KELLER AND HECKMAN LLP
Serving Business through Law and Science®

1001 G Street, N.W.
Suite 500 West
Washington, D.C. 20001
tel. 202.434.4100
fax 202.434.4646

Writer's Direct Access
Devon Wm. Hill
(202) 434-4279
hill@khlaw.com

April 8, 2011

Via Federal Express

Food and Drug Administration
Division of Animal Feeds (HFV-224)
Office of Surveillance and Compliance
Center for Veterinary Medicine
7519 Standish Place
Rockville, Maryland 20855

Re: CVM GRAS Notification for Hydrophobic Silica; Our File No. EM13458-01

Dear Sir or Madam:

On behalf of our client, Emerald Carolina Chemicals, LLC (the Notifier), we hereby respectfully request to participate in the pilot program for Generally Recognized as Safe (GRAS) determinations[1] for the safe use of hydrophobic silica (CAS Reg. No. 67762-90-7) as a component of the Notifier's FoamBlast® FMT defoamer, which is used as a processing aid in the production of distillers grains used in animal feed for food-producing animals. As discussed in detail in the enclosed dossier of information, the defoamer product is added to the condensed distillers solubles (*i.e.*, thin stillage concentrate) to assist in separating out corn oil during processing of grain from ethanol distillation. Accordingly, the hydrophobic silica defoamer component may be present at minute levels as an impurity in distillers grains fed to the food-producing animals.

A submission is provided, in triplicate, for the hydrophobic silica component of the defoamer. The submission includes a determination, based on scientific procedures, that hydrophobic silica is GRAS based on its presence as an impurity in animal feed as a result of its use in the processing of distillers grains.

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[1] *See* Substances Generally Recognized as Safe Added to Food for Animals; Notice of Pilot Program, 75 Fed. Reg. 31800 (June 4, 2010).

We trust that this submission satisfies the Agency's needs, and will be deemed accepted and complete. Should any questions arise, please contact us, preferably by telephone or e-mail, so that we can promptly respond.

Sincerely,

Devon Wm. Hill

Enclosure

Generally Recognized As Safe (GRAS) Notification for Hydrophobic Silica (CAS Reg. No. 67762-90-7)

Prepared for:

U.S. Food and Drug Administration

Center for Veterinary Medicine

Division of Animal Feeds (HFV-224)

7519 Standish Place

Rockville, MD 20855

Notifier:

Emerald Carolina Chemical, LLC

8309 Wilkinson Boulevard

Charlotte, NC 28214-9052

April 8, 2011

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APPENDICES

I. Introduction

On behalf of Emerald Carolina Chemical, LLC (Emerald or the Notifier), Keller and Heckman LLP submits the enclosed dossier of information in support of this notification that hydrophobic silica (CAS Reg. No. 67762-90-7), a component of the Notifier's FoamBlast® FMT defoamer, is Generally Recognized as Safe (GRAS) when present as an impurity in feed for the food-producing target animals, as a result of the defoamer's use as a processing aid in the production of dried and wet distillers grains (DG) with added solubles. More specifically, the 'whole' stillage produced during ethanol distillation is filtered by a mechanical centrifuge to remove water-soluble solids) to produce a 'thin stillage.' The 'thin stillage' is then condensed from 5-10% solids to up to 40% solids into 'condensed distillers solubles' (CDS), which contains corn syrup.

After the defoamer is added, the CDS is processed in a mechanical centrifuge to separate out the corn oil. CDS is a liquid byproduct that contains corn oil, as well as fermentation byproducts, spent yeast cells, and other nutrients which remain after corn grain has been fermented to produce ethanol. The Notifier's defoamer product is added to the CDS at levels up to 100 parts per million (ppm) to assist in separating the corn oil from the CDS. Hydrophobic silica is used up to a level of 20% of the Notifiers defoamer; thus the substance is added at levels up to 20 ppm to the CDS. Once the corn oil has been separated from the CDS, the resulting "de-oiled" CDS is then added to dried and wet DG to produce either wet distillers grains with solubles (WDGS) or dried distillers grains with solubles (DDGS). The WDGS and DDGS may then be used as a component of animal feed and fed to food-producing animals in accordance with normal feeding practice. In addition, the separated corn oil may be used in the production of biodiesel fuel, or added back into certain grades of DG fed to food-producing animals as a source of fat.

The defoamer and its components, including the hydrophobic silica, serve no technical purpose in the animal feed itself. Accordingly, the GRAS substance that is the subject of this notification is only present as a potential impurity in animal feed containing DG processed with the defoamer.

The determination of GRAS status is on the basis of scientific procedures, in accordance with 21 CFR § 170.30(b) and conforms to the guidance issued by the Food and Drug Administration (FDA) under *proposed* 21 CFR § 170.36, 62 Fed. Reg. 18938 (Apr. 17, 1997) and FDA's Notice of Pilot Program: Substances Generally Recognized as Safe Added to Food for Animals, 75 Fed. Reg. 31806 (June 4, 2010).

We submit information in the following areas:

- identity of the notified substance;
- intended conditions of use and technical effect;
- manufacturing specifications and stability certification;
- description of the ethanol production process and DDGS and WDGS manufacture method of the notified substance;
- toxicology summary;
- dietary exposure assessment for the food-producing target animal species;
- dietary exposure assessment for humans;
- estimation of daily intake for the notified substance; and
- GRAS determination for the notified substance, as a proposed conclusion determined by scientific procedures for use as a component of a processing aid (defoamer) in the production of DDGS and WDGS used in animal feed for food-producing target animals.

It is the Notifier's expectation that FDA will concur that the information presented fully supports the determination that the Notifier's hydrophobic silica is GRAS when present as an impurity in animal feed as a result of its use as a component of a processing aid (*i.e.*, the Notifier's defoamer product) in the production of WDGS and DDGS. This notification does not attempt to assess use in conjunction with DG as a component of food administered to companion or non-food producing animals.

II. Administrative Information

A. Claim Regarding GRAS Status

Hydrophobic silica is GRAS based on scientific procedures, when present at levels up to 20 ppm, as an impurity in animal feed for the food-producing target animal species as a result of its use as an emulsifier in the production of wet and dried distillers grain with added solubles (WDGS and DDGS, respectively). Hydrophobic silica serves no technical purpose in the animal feed itself. Accordingly, the GRAS substance that is the subject of this notification is only present as a potential impurity in the WDGS and DDGS due to its use in the processing of the CDS.

The use of hydrophobic silica in this manner as a component of the Notifier's FoamBlast® FMT defoamer has been determined to be exempt from the premarket approval requirements of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 301 *et. seq.*).

Devon Wm. Hill, Esq., Counsel for the Notifier

4-8-11

Date

B. Name and Address of the Notifier

Notifier	Acknowledgement of Receipt of Notification and Inquiries to be directed to:
Mr. Barry Ferguson Sales/Export Manager Emerald Carolina Chemical, LLC 8309 Wilkinson Boulevard Charlotte, NC 28214-9052 barry.ferguson@emeraldmaterials.com Office: 704-391-6419 Cell: 336-250-8533	Keller and Heckman LLP 1001 G Street N.W. Suite 500 West Washington, DC 20001 Mr. Devon Wm. Hill hill@khlaw.com Office: 202-434-4279 Fax: 202-434-4646

A letter authorizing Keller and Heckman to serve as agent for the Notifier is provided as **Appendix 1**.

C. Basis for GRAS Determination

This GRAS determination is based upon the publicly available scientific literature pertaining to the safety of the substance, and a dietary exposure assessment, as demonstrated herein.

D. Availability of Information

Much of the data and information that are the basis for the GRAS determination are enclosed with the notification. The Notifier also will retain copies of all of the data and information that form the basis for the GRAS determination, which are available for FDA's review at reasonable times, and copies will be sent to FDA upon request. Requests for copies and arrangements for review of materials cited herein may be directed to:

Keller and Heckman LLP
1001 G Street, N.W.
Suite 500 West
Washington, DC 20001
ATTN: Devon Wm. Hill, Esq.
hill@khlaw.com
202-434-4279 (tel.)
202-434-4646 (fax)

III. Detailed Information about the Identity of the Notified Substance

A. Names and Other Identities

Chemical Name: Hydrophobic Silica

CAS Reg. No.: 67762-90-7

B. Common or Usual Name of the Notified Substance

- Hydrophobic silica
- Synonyms: dimethyl siloxane reaction product with silica; siloxanes and silicones, di-Me, reactions products with silica

C. Intended Conditions of Use and Technical Effect of the Notified Substance

Hydrophobic silica will be used as a component (emulsifier constituent) of a processing aid (the Notifier's defoamer product) used in the production of WDGS and DDGS, respectively.

As noted above, the defoamer is added to the CDS at levels up to 100 ppm; the hydrophobic silica comprises up to 20% of the defoamer and thus is used at level of up to 20 ppm in the CDS. With respect to the intended technical effect, the defoamer is used as a chemical processing aid to assist in separating the corn oil from the CDS to produce "de-oiled" CDS[1], which is then added to the DDG and WDG to produce WDGS and DDGS, respectively. The WDGS and DDGS may then be used as components of animal feed for the food-producing target animals in accordance with normal feeding practice. The defoamer and its components, including the hydrophobic silica, serve no technical purpose in the animal feed itself. Accordingly, the GRAS substance that is the subject of this notification is only present as a potential impurity in the WDGS and DDGS due to its use in the processing of the CDS.

D. Manufacturing Specifications for the Notified Substance

(b) (4)

The Certificates of Analysis for each of the 5 lots are provided in **Appendix 2,** a Technical Data Sheet is provided in **Appendix 3** and a Food-Grade Assurance Letter from the Notifier's supplier is provided in **Appendix 4**.

[1] The CDS is put through a mechanical centrifuge to separate out the corn oil.

E. Stability Data

The hydrophobic silica used by the Notifier has been certified by the manufacturer as being stable for one year in an unopened package stored inside under normal conditions. See **Appendix 5** for the Certification letter provided by the Notifier's supplier.

F. Manufacturing Method of Notified Substance

(b) (4)

[redacted]

G. Detailed Description of Ethanol Distillation Process

Ethanol is distilled during the production of non-food grade and food grade ethanol. After distillation is performed to remove the ethanol from the fermentation mash, the remaining distillation residue, known as stillage (or whole stillage), is pumped from the bottom of the distilling column into centrifuges that separate the wet DG without solubles (WDG) from the stillage. The 'thin' stillage that remains after the WDG is removed from the whole stillage is a liquid that contains approximately 5-10% solids. The thin stillage is then routed to the fermentation tanks as make-up water, or sent to an evaporation system, which concentrates the thin stillage into CDS (which contains up to 40% solids). CDS, or concentrated thin stillage (which is also known as corn syrup), is high in protein and fat, and contains corn oil as well as fermentation byproducts, spent yeast cells, and other nutrients.

The Notifier's FoamBlast® FMT defoamer is then added at levels up to 100 ppm to the CDS to assist in separating out the corn oil from the corn syrup. Hydrophobic silica comprises a maximum 20% of the defoamer and thus is used at a maximum level of 20 ppm in the CDS.

