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TEMPLATE:

Columbia River Carbonates

[Insert petition number]

EPA has received a pesticide petition ([insert petition number]) from Columbia River Carbonates, 300 North Pekin Road, Woodland, Washington 98674 requesting, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 to establish an exemption from the requirement of a tolerance for the biochemical pesticide calcium carbonate.

Pursuant to section 408(d)(2)(A)(i) of FFDCA, as amended, Columbia River Carbonates has submitted the following summary of information, data, and arguments in support of their pesticide petition. This summary was prepared by Columbia River Carbonates and EPA has not fully evaluated the merits of the pesticide petition. The summary may have been edited by EPA if the terminology used was unclear, the summary contained extraneous material, or the summary unintentionally made the reader conclude that the findings reflected EPA's position and not the position of the petitioner.

I. Columbia River Carbonates Petition Summary

[Insert petition number]

A. Product Name and Proposed Use Practices

MICRONA™ Shield WP consists of 98.8% calcium carbonate (CAS No. 471-34-1; PC Code is 73502) obtained from mining naturally occurring mineral limestone (CAS

No. 1317-65-3) which is then processed into an ultrafine powder. Calcium carbonate acts as a mechanical insecticide by forming a barrier to an insect pest. The ultrafine particles that cover the crop plant repel and suppress the pest. Calcium carbonate absorbs the pests' moisture and leads to desiccation (dehydration) resulting in the death of sensitive insect life stages.

B. Product Identity/Chemistry

1. *Identity of the pesticide and corresponding residues.* Nature of the Residue data are conditionally required when Tier II and Tier III studies as listed in 40 CFR § 158.2040 are required and when tolerances are proposed. An exemption from tolerance is proposed for all raw agricultural commodities. MICRONA™ Shield WP consists of 98.8% calcium carbonate (CAS No. 471-34-1 for precipitated calcium carbonate; 13397-26-7 for calcite) obtained from mining the naturally occurring mineral limestone (CAS No. 1317-65-3) followed by processing into an ultrafine powder. The calcium carbonate is not obtained using any thermal or chemical process which might alter the characteristics of limestone.

2. *Magnitude of residues at the time of harvest and method used to determine the residue.* Magnitude of the Residue data are conditionally required when Tier II and Tier III studies as listed in 40 CFR § 158.2050 are required and when tolerances are proposed. An exemption from tolerance is proposed for all raw agricultural commodities.

3. *A statement of why an analytical method of detecting and measuring the levels of the pesticide residue are not needed.* A residue analytical method suitable for enforcement of tolerances is required when a numerical tolerance is proposed. An exemption from tolerance is proposed for all raw agricultural commodities.

C. Mammalian Toxicological Profile

Columbia River Carbonates submitted a rationale for using nanocalcium carbonate as a surrogate for their calcium carbonate product which is considered microcalcium carbonate. Consequently, mammalian toxicity studies were submitted on both microcalcium carbonate and nanocalcium carbonate and are summarized below.

1. Acute toxicity. Calcium carbonate (micro and nano) has low acute toxicity. The acute oral toxicity of micro- and nanocalcium carbonate is >2000 mg/kg bw. The acute dermal LD50 of nanocalcium carbonate was >2000 mg/kg bw and the acute inhalation LC50 of microcalcium carbonate was >3 mg/L. Microcalcium carbonate was minimally irritating to the rabbit eye and was non-irritating to rabbit skin. Nanocalcium carbonate was negative in a local lymph node assay and therefore is not considered to be a dermal sensitizer.

2. Genotoxicity. Studies on the potential genotoxicity of calcium carbonate are only available on nanocalcium carbonate which was tested in two Ames *Salmonella* assay, two *in vitro* chromosomal aberration assays, a mouse lymphoma assay and a mouse micronucleus test. Nano calcium carbonate was negative in both Ames *Salmonella* assays with and without metabolic activation in all *Salmonella* strains tested

and in *Escherichia coli* strain WP2uvrA. It was also negative for inducing chromosomal aberrations in Chinese hamster ovary fibroblasts and human lymphocytes both with and without metabolic activation and for inducing gene mutations in the mouse lymphoma assay both with and without metabolic activation. The mouse micronucleus test was negative up to the limit dose for this study (2000 mg/kg bw).

