium for age groups:

Table 9. Magnesium IOM ULs for All Age Groups	
Age Group	**ULs**

28/ 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).

29/ 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.

30/ 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.

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

Magnesium Safety Conclusion

Table 10. Magnesium IOM ULs for All Age Groups

Age Group	ULs	90th Percentile
Children 1 Through 3 Years of Age	65 mg of supplementary magnesium	37.45 mg/day
Children 4 Through 8 Years of Age	110 mg of supplementary magnesium	55 mg/day
Adolescents and Adults > 8 Years	350 mg of supplementary magnesium	117.32 mg/day

As the above table indicates, the magnesium EDIs for the 90th percentile consumers from the consumption of beverages fortified with dolomite are below the ULs of magnesium for all age groups. Further, the intended use of dolomite in the remineralization of purified water beverages is a substitutional use that would not increase dietary exposure to its main component magnesium.

6.2.3 Dolomite

While dolomite readily dissolves into calcium and magnesium ions when in contact with purified water injected with CO_2, out of an abundance of caution, we also conducted a safety review of dolomite. Dolomite is not mutagenic, and there are no indications of carcinogenicity. 31/ A natural mixture of dolomite, magnesite, and magnesium-phyllosilicates (talc and chlorite) was tested for mutagenicity in a bacterial reverses mutation test. 32/ 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*. 33/ The authors reported that none of the strains showed any evidence of mutagenesis in either the presence or absence of metabolic activation. 34/ The mixture that contains dolomite was also tested in an *in vitro* chromosome aberration test in human lymphocytes. 35/ Up to 1,500 µg/mL was used, and

31/ 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.
32/ *See id*.
33/ *See id*.
34/ *See id*.
35/ *See id*.

there is not any statistically significant increase in the number of cells with chromosome aberrations. 36/

The potential of oral exposure to dolomite was also analyzed using Wistar rats. 37/ In particular, animals received dolomite oral dosages of 500 and 1,500 mg/kg during the period of gestation. 38/ Maternal, embryo and fetal toxicity were evaluated. 39/ Dolomite exposure did not produce maternal toxicity assessed by clinical observations, body weight gain, hematology parameters and relative organs weight. 40/ 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. 41/ 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 901.32 mg/day (or 15.02 mg/kg bw/day).

6.2.4 Heavy Metals

Table 11. Heavy Metal Levels In the Remineralized Water Comparison

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

As the heavy metal levels in the remineralized water are much lower than the allowable levels under FDA's regulation 21 CFR 165.110(b)(4)(iii)(A), these impurities in the bottled water do not present any human safety concern.

36/ *See id*.
37/ 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.
38/ *See id*.
39/ *See id*.
40/ *See id*.
41/ *See id*.

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, in consistent 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 90.16 mg/L calcium and 55 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.

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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.

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