After the defoamer is added, the CDS enters a mechanical centrifuge that separates out the corn oil. The hydrophobic silica is a component in a defoamer used as a chemical additive in the separation of corn oil from the CDS. Once the corn oil has been separated from the CDS and recovered, the resulting solubles-rich "de-oiled" CDS is then mixed back in with the wet DG (without solubles) and/or dried DG (without solubles), creating DDGS and WDGS, respectively. The separated corn oil may be used in the production of biodiesel fuel, sold into the industrial or specialty chemicals market, or added back into certain grades of DG and fed to food-producing animals as a source of fat.

The DDGS and WDGS, which include the reintroduced solubles from the CDS syrup, may be used as a component of feed for food-producing animals in accordance with normal feeding practice.

This GRAS notification is for DG collectively, including at least four non-fermentable residue byproducts of ethanol fermentation including wet distillers grains without solubles (WDG), dried distillers grains without solubles (DDG), CDS, WDGS and DDGS. (We include WDG and DDG in this notification although they do not *per se* include any de-oiled CDS because they may include re-added corn oil; our calculations will provide for dietary exposure from any hydrophobic silica that may be present in the corn oil.) For this purpose, data is provided on DDGS to represent the "worst-case" for potential residues.[2] The reintroduction of the solubles into the grains (by adding the "de-oiled" CDS to the DDG or WDG) will bring any residual hydrophobic silica that may be in the solubles into the DDGS or WDGS, while subsequent drying of the grains will concentrate any residual hydrophobic silica in the DDGS or WDGS. Therefore, we consider as the "worst-case" that the residual hydrophobic silica will be highest in DDGS. *See* **Figure 1** be

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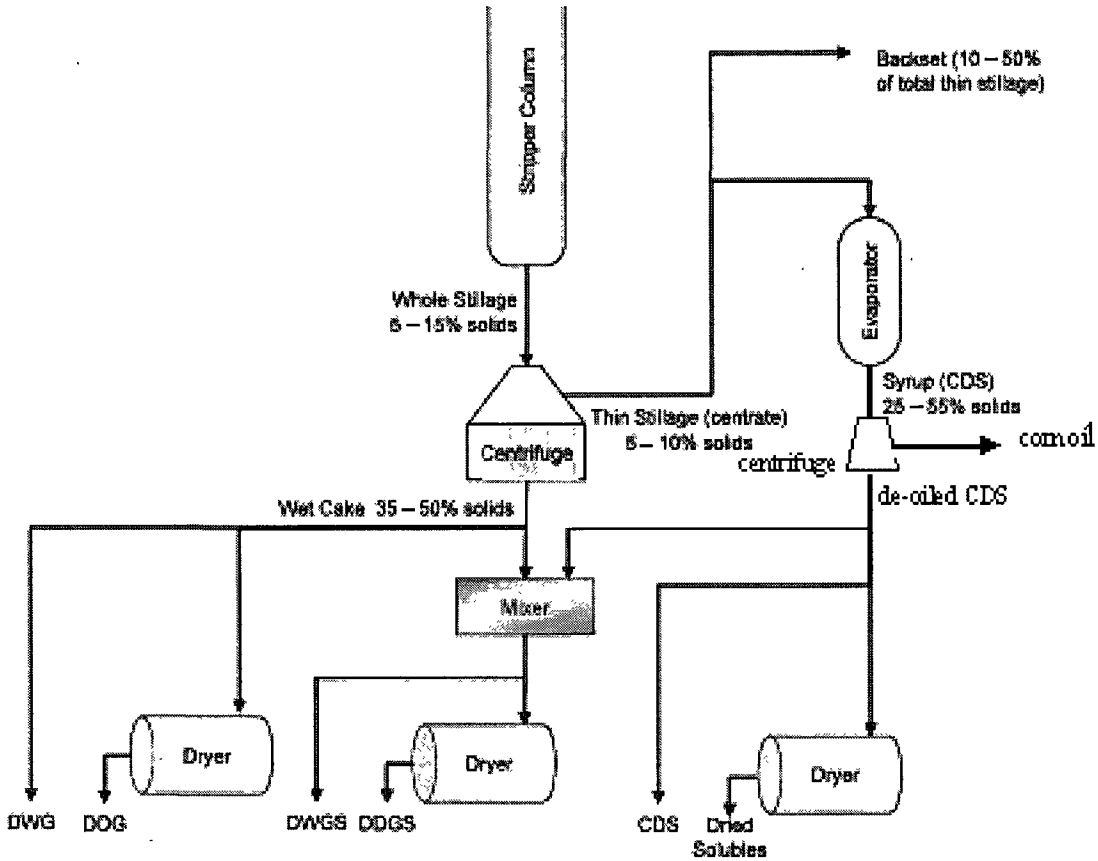
[2] Although CDS can be sold separately as a feed supplement when it is used to control dust and condition dry feed ratios, because de-oiled CDS has a much lower fat content and thus cannot provide a sizeable boost in energy level to animal feed, we expect that all de-oiled CDS will be added back to the distillers grains to produce wet and dry distillers grains with solubles. Therefore, the use of DDGS will provide the maximum dietary exposure to the defoamer components.

Figure 1: Ethanol production process.[3]



H. Calculated Residual Levels in Distillers Grains

As discussed above, to assist in separating the corn oil from the CDS grains, the defoamer is added to the CDS at levels up to 100 ppm; the hydrophobic silica comprises a maximum of 20% of the defoamer and thus is used at a maximum level of 20 ppm in the CDS. To determine the "worst-case" residual level of the hydrophobic silica present in the DDGS and WDGS, we conservatively assume that all of the Notifier's defoamer product added to the CDS

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[3] Ethanol Coproducts for Ruminant Livestock Diets. Kenneth Kalscheur and Alvaro Garcia, Dairy Science Department, SDSU, Kurt Rosentrater, USDA - Agriculture Research Service and Cody Wright, Department of Animal and Range Science, SDSU. August 2008. *See* http://www.thebeefsite.com/articles/1632/ethanol-coproducts-for-ruminant-livestock-diets.

will remain in the corn-oil free CDS (and thus, all of the hydrophobic silica present in the defoamer remains in the de-oiled CDS).[4] Because CDS has a maximum fat content of 10%[5], the maximum worst-case residual level of hydrophobic silica in the de-oiled CDS is 22.2 ppm (20 ppm ÷ 0.9 = 22.2 ppm).

IV. Detailed Summary of the Basis for Notifier's GRAS Determination

A. Safety Evaluations and Toxicology Summary

Hydrophobic silica can be prepared from two different processes. In the first process, untreated hydrophilic silica is reacted at high temperatures with dichlorodimethyl silane where Si-Cl groups associated with the dichlorodimethyl silane react with the silanol (Si-OH) groups present on the surface of the silica to form silyl methyl groups with the release of hydrochloric acid.[6] This reaction results in the formation of dimethyl silicone groups attached to the surface of the silica. In the second process, untreated hydrophilic silica is reacted with silicone oil (polydimethysiloxane) are high temperatures where the silicone oil condenses with the silanol groups on the surface of the silica resulting in the release of water and the reaction of the silicone

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4 This conservative assumption also ensures that all potential sources of dietary exposure to the hydrophobic silica are covered because, as noted above, the corn oil recovered from the CDS may, in some cases, be used as a component of animal feed (fat source) for food-producing animals.

5 CDS typically has a dry matter content of 25-30%, and a fat content (on a dry matter basis) of 20% (Using Distillers Grains in the U.S. and International Livestock and Poultry Industries, B.A> Babcock, D.J. Haynes, and J.D. Lawrence eds, The Midwest Agribusiness Trade Research and Information Center, 2008, *see* http://www.card.iastate.edu/books/distillers_grains). In some cases, CDS can have dry matter content as high as 45% (*see* http://beef.osu.edu/bee/beefAgst29.html); in that situation, the fat content can be as high as 20% x 45% = 9% in the CDS. We therefore conservatively assume that the entire 10% fat content in the CDS is attributable to the corn oil.

6 J. Lewison, W. Mayr, and H. Wagner, "Characterization and Toxicological Behavior of Synthetic Amorphous Hydrophobic Silica," Regulatory Toxicology and Pharmacology, 20, 37-57 (1994).

oil with the silica.[7] These two different process have been assigned two different CAS Registration Numbers; CAS Reg. No. 67762-90-7 is assigned to siloxanes and silicones, di-Me, reaction products with silica, and CAS Reg. No. 68611-44-9 is assigned to silane, dichlorodimethyl-, reaction products with silica. Both processes result in chemically equivalent hydrophobic silica products where the surface of the silica is methylated. Therefore, toxicology studies on hydrophobic silica prepared from dichlorodimethylsilane are equally applicable to hydrophobic silica prepared from the reaction silicone oil (polydimethylsiloxane) with silica.

Lewinson, *et al.* (1994) published an article on the toxicity of hydrophobic silica prepared with dichlorodimethylsilane, which supports the safety of hydrophobic silicas.[8] Supporting studies discussed in the article include acute oral and inhalation toxicity, subacute oral toxicity (rats, 8 weeks), chronic oral toxicity (rats, 6 months), carcinogenicity (rats, 2 years), mutagenicity (toluene extract of hydrophobic silica), and reproductive toxicity (rats, 6 months). Hydrophobic silica is not acutely toxic when administered orally or by inhalation. The oral LD_{50} for male and female Wistar rats was greater than 7.9 gm/kg. The toluene extract from hydrophobic silica was not mutagenic in *S. typhimurium* strains TA98, TA100, and TA1537, or in E. coli with or without metabolic activation. The dry weight of the toluene extract from 100 grams hydrophobic silica was 0.1 grams. Quantities of 5 to 1580 µg-extract/plate were used in the experiments.

In an eight-week, subchronic feeding study, hydrophobic silica was administered in the diet to four groups of 10 male and 10 female Wistar rats at 0, 500, 1000, or 2000 mg/kg bw/day. Rats in the low- and mid-dose groups received the test substance for 5 weeks. Because the animals tolerated 2000 mg/kg bw/day, the high dose was elevated to 4000 mg/kg bw/day after 14 days, to 8000 mg/kg bw/day after another 14 days, and finally to 16,000 mg/kg bw/day for a total test period of eight weeks. Treatment-related effects were seen at 16,000 mg/kg bw/day

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[7] R. E. Patterson, Chapter 60. "Preparation and Uses of Silica Gels and Precipitated Silicas," in Colloidal Silica Fundamentals and Applications, H. E. Bergna and W. O. Roberts, ed., CRC Press, 2006, pp 779-787.

[8] J. Lewinson, W. Mayr, and H. Wagner, *Characterization and Toxicological Behavior of Synthetic Amorphous Hydrophobic Silica* 20 Reg. Toxicol. & Pharm. 37-57 (1994).

(about 25% of the daily food intake). Effects included behavioral changes and cachexia (severe disorders associated with malnutrition), and two males and two females died. Microscopic examination of the liver of the high dose animals revealed severe atrophy of the epithelium. Because this effect, to a lesser extent, was observed in the livers of two females in the 1000 mg/kg bw/day group, the no observed effect level (NOEL) was established as 500 mg/kg bw/day.[9]

In a 6-month, chronic feeding study, 20 male and 20 female Wistar rats were fed hydrophobic silica at 500 mg/kg bw/day. Histopathological examination revealed an increased lipid content in the adrenal glands, but the effects were reversible in a three-week recovery period and were considered to be stress related. The 500 mg/kg bw/day dose level was regarded as the NOEL in the study.

In a two-year carcinogenicity bioassay, no carcinogenic or other treatment-related effects were observed after administration of hydrophobic silica in the diet of 20 male and 20 female Wistar rats at 100 mg/kg bw/day for 24 months. Applying a safety factor of 100 to the NOEL of 100 mg//kg bw/day, we calculate an ADI of 1 mg/kg bw/day for hydrophobic silica (100 mg/kg bw/day ÷ 100 = 1 mg/kg bw/day).[10]

To identify possible reproductive effects, 10 female Wistar rats in the control group and 10 females treated with 500 mg/kg bw/day hydrophobic silica were mated at weeks 8 and 17 with males from the chronic 6-month study. Progeny from the two litters were examined for gross anomalies immediately after birth. The total treatment time of the parental females was 6 months. At autopsy, the parental organs were weighed, and macroscopic and microscopic examinations were performed. No treatment-related effects were found either in the parents or the progeny. The NOEL was established as 500 mg/kg bw/day.

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9 NOEL (no observed effect level) and NOAEL (no observed adverse effect level) are interpreted to mean a level of exposure that results in no treatment related adverse effects to the test animals relative to the control group.

10 We have used the lowest reported NOEL of 100 mg/kg bw/day based on chronic feeding studies for hydrophobic silica to calculate an ADI.

Three extended toxicological dietary exposure studies were conducted using DDS hydrophobic silica. No toxicological effects due to direct systemic interaction with target organs were attributable to the addition of hydrophobic silica to the diet of the test animals. Adverse effects were observed in the subchronic exposure, but these were secondary effects due to the malnutrition of the test animals that consumed up to 40% of their diet as hydrophobic silica. In the six-month exposure some effects on the liver were observed, but these were transient should not be regarded as toxic effects. No adverse effects were found in the two-year exposure. Thus, exposures for two years to 100 mg/kg bw/day; exposures for six months to 500 mg/kg bw/day; and for up to eight weeks to as high as 16,000 mg/kg bw/day resulted in no significant treatment related effects.

It should be noted that FDA has reviewed the data discussed above and concluded, in an animal feed GRAS affirmation final rule, that "the data on DDS hydrophobic silica indicate that it is nontoxic and that the lack of toxicity is due to hydrophobic silica's nonabsorbability". 61 Fed. Reg. 43451- 43454 (August 23, 1996). The Agency determined that the safety of DDS hydrophobic silica is supported by both data on the compound and the essential similarity of its toxicological profile to that of silica/silicon dioxide. FDA concluded that the hydrophobic surface modification of silica did not change the inherent safety of the silica and that it was appropriate to extend the safety determination for the components (silica and PDMS) to the hydrophobic silica.

B. Toxicology Data on Silicon Dioxide

Silicon dioxide and various silicates have a wide range of clearances in FDA's food additive regulations for use in food. For example, silica aerogel, a form of silicon dioxide, is listed as "Generally Recognized as Safe" (GRAS) as a component of antifoaming agents at 21 C.F.R. Section 182.1711. Silicon dioxide is also cleared in FDA's food additive regulations as an anticaking agent at Section 172.480 and as a defoaming agent at Section 173.340.

The safety of silicon dioxide (including amorphous silicon dioxide) and other silicates rests primarily on the fact that they are chemically inert and generally are not absorbed from the gastrointestinal tract.[11] In evaluating the safety of silicates as food ingredients, expert bodies have also noted that, due to the ubiquity of silicates in the environment and as a natural component of plants and animals, natural exposure to silicates dwarfs intake from their use as food additives/ingredients. The European Union's (EU) Scientific Committee for Food placed silicon dioxide in the category of "ADI not specified." "ADI not specified" is a term used when, on the basis of the available toxicological, biochemical, and clinical data, the total daily intake of the substance will not represent a hazard to health. The Committee concluded as follows:

> The available data on orally administered silica and silicates, including amorphous silicon dioxide, appear to substantiate the biological inertness of these compounds. Any silicate absorbed is excreted by the kidneys without evidence of toxic accumulation in the body, except for the reported damage to dog kidney by magnesium trisilicate and sodium silicate.

The Federation of American Societies for Experimental Biology's (FASEB) Scientific Committee on GRAS Substances (SCOGS) reviewed silicon dioxide for the FDA in 1979.[12] Except for the species-specific effects of magnesium trisilicate and sodium silicate, cited above, the only toxicity observed with silicates, including silicon dioxide, relates to inhalation, and the observed inhalation toxicity is due to particle size, not to any systemic toxicity. The SCOGS panel noted that silicon dioxide and other silicates occur abundantly in the earth's crust, and are present in practically all natural waters, animals and plants. This fact led the panel to observe that silicon compounds consumed as food ingredients constitute only a minor portion of total dietary silicon intake.

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[11] Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, WHO Tech. Report Series; 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53.

[12] FASEB (1979). Evaluation of the Health Aspects of Certain Silicates as Food Ingredients. U.S. Department of Commerce, National Technical Information Service PB-301 402.

C. Toxicology Data on Polydimethylsiloxane (PDMS)

PDMS is cleared for use as a defoaming agent by FDA under 21 C.F.R. § 173.340. PDMS is also the subject of a number of clearances as a component of food-contact materials. In addition, PDMS is widely used in the pharmaceutical industry under the names of dimethicone and simethicone, sold in over-the-counter drugs as antiflatulence agents.

Toxicity data on PDMS generated through 1978 have been reviewed by FASEB's SCOGS panel for FDA.[13] PDMS is poorly absorbed from the gastrointestinal tract, although limited metabolism of lower molecular weight species may occur. In one study, two monkeys were fed 100 gm and two others 300 gm 5 days weekly for 8 months. One monkey receiving the larger dose vomited continually during the first month. Otherwise, only occasional diarrhea was observed.[14] FASEB concluded that "[t]he methylpolysilicones used in food have been demonstrated to be of low acute and chronic toxicity to animals and man when administered orally."

More recently, a British Industrial Biological Research Association (BIBRA) working group reviewed existing data generated prior to 1991.[15] The report concluded in part:

> Limited oral and dermal studies have provided no convincing evidence of reproductive toxicity in rats and rabbits, and limited long-term feeding studies in rodents have given no conclusive indication of carcinogenicity. No evidence of genotoxic potential was found in rodent treated by injection, in mammalian cells in culture or in Ames bacterial tests.

Data from an extensive series of toxicity studies by Dow Corning on various PDMSs were reported in 1994. These studies included a teratology study on New Zealand rabbits in which a food grade PDMS produced no developmental effects, including teratology effects, when

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13 FASEB (1981). Evaluation of the Health Aspects of Methylpolysilicones as Food Ingredients. Contract No. FDA 223-78-2100.

14 FASEB (1981). Page 13.

15 BIBRA Working Group (1991). Polydimethylsiloxane, Toxicity Profile, BIBRA Toxicology International, 9 pages.

administered to pregnant rabbits during organogenesis at dietary levels up to 2.5%.[16] Dow Corning also sponsored a 12-month study in which hydroxyl-terminated PDMS was fed to 5 male and 5 female rats at a dietary level of 0.05%. Treated males gained significantly more weight than control males, but no treatment-related effects on hematology, clinical chemistry, or urinalysis parameters or changes in gross pathology or histopathology were observed.[17] An 8-month study was conducted in which hydroxyl-terminated PDMS was fed to 6 male and 6 female albino rabbits at a dietary level of 0.05%. No treatment-related effects were observed.[18] In addition, Dow Corning performed a series of 90-day feeding studies in which PDMSs having viscosities of 50; 350; 1000; 10,000; or 60,000 centipoise were administered to groups of 5 male and 5 female SD rats at a dietary level of 1%. No treatment-related effects were observed.[19] A 13-week study was carried out in which beagle dogs (3/sex/group) were orally administered 0, 120, 380, or 1200 mg/kg silica filled PDMS. No treatment-related effects were observed, as above.[20] Dow Corning performed a 13-week feeding study in which 15 male and 15 female CD1 mice per group received 0, 5, or 10% PDMS having a viscosity of 35 centistokes. Although mice in the 10% group exhibited oily fur and anal leakage, there were no deaths or behavioral abnormalities, no significant differences in body weights or organ weights, and no significant treatment-related effects on gross pathology or histopathology.[21] Dow Corning also conducted

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16 W.H. Siddiqui, *Developmental toxicity evaluation of Dow Corning Antifoam A compound, food grade in rabbits* 49 Teratology 397 (1994).

17 Chronic (one-year) feeding studies with Dow Corning special polysiloxane in rats with cover letter dated 04/20/94. (1994). EPA/OTS; Doc #86940001086. NTIS Order No.: NTIS/OTS0556540.

18 Chronic (8-month) feeding studies with DC 360 fluids in rabbits with cover letter dated 04/20/94. (1994). EPA/OTS; Doc #86940001085. NTIS Order No.: NTIS/OTS0556539.

19 Report prepared for the Dow Corning Corporation, Midland Michigan on five silicone materials (Dow Corning 200 Fluid) with cover letter dated 04/20/94. (1994). EPA/OTS; Doc #86940001039. NTIS Order No.: NTIS/OTS0556493.

20 DC Medical Antifoam 351 Compound; a thirteen-week feeding study in dogs with cover letter dated 04/20/94. (1994). EPA/OTS; Doc #86940001520. NTIS Order No.: NTIS/OTS0590154.

21 A 90-day subchronic oral toxicity study with polydimethylsiloxane fluid in the mouse with cover letter dated 04/20/94. (1994). EPA/OTS; Doc #86940001392. NTIS Order No.: NTIS/OTS0590096.

two 13-week rat studies. In one of these rat studies, 9 groups of 20 male and 20 female SD rats received 1, 5, or 10% PDMS having a viscosity of 35, 350, or 1000 centistokes. Males exhibited increased feed consumption, but no treatment-related effects were observed on hematology, clinical chemistry, or urinalysis parameters or on gross pathology or histopathology.[22] In the second study performed by Dow Corning, 5 groups of 100 male rats (2 control groups) orally received 10% PDMS having viscosities 35, 350, or 1000 centistokes. Again, no statistically significant treatment-related effects were observed.[23]

The structure of hydrophobic silica consists primarily of silica with the surface structure containing a Si-O-Si backbone with each silicon atom bonded to two methyl groups. Hydrophobic silica can also be prepared by the reaction of silicon dioxide with dichlorodimethylsilane where silica present on the surface of the silica is attached to two methyl groups resulting in the hydrophobization of silica. Thus, hydrophobic silica described as Silane, Dichlorodimethyl-, reaction products with Silica with CASRN 68611-44-9 is affirmed as GRAS for use in feed and drinking water for animals.[24] In considering the GRAS status of hydrophobic silica, FDA reviewed the available toxicity data and concluded that the data indicate that hydrophobic silica is nontoxic and its lack of toxicity is the result of its "nonabsorbability."[25] More specifically, the Agency determined that the safety of the hydrophobic silica is supported by data on the compound and its similarity from a toxicological standpoint to silica/silicon

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22 A 90-day subchronic oral toxicity study with polydimethylsiloxane fluids in the rat with cover letter dated 04/20/94. (1994). EPA/OTS; Doc #86940001394. NTIS Order No.: NTIS/OTS0590098.

23 A 90-day subchronic oral toxicity study with polydimethylsiloxane fluids in male rats with cover letter dated 04/20/94. (1994). EPA/OTS Doc #86940001395. NTIS Order No.: NTIS/OTS0590099.

24 See 21 C.F.R. §584.700 ("Hydrophobic silicas"). We note that the Act's definition of "food" includes articles used for food and drink for man *and other animals*. Because GRAS substances are excluded from the "food additive" definition and the definition of "food" includes animal feed, one interpretation of the law could be that substances affirmed as GRAS for use in animal feed applications also may be considered to be GRAS in food-contact use. FDA has not confirmed this interpretation in its regulations, however; therefore, we consider it prudent to document additional support for a GRAS determination in this case.

25 *See* 61 Fed. Reg. 43451, 43453 (August 23, 1996).

dioxide, which, as noted above, is GRAS in Section 182.1711. FDA concluded that the hydrophobic surface modification of the silica does not change the inherent safety of the silica, and therefore that it is appropriate to extend the safety determination for the components to the hydrophobic silica.[26]

Considered as a whole, the results discussed in this section are more than sufficient to assure the safety of hydrophobized silica for the intended use as a component of the Notifier's defoamer product.

V. Correlation of Data to Target Animal Species

Although the animal species tested were predominantly rats, and the target species are livestock animals consisting of both poultry and ruminants, we believe the toxicology data presented above is equally applicable to the target animal species. Hydrophobic silica is completely insoluble, does not hydrolyze, and is not expected to be absorbed within the digestive tracts of either type of animal, and will be completely eliminated with the feces. As hydrophobic silica will not be metabolized by the action of microorganisms that may be present in ruminal fluids of certain target animals, the substance will pass completely through the digestive track of ruminants. Thus, the findings of the toxicology studies presented above can appropriately be applied to the target animal species in this GRAS notification. Accordingly, the ADI presented above is equally applicable to all target animals.

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[26] As a reactant, dichloromethylsilane is highly reactive and not expected to be present in hydrophobic silica to any significant extent. Dichloromethylsilane tested negative in the Ames assay, mouse lymphoma assay, and did not induce mitotic gene conversion in saccharomyces cerevsiae. In an *in vitro* chromosomal aberration assay, the substance was clastogenic, both in the presence and absence of metabolic activation. However, in an *in vivo* chromosomal aberration assay, no aberrations were induced in the bone marrow cells of rats. Therefore, the weight of the evidence suggests dichloromethylsilane is not genotoxic.

VI. Dietary Exposure Assessment for Target Animals

As discussed above, the Notifier intends to use the defoamer at a maximum use level of 100 ppm in the CDS; the hydrophobic silica comprises up to 20% of the defoamer and thus is used at level of up to 20 ppm[27] in the CDS. Once the defoamer has been added to the CDS, and the corn-oil separated out, the de-oiled CDS is then added to either dried DG to create DDGS or wet DG to create WDGS, which can then be used as components of animal feed for the food-producing target animals. As indicated above, the worst-case residual level of the hydrophobic silica in the de-oiled CDS is approximately 22.2 ppm, conservatively assuming the entire 10% fat content in CDS is attributable to the removed corn oil. Once de-oiled, CDS syrup is then incorporated into the distillers grains at a level of 25% on a solids weight basis;[28] the resulting solubles-enriched DG product (either as WDGS or DDGS) is typically added to animal feed at a maximum level of 30% on a solids basis.[29] Although the corn-oil free CDS can be sold separately as a feed supplement when it is used to control dust and condition dry feed ratios,

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[27] (100 ppm)(0.20) = 20 ppm.

[28] Whole stillage with an 85-90% water content (10%-15% solids) is separated into a wet DG stream with a water content of 65-70% (*i.e.*, 30-35% solids) and a thin stillage stream with a water content of 90-95% (*i.e.*, 5 -10% solids). The thin stillage stream is condensed in an evaporator into CDS with a water content of 60% (*i.e.*, 40% solids). While the water and solids contents noted above vary depending on the production plant and processing techniques, and although a portion of the thin stillage is recycled back to the fermentation vessel, we can use the approximate water and solid contents to conservatively determine the maximum amount of CDS solids that are added to wet or dry DG to make WDGS or DDGS, respectively. In this regard, we note that a whole stillage stream with 1 kg of DG contains approximately 7.3 kg of water. The whole stillage stream is then separated into wet DG with a maximum solids content of 35% (which we assume contains the bulk of the 1kg of DG), and into a thin stillage stream with a solids content of about 5% (consisting of 5.5 kg of water and 0.33 kg of solids). The thin stillage is then condensed to 40% solids, but still contains 0.33 kg of solids which is then added back to the 1 kg of solids in the wet DG prior to drying. Therefore, the "addition rate" of the CDS to DG is 0.33/1.33 kg or 25% on a solids basis. In an actual process, the ratio of solids in the condensed thin stillage stream is expected to be much less than 25%, so this provides a worst-case addition of CDS containing hydrophobic silica to the DDGS.

[29] "Using Distillers Grains in the U.S. and International Livestock and Poultry Industries," B.A. Babcock, D.J. Haynes, and J.D. Lawrence eds, The Midwest Agribusiness Trade Research and Information Center, 2008, *see* http://www.card.iastate.edu/books/distillers_grains.

because of its much lower fat content, the de-oiled CDS cannot provide a sizeable boost in energy level when added directly into animal feed. Accordingly, we expect that all de-oiled CDS will be added back to the DG to produce WDGS and DDGS. Therefore, the use of DDGS will provide the maximum dietary exposure to the defoamer components.

De-oiled CDS typically has a solids content of 40% with a polyoxyethylene (20) sorbitan monostearate concentration of 22.2 ppm. Hydrophobic silica has a concentration of 55.5 ppm based on CDS solids.[30]

Because the de-oiled CDS is added to the DG at 25% on a solids basis, the maximum potential concentration of hydrophobic silica in animal feed is: (55.5 ppm) (0.25) = 13.9 ppm on a solids basis.

Distiller's grains are typically fed as a portion of daily feed to target animals such as cattle, diary cows, sheep, swine, turkeys, and broiler chickens. The recommended daily feed diets for cattle, diary cows, sheep, turkeys and swine include up to 30% distillers grains on a dry weight basis. The daily feed intake of broiler chickens may include up to 15% by weight dry distillers grains.[31]

The Distillers Grain Technology Council has stated that DG can be used in daily feed for the food-producing target animals as presented in Table 1 below.[32] Weights and intakes of feed are nominal, meaning that they are representative of populations of animals generally, and may not be specific to particular categories of food-producing animals raised under specific conditions.[33] The quantity of food consumed per day per animal may not be representative of

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30 22.2 ppm ÷ 0.40 = 55.5 ppm.

31 Using Distillers Grains in the U.S. and International Livestock and Poultry Industries, *see* http://www.matric.iastate.edu/DGbook/distillers_grain_book.pdf.

32 Distillers Grains Technology Council, University of Louisville, Lutz Hall Room 435, Louisville, Kentucky 40292: www.distillersgrains.org.

33 SAX'S Dangerous Properties of Industrial Materials. Ninth Edition (1996). Table 2. Van Nostrand Reinhold Company. New York.

food intakes for a specific period of time during growth, but rather reflect an average that approximates intakes over an expected lifetime.

TABLE 1. Feeding Data for Food-Producing Target Animals

Target Animal Species	Weight (kg)	Food Consumed (g/day)	Distillers Grains (dry weight basis) Consumed per Day		
			(%)	(g/day)	g/kg bw/day
Beef Cattle	500	10,000	30%	3,000	6
Dairy Cattle	500	10,000	30%	3,000	6
Poultry[34] (broiler)	2.5	232.5	15%	34.9	14
Sheep	60	2,400	30%	720	12
Swine	60	2,400	30%	720	12

The amount of distillers grains consumed on a dry basis for each animal is calculated as follows for cattle:

(10,000 g-food/500 kg bw) x (0.3 g-distillers grains/g-food)

= 6 g-distillers grains/kg bw

The maximum distillers grains consumed by beef cattle, on a dry weight basis, is 6 g/kg bw/day. With a maximum residual level of 13.9 mg/kg of hydrophobic silica in distiller's grains on a dry weight basis, a maximum dietary intake for beef cattle is calculated as follows:

6 g-distillers grain/kg bw x (13.9 mg- HPS/kg-distillers grains) x (kg/1000 g)

= 0.08 mg HPS/kg bw/day

The dietary intake of hydrophobic silica by other food-producing target animals is similarly calculated and presented in the table below:

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[34] The feed consumption for broiler chickens is reported to be 93 mg/kg bw/day – Predicting Feed Intake of Food-Producing Animals, Subcommittee on Feed Intake, Committee on Animal Nutrition, Board on Agriculture, National Research Council, National Academy Press, Washington, D.C., 1987.

TABLE 2. EDIs for Target animals

Target Animal Species	EDI (mg/kg-bw/day) for Hydrophobic Silica
Beef Cattle	0.08
Dairy Cattle	0.08
Poultry (Broiler)	0.2[35]
Sheep	0.17[36]
Swine	0.17[37]

Poultry consume the highest amount of DG per body weight per day among all the food-producing target animals, thus providing a worst-case dietary intake of 0.2 mg/kg bw/day for hydrophobic silica for all food-producing target animals. As shown above, a very conservative ADI of 1 mg/kg-bw/day has been established for hydrophobic silica for the target animals. Accordingly, we conclude that the residual hydrophobic silica that may be present in the animal feed as an impurity, as a result of the use hydrophobic silica in the Notifier's defoamer product, as described above, is safe for the target animals.

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[35] 14 g-distillers grain/kg bw x (13.9 mg-HPS/kg-distillers grains) x (kg/1000 g) = 0.2 mg HPS/kg bw/day.

[36] 12 g-distillers grain/kg bw x (13.9 mg-HPS/kg-distillers grains) x (kg/1000 g) = 0.17 mg HPS/kg bw/day.

[37] 12 g-distillers grain/kg bw x (13.9 mg-HPS/kg-distillers grains) x (kg/1000 g) = 0.17 mg HPS/kg bw/day.

VII. Dietary Exposure Assessment for Humans of Hydrophobic Silica

Table 3. EDI Summary for Hydrophobic Silica

Dietary Exposure	EDI (mg/kg bw/day)
Animal Dietary Exposure to Hydrophobic Silica	0.2 mg/kg bw/day
Human Dietary Exposure to Hydrophobic Silica	0.007 mg/kg bw/day

As described above, it is well understood that hydrophobic silica is not absorbed by the gastrointestinal tract and, therefore, is not expected to reside in the edible tissues of the target animals. As such, no exposure to hydrophobic silica is expected based on the consumption of any component of the animal, which includes tissues, fat, edible organs, eggs, and milk.

As there is no expectation of accumulation of hydrophobic silica in the tissues of the food-producing target animals, there is little likelihood of any significant human exposure as a result of consuming food products derived from the target animals. Nevertheless, for the sake of conservatism, we will assume, as worst-case, that at slaughter, hydrophobic silica may be present in the edible portions of the carcass at levels equal to the amount of the compound consumed on that day.[38] We will also conservatively assume that the compound is equally distributed throughout the carcass and in any milk or eggs that may be produced by the target animals.

To determine the dietary intake of hydrophobic silica by the consumption of edible parts of a species of target animals, FDA assigns consumption values for different edible products of each species, based on the relative amount of each organ or tissue that is consumed by

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[38] This is a conservative assumption in that hydrophobic silica is insoluble and is not readily absorbed through the intestinal tract and thus not stored in any animal tissues and organs. Furthermore, any hydrophobic silica that could possibly be absorbed through the intestinal tract would be directly excreted. As all of the hydrophobic silica will pass directly through the digestive system, this clearly provides a worst-case for human dietary exposure.

individuals.[39] Specifically, according to FDA's Guidance for Industry: *General Principles for Evaluating the Safety of Compounds used in Food-Producing Animals*, FDA assumes that these consumption values (*i.e.*, grams consumed per person per day) are applied to all species of the target animals, as it is assumed that when an individual consumes a full portion[40] of a meat product from one species, that individual will not also consume a full portion of a meat product from another species. Additionally, FDA assumes that on a daily basis an individual consumes a full portion of milk in addition to a full portion of eggs[41] in addition to the full portion of edible muscle and organ tissue (from one animal species). These values are used to determine the exposure of hydrophobic silica, based on the level of hydrophobic silica in each edible portion of the target animal. The consumption values and the hydrophobic silica levels are summarized in the table below, based on the assumptions that (1) the maximum daily intake of hydrophobic silica of 0.2 mg/kg bw/day is evenly distributed throughout the muscle tissues, organs, milk, and eggs of the food-producing target animals and (2) the hydrophobic silica is metabolized on a daily basis:

TABLE 11. Consumption Values for Hydrophobic Silica

Edible Product	Consumption (g food/day)	Hydrophobic Silica Level (µg/g tissue)
Muscle	300 g	0.2
Liver	100 g	0.2
Kidney	50 g	0.2
Fat	50 g	0.2
Milk	1.5 L	0.2
Eggs	100 g	0.2

[39] As described in *FDA's Guidance for Industry: General Principles for Evaluating the Safety of Compounds used in Food-Producing Animals*; http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052180.pdf.

[40] According to FDA's guidance on *General Principles for Evaluating the Safety of Compounds used in Food-Producing Animals*, a full portion of meat consists of 300 g of muscle tissue, 100 g of liver, 50 g of kidney, and 50 g of fat.

[41] According to FDA, the estimated daily intake is 1.5 liters for milk and 100 grams for eggs.

To estimate the dietary exposure of hydrophobic silica, the Notifier considered each edible portion of cattle. In addition, based on FDA's assumptions discussed above, the Notifier assumed that a full portion of milk and eggs are consumed in addition to a full portion of edible muscle or organ tissues. Based on this, the Notifier calculated the relative level of hydrophobic silica in each edible product to obtain, in essence, a dietary exposure for individual human consumers. The exposures due to milk and eggs, as well as the sum of all the exposure values (to obtain a cumulative dietary exposure level) are calculated as follows:

Muscle:

(0.2 μg HPS /1 g muscle) x (300 g muscle/person/day)

= 60 μg HPS /person/day

Liver:

(0.2 μg HPS /1 g liver) x (100 g liver/person/day)

= 20 μg HPS /person/day

Kidney:

(0.2 μg HPS /1 g kidney) x (50 g kidney/person/day)

= 10 μg HPS /person/day

Fat:

(0.2 μg HPS /1 g fat) x (50 g fat/person/day)

= 10 μg HPS /person/day

The total dietary exposure to hydrophobic silica for a individual consumer <u>not</u> consuming eggs and milk is calculated as follows:

60 μg HPS /person/day (muscle) + 20 μg HPS /person/day (liver) + 10 μg HPS /person/day (kidney) + 10 μg HPS /person/day (fat)

= 100 μg HPS /person/day

The dietary exposure to hydrophobic silica for a individual consumer who does consume eggs and milk is calculated as follows:

Milk:

(0.2 mg HPS / 1.0 L milk) x (1.5 L milk/person/day)

= 0.3 mg HPS /person/day

Eggs:

(0.2 µg HPS / 1 g egg) x (100 g egg/person/day)

= 20 µg HPS /person/day

Thus, the cumulative exposure to hydrophobic silica from the consumption of all animal (cattle) products (*i.e.*, muscle tissue, organ tissue (liver and kidney), and fat), and milk and eggs (poultry) provides us with the estimated daily intake (EDI) for the GRAS substance as follows:

0.1 mg + 0.3 mg + 0.02 mg = 0.42 mg HPS /person/day

Assuming an individual consumes 3 kg of food per day, this calculates to a dietary concentration of 0.42 ÷ 3 kg = 0.14 ppm per day. The estimated daily intake (EDI) for hydrophobic silica is calculated as follows:

EDI (HPS) = 0.14 mg/kg x 3 kg-food/p/d = 0.42 mg/p/d

Assuming that an average individual weighs 60 kg, the EDI also may be expressed as

0.42 mg/p/d ÷ 60 kg bw = 0.007 mg/kg bw/d.

VIII. Conclusion

Based on the dossier of information provided in this GRAS notification, and on the scientific procedures discussed herein, the Notifier has concluded that hydrophobic silica (CAS Reg. No. 67762-90-7), a component of the Notifier's FoamBlast® FMT defoamer, is Generally Recognized As Safe (GRAS) when present as an impurity in the feed for the food-producing target animals, as a result of the defoamer's use as a processing aid at levels up to 20 ppm in the production of dried and wet distillers grains with added solubles.

APPENDIX 1

Emerald Performance Materials

February 28, 2011

U.S. Food and Drug Administration
Center for Veterinary Medicine
Division of Animal Feeds (HFV-224)
7519 Standish Place
Rockville, Maryland 20855

Re: Authorization to Act as Agent for Carolina Chemical LLC

Dear Sir or Madam:

This is to advise that the law firm of Keller and Heckman LLP, its employees, associates, and agents, specifically including, but not limited to Devon Wm. Hill, are authorized to act as agents on behalf of Carolina Chemical LLC (a subsidiary of Emerald Performance Materials, LLC) with regard to its Generally Recognized as Safe (GRAS) Notification for Hydrophobic Silica (CAS Reg. No. 67762-90-7), submitted to the U.S. Food and Drug Administration, Center for Veterinary Medicine.

This letter is our authorization to you to permit said firm to undertake appropriate communications relevant to making submissions or inquiring as to the status of the above referenced GRAS Notification filed by or on behalf of Carolina Chemical LLC, including examination of all relevant information including confidential business, proprietary, and trade secret information submitted or developed under the Federal Food, Drug and Cosmetic Act.

Sincerely,

Barry Ferguson

Barry Ferguson
Sales/Export Manager

Emerald Carolina Chemical, LLC
8309 Wilkinson Blvd / Charlotte, NC, 28214 / Phone. 704-393-0089 / Fax 704-391-7340
www.emeraldmaterials.com

APPENDIX 2

(b) (4)

Certificate of Analysis

Dumacil 100-FG-K

Lot No. (b) (4)

Date of Manufacture: 10-01-10

Resource # Z1032

Property	Method	Specification	Units	Result
Hydrophobicity	LP0002	≤ 2		1
Appearance	LP0005	White Powder		Pass
Naphtha Residue	LP0009	≤ 10 Black Specks		0
pH	LP0015	*8 - 11*		9

Authorized By:

Customer: Emerald Performance Materials

(b) (4)

PD

For further information please contact:

(b) (4)

11/2/10

(b) (4)

Certificate of Analysis

Dumacil 100-FG-K

Lot No. (b) (4)

Date of Manufacture: 10-04-10

Resource # Z1032

Property	Method	Specification	Units	Result
Hydrophobicity	LP0002	≤ 2		1
Appearance	LP0005	White Powder		Pass
Naphtha Residue	LP0009	≤ 10 Black Specks		0
pH	LP0015	*8 - 11*		9

Authorized By:

(b) (4)

Customer: Emerald Performance Materials

For further information please contact:

(b) (4)

10·22·10

(b) (4)

Certificate of Analysis

Dumacil 100-FG-K

Lot No. (b) (4)

Date of Manufacture: 09-01-10

Resource # Z1032

Property	Method	Specification	Units	Result
Hydrophobicity	LP0002	≤ 2		1
Appearance	LP0005	White Powder		Pass
Naphtha Residue	LP0009	≤ 10 Black Specks		0
pH	LP0015	*8 - 11*		9

Authorized By:

Customer: Emerald Performance Materials

(b) (4)

For further information please contact

(b) (4)

9.14.10

(b) (4)

Certificate of Analysis

Dumacil 100-FG-K

Lot No.(b) (4)

Date of Manufacture: 08-06-10

Resource # Z1032

Property	Method	Specification	Units	Result
Hydrophobicity	LP0002	≤ 2		1
Appearance	LP0005	White Powder		Pass
Naphtha Residue	LP0009	≤ 10 Black Specks		0
pH	LP0015	*8 - 11*		9

Authorized By:

Customer: Emerald Performance Materials

(b) (4)

For further information please contact:

(b) (4)

5/16/10

(b) (4)

Certificate of Analysis

Dumacil 100-FG-K

Lot No. (b) (4)

Date of Manufacture: 08-05-10

Resource # Z1032

Property	Method	Specification	Units	Result
Hydrophobicity	LP0002	≤ 2		1
Appearance	LP0005	White Powder		Pass
Naphtha Residue	LP0009	≤ 10 Black Specks		0
pH	LP0015	*8 - 11*		9

Authorized By:

(b) (4)

Customer: Emerald Performance Materials

For further information please contact:

(b) (4)

5/12/10

APPENDIX 3

(b) (4)

Technical Bulletin

(b) (4)

Dumacil 100-FG-K

Dumacil 100-FG-K is a micro-fine silica treated with an organic silicone compound. The resultant hydrophobic silica is extremely water repellent and easily dispersed in organic systems. Dumacil 100-FG-K provides excellent performance in defoamers for use in paint, paper, latex and textile industries.

Identity

Appearance	White powder

Typical Properties

Bulk Density, lbs/cu ft	9
pH	9.5
Ignition Loss, 1000°C	8%

Storage and Handling

Prolonged breathing of hydrophobic silica dust may cause irritation of the respiratory tract. Therefore, as with all dusty materials, proper ventilation and personal protective equipment should be used.

Regulatory Status

Dumacil 100-FG-K meets the requirements of FDA 21 CFR

- 173.340 Defoaming agents
- *175.105 Adhesives*
- *175.300 Resinous and Polymeric coatings*
- *176.170 Components of paper and paperboard in contact with aqueous and fatty foods*
- *176.180 Components of paper and paperboard in contact with dry foods*
- 176.200 Defoaming agents used in Coatings
- 176.210 Defoaming agents used in the Manufacture of paper and Paperboard

Dumacil 100-FG-K complies with the Toxic Substances Control Act PL 94-469.

Dumacil 100-FG-K is a Kosher certified product

For further information please contact:

(b) (4)

APPENDIX 4

(b) (4)

(b) (4)

(b) (4)

(b) (4)

19 August 2009

To Whom It May Concern:

(b) (4) D-100 FGK is food grade and meets the criteria in 21 CFR §173.340.

(b) (4) D-100 FGK also meets the criteria in 21 CFR §582.1 as related to substances generally recognized as safe in animal feeds.

The constituents of this product is also listed in the Current EU approved additives and their E Numbers. Therefore it complies with the Directive 95/2/EC on Food Additives other than Colours and Sweeteners.

Sincerely,

(b) (4)

APPENDIX 5

(b) (4)

(b) (4)

(b) (4)

To whom it may concern:

Dumacil 100 is expected to be stable for 1 year in an unopened package stored inside under normal conditions.

(b) (4)

(b) (4)

Krause, Andrea

From: Krause, Andrea
Sent: Friday, December 16, 2011 2:28 PM
To: 'hill@khlaw.com'
Cc: Wong, Geoffrey K
Subject: Reference Request: AGRN 000-005 and 000-007

Attachments: References_AGRN 000-007.pdf; References_AGRN 000-005.pdf

Mr. Hill,
Attached are the lists of references that we were unable to locate. Please let me know if you have any questions.

Regards,

Andrea Krause, Ph.D.
Staff Fellow Chemist
FDA, Center for Veterinary Medicine
Division of Animal Feeds, HFV-224
5219 Standish Place
Rockville, MD 20855
Phone: (240) 276-9768
Fax: (240) 453-6882
email: andrea.krause@fda.hhs.gov


References_A000-007.pdf References_A000-005.pdf

References Requested by CVM for AGRN000-005, December 16, 2011

Hydrophobic Silica (AGRN 000-005)

11.
Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, WHO Tech. Report Series; 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53.

12.
FASEB (1979). Evaluation of the Health Aspects of Certain Silicates as Food Ingredients. U.S. Department of Commerce, National Technical Information Service PB-301 402.

15.
BIBRA Working Group (1991). Polydimethylsiloxane, Toxicity Profile, BIBRA Toxicology International, 9 pages.

Krause, Andrea

From: Hill, Devon W. [Hill@khlaw.com]
Sent: Wednesday, December 21, 2011 4:15 PM
To: Krause, Andrea; Wong, Geoffrey K
Cc: Chowdhury, Azim
Subject: Reference Request: AGRN 000-005 and 000-007
Attachments: KH.zip

Dear Dr. Krause,

With the Holidays fast approaching, we wanted to give you an update on where things stand with respect to the requested reports referenced in AGRN 000-005 and AGRN 000-007. We have experienced a bit more difficulty in pulling these documents than we initially expected, in part because our staff toxicologist who worked on these GRAS notifications last year has since left the firm and some of his files became dispersed As a result, we've had to re-order several of the reports which we were not able to locate in our files.

Attached please find the following with respect to **AGRN 000-005**:

file wouldn't open

- Footnote 11: Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, WHO Tech. Report Series; 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53; and
- Footnote 12: FASEB (1979). Evaluation of the Health Aspects of Certain Silicates as Food Ingredients. U.S. Department of Commerce, National Technical Information Service PB-301 402.

The report cited in footnote 15 of AGRN 000-005, "BIBRA Working Group (1991). Polydimethylsiloxane, Toxicity Profile, BIBRA Toxicology International" has been ordered. We expect to receive a copy next week.

Attached please find the following with respect to **AGRN 000-007**:

- Footnote 7: Evaluation of Polysorbates 20,40,60,65,80 (paragraph 12), Reports of the Scientific Committee for Food (Fifteenth Series) (1985);
- Footnote 7: Opinion on Polyoxyethylene (20) Sorbitan Mono-Oleate (Polysorbate 80), Reports of the Scientific Committee for Food (Thirtyfourth Series) (September 17,1993);
- Footnote 8: Cosmetic Ingredient Review (CIR) - Final Report on Safety Assessment of Cosmetic Ingredients;
- Footnote 16: Marszall L, et. al - Toxicologial aspects of the use of span and tween products;
- Footnote 19: Kawachi T, et. al - Cooperative Program on Short-term assays for carcinogenicity in Japan;
- Footnote 23: Kada T, et. al - Screening of Environmental Chemical Mutagens;
- Footnote 36: FAO-WHO Expert Committee on Food Additives (1974);
- Footnote 46: 17th JECFA (1973) - POE 20 Sorbitan Monooleate;
- Footnote 48: [Same as Footnote 7];
- Footnote 52: [Same as Footnote 7]; and
- Footnote 64: Page SC. Jr. (1949). Experimental safety of sorbitan monostearate and its Polyoxyethylene derivatives. Fed. Proc. 8, 323.

The report cited in footnote 35, "Sugimura T. et al. 1976. Fundamentals in cancer prevention. Ed. Magee PN. et al. University of Tokyo p.191" has been ordered. We expect to receive a copy next week.

Regarding footnotes 13 and 15 in AGRN 000-007, we have not been able to locate the actual reports cited (they

are unpublished). However, we have located the attached "Final Report on the Safety Assessment of Polysorbates 20, 21, 40, 60, 61, 65, 80, 81 and 85" from the International Journal of Toxicology (1984), which similarly references those reports (see footnotes 233 and 235 therein). Rather than citing to the unpublished reports in the GRAS notification, our toxicologist should have instead cited the attached Final Report (see page 41 therein) regarding the acute oral toxicity of the polysorbates. We apologize for this oversight.

Finally, regarding the BIBRA reports in footnotes 49 and 51 of AGRN 000-007, we have ordered these and expect to receive copies next week. We are still also searching our files for the report cited in Footnote 55 "January 28, 1960 Memorandum From Division of Pharmacology to Mr. Alan T. Spiher." We will let you know as soon as we are able to locate this memorandum.

If you have any further questions or concerns, please do not hesitate to let us know.

Best regards and Happy Holidays,

Devon Hill

Devon Wm. Hill
Partner
tel: 202.434.4279 | fax: 202.434.4646 | hill@khlaw.com
1001 G Street, N.W., Suite 500 West | Washington, D.C. 20001

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From: Krause, Andrea [mailto:Andrea.Krause@fda.hhs.gov]
Sent: Friday, December 16, 2011 2:28 PM
To: Hill, Devon W.
Cc: Wong, Geoffrey K
Subject: Reference Request: AGRN 000-005 and 000-007

Mr. Hill,
Attached are the lists of references that we were unable to locate. Please let me know if you have any questions.

Regards,

Andrea Krause, Ph.D.
Staff Fellow Chemist
FDA, Center for Veterinary Medicine
Division of Animal Feeds, HFV-224
5219 Standish Place
Rockville, MD 20855
Phone: (240) 276-9768
Fax: (240) 453-6882
email: andrea.krause@fda.hhs.gov

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Pages 49-90 have been removed in accordance with copyright laws. Please see footnotes/emails in document for list of references of copyrighted information.

Krause, Andrea

From: Chowdhury, Azim [chowdhury@khlaw.com]
Sent: Friday, December 23, 2011 2:24 PM
To: Krause, Andrea
Cc: Hill, Devon W.
Subject: RE: Reference Request: AGRN 000-005 and 000-007
Attachments: Cosmetic Ingredient Review - Final Report on Safety Assessment of cosmetic ingredients.pdf; Evaluation of the Health Aspects of Certain Silicates as Food.pdf; Sugimura T. et al. 1976. Fundamentals in cancer prevention. Ed. Magee PN. et al. University of Tokyo p.191.pdf

Dear Dr. Krause,

Devon Hill asked me to respond to your below request. Please find attached PDFs of "Evaluation of the Health Aspects of Certain Silicates as Food" and "Cosmetic Ingredient Review-Final Report on Safety Assessment of Cosmetic Ingredients." I've also attached the missing footnote 35 from AGRN 000-007, "Sugimura T. et al. 1976. Fundamentals in cancer prevention. Ed. Magee PN. et al. University of Tokyo p.191." If you have any problems opening these electronic files, please let us know.

We are trying to locate an English translation of the Marszall article, and will get back to you as soon as possible.

If there is anything else you need, please do not hesitate to let us know.

Best regards and Happy Holidays,

Azim

Azim Chowdhury
Associate
tel: 202.434.4230 fax 202.434.4646 | chowdhury@khlaw.com
1001 G Street, N.W., Suite 500 West | Washington, D.C. 20001

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From: "Krause, Andrea" <Andrea.Krause@fda.hhs.gov>
Date: December 23, 2011 11:51:58 AM EST
To: "'Hill, Devon W.'" <Hill@khlaw.com>
Subject: RE: Reference Request: AGRN 000-005 and 000-007

Mr. Hill,
Thank-you for your prompt reply. We are unable to open two of the files you sent ("Evaluation of the Health Aspects of Certain Silicates as Food" and "Cosmetic Ingredient Review-Final Report on Safety Assessment of Cosmetic Ingredients"). If you could resend those two files at your convenience, it would be much appreciated. Also, the article by Marszall L, et al. (Tox aspects of the use of span and tween products) is in another language. If you have a translation of that in your possession, could you send it as well? If you don't have it, there's no need to get it--we can make do without--just thought I'd check. Thanks again.

Regards,
Andrea

From: Hill, Devon W. [mailto:Hill@khlaw.com]
Sent: Wednesday, December 21, 2011 4:15 PM
To: Krause, Andrea; Wong, Geoffrey K
Cc: Chowdhury, Azim
Subject: Reference Request: AGRN 000-005 and 000-007

Dear Dr. Krause,

With the Holidays fast approaching, we wanted to give you an update on where things stand with respect to the requested reports referenced in AGRN 000-005 and AGRN 000-007. We have experienced a bit more difficulty in pulling these documents than we initially expected, in part because our staff toxicologist who worked on these GRAS notifications last year has since left the firm and some of his files became dispersed As a result, we've had to re-order several of the reports which we were not able to locate in our files.

Attached please find the following with respect to **AGRN 000-005**:

- Footnote 11: Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, WHO Tech. Report Series; 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53; and
- Footnote 12: FASEB (1979). Evaluation of the Health Aspects of Certain Silicates as Food Ingredients. U.S. Department of Commerce, National Technical Information Service PB-301 402.

The report cited in footnote 15 of AGRN 000-005, "BIBRA Working Group (1991). Polydimethylsiloxane, Toxicity Profile, BIBRA Toxicology International" has been ordered. We expect to receive a copy next week.

Attached please find the following with respect to **AGRN 000-007**:

- Footnote 7: Evaluation of Polysorbates 20,40,60,65,80 (paragraph 12), Reports of the Scientific Committee for Food (Fifteenth Series) (1985);
- Footnote 7: Opinion on Polyoxyethylene (20) Sorbitan Mono-Oleate (Polysorbate 80), Reports of the Scientific Committee for Food (Thirtyfourth Series) (September 17,1993);
- Footnote 8: Cosmetic Ingredient Review (CIR) - Final Report on Safety Assessment of Cosmetic Ingredients;
- Footnote 16: Marszall L, et. al - Toxicologial aspects of the use of span and tween products;
- Footnote 19: Kawachi T, et. al - Cooperative Program on Short-term assays for carcinogenicity in Japan;
- Footnote 23: Kada T, et. al - Screening of Environmental Chemical Mutagens;

- Footnote 36: FAO-WHO Expert Committee on Food Additives (1974);
- Footnote 46: 17th JECFA (1973) - POE 20 Sorbitan Monooleate;
- Footnote 48: [Same as Footnote 7];
- Footnote 52: [Same as Footnote 7]; and
- Footnote 64: Page SC. Jr. (1949). Experimental safety of sorbitan monostearate and its Polyoxyethylene derivatives. Fed. Proc. 8, 323.

The report cited in footnote 35, "Sugimura T. et al. 1976. Fundamentals in cancer prevention. Ed. Magee PN. et al. University of Tokyo p.191" has been ordered. We expect to receive a copy next week.

Regarding footnotes 13 and 15 in AGRN 000-007, we have not been able to locate the actual reports cited (they are unpublished). However, we have located the attached "Final Report on the Safety Assessment of Polysorbates 20, 21, 40, 60, 61, 65, 80, 81 and 85" from the International Journal of Toxicology (1984), which similarly references those reports (see footnotes 233 and 235 therein). Rather than citing to the unpublished reports in the GRAS notification, our toxicologist should have instead cited the attached Final Report (see page 41 therein) regarding the acute oral toxicity of the polysorbates. We apologize for this oversight.

Finally, regarding the BIBRA reports in footnotes 49 and 51 of AGRN 000-007, we have ordered these and expect to receive copies next week. We are still also searching our files for the report cited in Footnote 55 "January 28, 1960 Memorandum From Division of Pharmacology to Mr. Alan T. Spiher." We will let you know as soon as we are able to locate this memorandum.

If you have any further questions or concerns, please do not hesitate to let us know.

Best regards and Happy Holidays,

Devon Hill

Devon Wm. Hill
Partner
tel: 202.434.4279 | fax: 202.434.4646 | hill@khlaw.com
1001 G Street, N.W., Suite 500 West | Washington, D.C. 20001

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From: Krause, Andrea [mailto:Andrea.Krause@fda.hhs.gov]
Sent: Friday, December 16, 2011 2:28 PM
To: Hill, Devon W.
Cc: Wong, Geoffrey K
Subject: Reference Request: AGRN 000-005 and 000-007

Mr. Hill,
Attached are the lists of references that we were unable to locate. Please let me know if you have any questions.

Regards,

Andrea Krause, Ph.D.
Staff Fellow Chemist
FDA, Center for Veterinary Medicine
Division of Animal Feeds, HFV-224
5219 Standish Place
Rockville, MD 20855
Phone: (240) 276-9768
Fax: (240) 453-6882
email: andrea.krause@fda.hhs.gov

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Krause, Andrea

From: Hill, Devon W. [Hill@khlaw.com]
Sent: Tuesday, January 10, 2012 11:00 AM
To: Krause, Andrea; Wong, Geoffrey K
Cc: Chowdhury, Azim
Subject: Reference Request: AGRN 000-005 and 000-007
Attachments: JC Krantz - 1951 36 BullSchMedUnivMD 48.pdf; Reports of the Scientific Committee for Food (Fifteenth Series) (1985);(2).pdf

Dear Dr. Krause,

I apologize that I missed your call this morning as I was in a meeting. I will plan to call you this afternoon, but first I wanted to provide you with a substantive response regarding our efforts to respond to FDA's request for certain references mentioned in our filing.

Following up on your request for the references cited in AGRN 000-005 and AGRN 000-007, the purpose of this e-mail is to provide you with an update on the status of our search. Unfortunately, we were unable to locate an English translation of the Marszall article in our files; if you would like us to have the article translated, please let us know.

Additionally, we were unable to locate the unpublished data sited in Footnote 15 of AGRN 000-007 by Krantz JC. However, in lieu of that unpublished information, please see the attached article by the same author (Krantz), "Sugar Alcohols -- XXVII. Toxicological, Pharmacodynamic and Clinical Observations on Tween 80." We believe this article summarizes the safety data on Tween 80, polyoxyethylene (20) sorbitan oleate, and the C18 oleate analog of polyoxyethylene (20) sorbitan stearate. This article cites to studies and presents data from studies conducted in the time period of 1943-1947 on the Tween (Polysorbate) products. The article provides support to the LD50 values that were supported by the unpublished data on the Tween (Polysorbate) products cited in the unpublished dated referred to in AGRN 000-0007.

Regarding the BIBRA reports cited, we were unable to find copies of the reports in our files. We contacted BIBRA, and have ordered the report referenced in AGRN 000-0005, "BIBRA Working Group (1991). Polydimethylsiloxane, Toxicity Profile, BIBRA Toxicology International." We expect to receive a copy of this report this week (it was mailed to us on 12/23/11), and will send it to you as soon as we do. Regarding the two BIBRA reports cited in AGRN 000-007, we were also unable to locate these in our files, unfortunately. We contacted BIBRA to re-order the reports, but were informed that these particular reports are no longer maintained in BIBRA's files (many of the old reports such as these have apparently been destroyed or sent back to the study sponsers). In lieu of these BIBRA reports, please see the attached "Reports of the Scientific Committee for Food (Fifteenth Series)," which was previously provided to you. We note that both the 1981 short-term (13 week) study in rats with polyoxyethylene (20) sorbitan monostearate (Footnote 49) and the 1983 review of the status of polysorbates (Footnote 51) are cited as references here (see bottom of page 7). Please let us know if this will be sufficient for your needs.

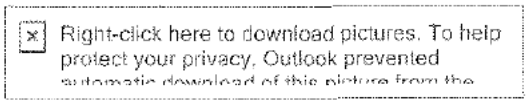
I look forward to speaking with you. As always, if you have any additional questions or concerns, or if you would like to set up a conference call to discuss, please do not hesitate to let us know.

Best regards,

Devon Hill

Devon Wm. Hill

Partner
tel: 202.434.4279 | fax: 202.434.4646 | hill@khlaw.com
1001 G Street, N.W., Suite 500 West | Washington, D.C. 20001



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tel. 202.434.4100
fax 202.434.4646

T-2

Writer's Direct Access
Devon Wm. Hill
(202) 434-4279
hill@khlaw.com

February 14, 2012

Via Electronic Mail and Federal Express

Dr. Andrea Krause, Ph.D.
Food and Drug Administration
Division of Animal Feeds (HFV-224)
Center for Veterinary Medicine
7519 Standish Place
Rockville, Maryland 20855

Re: Amendment to AGRN 000-005; GRAS Notification for Hydrophobic Silica; Our File No. EM13458-01

Dear Dr. Krause:

On behalf of our client, Emerald Carolina Chemicals, LLC (the Notifier), we hereby respectfully submit the enclosed Amendment to the Generally Recognized as Safe (GRAS) notification for hydrophobic silica, designated AGRN 000-005, filed on April 8, 2011. As discussed in detail in AGRN 000-005, the Notifier's defoamer product is added to the condensed distillers solubles (*i.e.*, thin stillage concentrate) to assist in separating out corn oil during processing of grain from ethanol distillation. Accordingly, the hydrophobic silica defoamer component may be present at minute levels as an impurity in distillers grains fed to the food-producing animals.

Pursuant to our telephone conferences on January 26, 2012 and February 3, 2012, you asked us to provide (1) assurance that the Notifier's hydrophobic silica meets the specifications set forth in 21 C.F.R. § 584.700 ("Hydrophobic Silica"); (2) a description for how the hydrophobic silica functions as a defoamer; (3) a revised GRAS Status Claim which specifies the food-producing target animal species that are subject to the notification; and (4) a description of why turkeys, egg laying hens and goats should be included among the types of food-producing target animal species subject to this GRAS notification.

Accordingly, the enclosed Amendment to AGRN 000-005 includes the following:

(1) Signed Letter, dated February 2, 2012, from (b) (4) (b) (4), stating that their (b) (4) Dumacil 100 FGK hydrophobic silica product meets all the specifications listed in 21 C.F.R. §

584.700, except for the dicholorodimethylsilane content, which does not apply to the Dumacil 100 FGK.[1]

(2) A detailed description of hydrophobic silica's chemical and physical properties that enable it to function as a defoamer (*i.e.*, its defoaming mechanism).

(3) A detailed description and dietary intake calculations demonstrating why turkeys, egg laying hens and goats should be included among the types of food-producing target animal species subject to this GRAS notification.

(4) A revised GRAS Status Claim which states that the hydrophobic silica is GRAS when present as an impurity in animal feed for the following food-producing target animal species: beef cattle, dairy cattle, poultry (turkey, broiler chickens and egg laying hens), sheep, goat and swine.

The enclosed Amendment to AGRN 000-005 is provided in triplicate. We trust that this Amendment satisfies the Agency's needs, and will be deemed accepted and complete. Should any questions arise, please contact us, preferably by telephone or e-mail, so that we can promptly respond.

Sincerely,

Devon Wm. Hill

Cc: Geoffrey Wong, Ph.D.

Enclosure

[1] The (b) (4) Dumacil 100 FGK is produced by reacting untreated hydrophobic silica with silicone oil (polydimethylsiloxane) at high temperatures (rather than with dicholorodimethylsilane).

Amendment to AGRN 000-005
Generally Recognized as Safe (GRAS) Notification for Hydrophobic Silica (CAS Reg. No. 67762-90-7)

Prepared for:

U.S. Food and Drug Administration
Center for Veterinary Medicine
Division of Animal Feeds (HFV-224)
7519 Standish Place
Rockville, MD 20855

Notifier:

Emerald Carolina Chemical, LLC
8309 Wilkinson Boulevard
Charlotte, NC 28214-9052

February 14, 2012

Table of Contents

I. Assurance Letter from (b) (4)

Please see attached (**Attachment 1**) the signed letter, dated February 2, 2012, from (b) (4), stating that the (b) (4) Dumacil 100 FGK hydrophobic silica product meets all the specifications listed in 21 C.F.R. § 584.700, except for the dicholorodimethylsilane content, which does not apply to the (b) (4) Dumacil 100 FGK. More specifically, the (b) (4) Dumacil 100 FGK, as described in AGRN 000-005, is produced by reacting untreated hydrophobic silica with silicone oil (polydimethylsiloxane) at high temperatures (rather than with dicholorodimethylsilane). Accordingly, the specification in Section 584.700 regarding the dicholorodimethylsilane content is not applicable to the Notifier's product.

II. Hydrophobic Silica Defoaming Mechanism

Hydrophobic silica is used as a component of a defoamer that is added to condensed distillers solubles (CDS) prior to processing in a mechanical centrifuge that separates corn oil from the aqueous CDS. A defoamer is a chemical additive that functions to reduce and inhibit the formation of foam in industrial process liquids. This action eliminates problems that occur with the presence of surface foam or entrapped air that can lead to reduced efficiency in industrial processes such as pumping, separation, and centrifugation.

Foam is frequently produced in hydrophilic-hydrophobic mixtures, and will especially be formed during the separation of hydrophobic corn oil from aqueous concentrated stillage or CDS in the production of distillers grains at ethanol production plants. Generally a defoamer is insoluble in the foaming medium and has surface active properties such that it has an affinity to the air-liquid surface where it destabilizes foam lamellas causing the rupture of air bubbles and breakdown of surface foam.

The properties of a defoamer which facilitate the rupture of the foam film include (1) insolubility in the foam medium, (2) facile dispersability in the foam medium, (3) chemical inertness, and (4) a lower surface tension than the foam medium. Insolubility is important because if a defoamer was soluble in a foam film, its surfactant properties would lead to reinforced foam formation. Easy dispersability allows the defoamer to be dispersed in the medium quickly with agitation. Chemical inertness is important to ensure that a defoamer will not react with any components in the medium.

Hydrophobic silica, with its hydrophobic surface, will function as a defoamer when used in combination with surfactants in the application of interest. The surfactants allow the hydrophobic silica to become dispersed in the CDS medium from which it is transferred to the air-liquid surface where it enters the foam interface and bridges across adjacent foam films. Due to its low surface tension, the hydrophobic surface of the silica "punctures" the foam film surface which leads to a foam film contraction, and eventual rupture of the foam film.

III. Inclusion of Turkeys, Egg Laying Hens and Goats to List of Target Animal Species

AGRN 000-005 provides that, although the animal species tested were predominantly rats, the toxicology data is equally applicable to the following food-producing target animal species: beef cattle, dairy cattle, poultry (broiler chickens), sheep and swine. For the reasons set forth herein, **turkeys, egg laying hens and goats** should be included in the list of food-producing target animals subject to this notification. The calculations below demonstrate that the maximum dietary intake of hydrophobic silica for each of the new target animal species is below the conservative Acceptable Daily Intake (ADI) of 1 mg/kg-bw/day.

First, we calculate the amount of distillers grains consumed on a dry basis for each animal. Next, using the maximum residual level of 13.9 mg/kg of hydrophobic silica in the distillers grains on a dry basis, we calculate the maximum amount of hydrophobic silica consumed (*i.e.*, the maximum dietary intake) for each target animal species. This value is then compared to the very conservative ADI for hydrophobic silica for the target animal species.

a. Amount of Distillers Grains Consumed by Target Animal Species

An egg laying hen has an average body weight of 4.2 lb (1.9 kg) and consumes 52 g of dry feed per day for a food consumption of 52 g/1.9kg = 27 g/kg bw/day[1]. Assuming that egg laying hens consume no more than 15% by weight dry distillers grains in feed[2], the maximum daily consumption of distillers grains for egg laying hens is 27 g/kg bw/day x 15% = 4.1 g/kg bw/day.

A female turkey is reported to have an average body weight of 8.1 kg and consumes 2.23 kg of dry feed per week (2.23 kg/wk x 1000 g/kg ÷ 7 days/wk = 320 g/day) or 320 g/day for a daily feed intake of 320 g/day ÷ 8.1 kg bw = 39.5 g/kg bw/day.[3] Additionally, a male turkey is reported to have an average body weight of 12.8 kg and consumes 3.6 kg of dry feed per week or 514 g of feed per day (3.6 kg x 1,000 g/kg ÷ 7 days/wk = 514 g) for a daily intake of 514 g/ 12.8 kg bw= 40 g/kg bw/day. Assuming that female turkeys consume no more than 15% by weight of dry distillers grains[4], and male turkeys consume no more than 20% by weight dry

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1 "Revisions of Feedstuffs in Table 1 of OPPTS Test Guideline 860.100 and Guidance on Constructing Maximum Reasonably Balanced Diets (MRBD)," United States Environmental Protection Agency, Jan. 30, 2008. page 5, available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0155-0003.

2 Using Distillers Grains in the U.S. and International Livestock and Poultry Industries, *see* http://www.card.iastate.edu/books/distillers_grains/pdfs/distillers_grains_book.pdf.

3 J.D. Furman. Nutrient Requirements of Chickens and Turkeys. 8th ed. 1984. National Academy Press. Washington, D.C., see http://www.afn.org/~poultry/flkman9.htm.

4 B.A. Babcock, D.J. Hayes, J.D. Lawrence. Using Distillers Grains in the U.S. and International Livestock and Poultry Industries. The Midwest Agribusiness Trade Research and

distillers grains[5], the maximum daily amount of distillers grains consumed is 6 g/kg bw/day[6] for female turkeys and 8 g/kg bw/day for male turkeys.[7]

The maximum daily dry feed intake for goats is 4% of their body weight or 40 g/kg bw/day (0.04 kg/kg bw/day x 1000 g/kg = 40 g/kg bw/day).[8] Assuming a goat consumes no more than 30% by weight dry distillers grains in their feed[9], the maximum daily consumption of distillers grains is 40 g/kg bw/day x 30% = 12 g/kg bw/day.

b. Maximum Dietary Intake of Hydrophobic Silica for each Target Animal Species

As the concentration of hydrophobic silica in distillers grains is 13.9 mg-hydrophobic silica/kg-distillers grains, the maximum dietary intake of the substance in turkey, egg laying hens, and goats are presented in the following revised tables:

TABLE 1. Feeding Data for Food-Producing Target Animals

Target Animal Species	Weight (kg)	Food Consumed (g/day)	Distillers Grains (dry weight basis) Consumed per Day		
			(%)	(g/day)	g/kg bw/day
Beef Cattle	500	10,000	30%	3,000	6
Dairy Cattle	500	10,000	30%	3,000	6

Information Center. 2008. p.128, available at http://www.card.iastate.edu/books/distillers_grains/pdfs/distillers_grains_book.pd.

[5] See "Value-added Feed Source for Beef, Diary Beef, Dairy, Poultry, Swine, Sheep," National Corn Growers Association (NCGA), September 9, 2008, available at http://www.ethanol.org/pdf/contentmgmt/NCGA_Distillers_Grain_908-1.pdf.

[6] 40 g/kg bw/day x 15% = 6 g/kg bw/day.

[7] 40 g/kg bw/day x 20% = 8 g/kg bw/day.

[8] M. Rashid, "Goats and their Nutrition," Manitoba Goat Association, *see* http://www.gov.mb.ca/agriculture/livestock/goat/pdf/bta01s08.pdf.

[9] T. Hutchens and R. Harmon. Adding Value to Kentucky Products by Feeding Distillers Dried Grains (Report Summer 2005). Goat Producer's Newsletter. University of Kentucky. November 2005. Available at http://www.distillersgrains.org/files/feedsource/Hutchens_11_05.pdf

Target Animal Species	Weight (kg)	Food Consumed (g/day)	Distillers Grains (dry weight basis) Consumed per Day (%)	(g/day)	g/kg bw/day
Poultry[10]					
(broiler)	2.5	232.5	15%	34.9	14
Egg laying hen	1.9	52	15%	7.8	4.1
Female turkey	8.1	320	15%	48	6
Male turkey	12.8	514	20%	102.8	8
Sheep	60	2,400	30%	720	12
Swine	60	2,400	30%	720	12
Goat	-	4% (maximum of body weight)	30%		12[11]

With a maximum residual level of 13.9 mg/kg of hydrophobic silica in distiller's grains on a dry weight basis, a maximum dietary intake for laying hens is calculated as follows:

4.1 g-distillers grain/kg bw x (13.9 mg- HPS/kg-distillers grains) x (kg/1000 g)

= 0.08 mg HPS/kg bw/day

The dietary intake of hydrophobic silica by the other food-producing target animals is similarly calculated and presented in the table below:

TABLE 2. EDIs for Target Animals

Target Animal Species	EDI (mg/kg-bw/day) for Hydrophobic Silica
Beef Cattle	0.08
Dairy Cattle	0.08
Poultry	
(Broiler)	0.2
(Egg Laying Hen)	0.06[12]

[10] The feed consumption for broiler chickens is reported to be 93 mg/kg bw/day – Predicting Feed Intake of Food-Producing Animals, Subcommittee on Feed Intake, Committee on Animal Nutrition, Board on Agriculture, National Research Council, National Academy Press, Washington, D.C., 1987.

[11] 40 g/kg bw/day x 30% = 12 g/kg bw/day.

[12] 4.1 g-distillers grain/kg bw x (13.9 mg-HPS/kg-distillers grains) x (kg/1000 g) = 0.06 mg HPS/kg bw/day.

Target Animal Species	EDI (mg/kg-bw/day) for Hydrophobic Silica
(Turkey - Female) (Turkey – Male)	0.08[13] 0.1[14]
Sheep	0.17
Swine	0.17
Goat	0.17[15]

IV. Revised GRAS Status Claim

Hydrophobic silica is GRAS based on scientific procedures, when present at levels up to 20 ppm, as an impurity in animal feed for food-producing target animal species (*e.g.*, beef cattle, dairy cattle, poultry (turkey, broiler chickens and egg laying hens), sheep, goat and swine) as a result of its use as an emulsifier in the production of wet and dried distillers grain with added solubles (WDGS and DDGS, respectively). Hydrophobic silica serves no technical purpose in the animal feed itself. Accordingly, the GRAS substance that is the subject of this notification is only present as a potential impurity in the WDGS and DDGS due to its use in the processing of the CDS.

The use of hydrophobic silica in this manner as a component of the Notifier's defoamer product has been determined to be exempt from the premarket approval requirements of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 301 *et. seq.*).

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[13] 6 g-distillers grain/kg bw x (13.9 mg-HPS/kg-distillers grains) x (kg/1000 g) = 0.08 mg HPS/kg bw/day.

[14] 8 g-distillers grain/kg bw x (13.9 mg-HPS/kg-distillers grains) x (kg/1000 g) = 0.1 mg HPS/kg bw/day.

[15] 12 g-distillers grain/kg bw x (13.9 mg-HPS/kg-distillers grains) x (kg/1000 g) = 0.17 mg HPS/kg bw/day.

Attachment 1

(b) (4)

(b) (4)

(b) (4)

February 2, 2012

To whom it may concern:

Our product, (b) (4) Dumacil 100 FGK, is a hydrophobic silica product that meets all of the specifications listed in 21 CFR 584.700, other than the dicholorodimethylsilane content which does not apply to (b) (4) Dumacil 100 FGK.

Sincerely,

(b) (4)