3. Reproductive and developmental toxicity.

a) The calcium carbonate (98.62% purity) used in the developmental toxicity study was US Pharmacopeia-grade and was obtained from Pfizer. In this study, Charles River CD.VAF Plus female rats (~50/group) were administered 0.5 (control), 0.75, 1.0 or 1.25% dietary calcium as calcium carbonate (98.62% purity) in AIN-76A diet for six weeks prior to mating, during mating and for 20 days during gestation. The mineral mix of the AIN-76A diet was modified slightly to maintain the concentrations of calcium carbonate of the test diets and a phosphorous level of 0.40%. After the six-week premating period, the females were mated to males in a 2:1 ratio. The day on which sperm was found in the vaginal smear was considered to be day 0 of gestation. The dams were killed on day 20 of gestation. The following clinical signs were observed: alopecia, exudate around the eyes, exudate around the nose, bent teeth, lumps in the left flank or leg and mammary lump. Three females died on study; however, the deaths were not attributed to dietary calcium. Two deaths were due to accidents and the third animal was found moribund and bleeding from the urethra. There were no consistent effects on body weight gain across groups. The dams on the excess calcium diets tended to eat more than the control group, but not all the increases were statistically significant. No adverse effects were observed on reproductive parameters. Significant increases were seen in implantation efficiency at the 1.25% dietary level and in the average number of viable female fetuses at 0.75 and 1.25% dietary calcium. These increases were not dose related and were not considered to be caused by dietary calcium or calcium carbonate. Fetal body weights and crown-rump length were unaffected by excess dietary calcium or calcium carbonate. In addition, there were no effects on the number of litters with runts. No treatment-related effects were observed on the incidence of external, visceral or skeletal abnormalities. The no observed adverse effect level (NOAEL) was considered to be a concentration of 1.25% in the diet. This level equates to a NOAEL of 1963 to 2188 mg/kg bw/day for calcium carbonate.

b) A combined repeated dose study with reproduction/developmental toxicity screening test was conducted according to OECD guideline 422 on nanocalcium carbonate. Nanocalcium carbonate (98.5% purity) was administered to male and female Wistar Han™:WIST rats (10/sex/group) by gavage for up to 48 days (including a two-week maturation phase, pairing, gestation and early lactation for females) at dose levels of 0 (distilled water), 100, 300 and 1000 mg/kg bw/day. Prior to the start of treatment and at weekly intervals thereafter, all animals were observed for signs of functional/behavioral toxicity. Function performance tests were performed on 5 males and 5 females from each dose group prior to termination together with an assessment of sensory reactivity to various stimuli. Individual body weights were recorded and food consumption was monitored. The following was recorded for each female: date of pairing, date of mating, date and time of observed start of parturition and date and time of

observed completion of parturition. The following reproductive indices were calculated: pre-coital interval, mating index and pregnancy index. Gestation length, parturition index, percent pre-implantation loss, post-implantation loss, live birth index, viability index and sex ration were also calculated. The following was recorded for each litter: number of offspring, number of live offspring, sex on days 1 and 4 of lactation, clinical condition of offspring from birth to day 5 postpartum and body weights on days 1 and 4 postpartum. All live offspring were assessed for surface righting reflex on day 1 postpartum. Parental animals were evaluated for hematology, coagulating and clinical chemistry parameters on day 42 for males and day 4 postpartum for females. A complete necropsy was performed on all animals on study. The uterus was examined for signs of implantation and the number of uterine implantations in each horn. The following organs were weighed: adrenals, brain, epididymides, heart, kidneys, liver, pituitary, seminal vesicles, spleen, testes, thymus, ovaries, prostate and thyroid. A full set of tissues/organs was saved for possible microscopic examination. The tissues from five selected control and high dose group animals and any animals dying on study were prepared for microscopic examination. One male in the high dose group was killed in extremis. The cause of death was determined to be a gavage error. There were no other deaths on study. No toxicologically significant clinical signs were observed. No treatment-related effects were noted on behavioral assessments, functional performance tests or sensory reactivity tests. Body weights, body weight gain and food consumption were unaffected by treatment in the parental animals. Treatment did not result in any effects on reproductive performance or effects on offspring. Males in the high dose group had a statistically significant reduction in MCH and MCV; however, all values were with the normal range for rats of this strain and age and therefore, the changes were not considered to be of toxicological importance. A statistically significant decrease in total protein and increase in chloride concentration was observed in males in the high dose group. All individual values were within the normal range and were therefore the changes were not considered to be of toxicological relevance. No treatment-related effects were observed on organ weights nor were there any effects of treatment observed upon gross necropsy of the parental animals or their offspring. Histopathology did not reveal any treatment-related effects on the tissues/organs examined. The NOAEL for systemic and reproductive toxicity was considered to be 1000 mg/kg bw/day.

4. Subchronic toxicity.

a) A 90-day oral toxicity study was conducted on nanocalcium carbonate. The nano form of calcium carbonate was tested because this form was anticipated to represent the worst case as it is likely to be more soluble than the bulk form due to the smaller particle size and hence greater surface area for systemic absorption. Male and female Sprague-Dawley rats (10/sex/group) were administered nanocalcium carbonate (>98% purity) by gavage at dose levels of 0, 250, 500 or 1000 mg/kg bw/day for 90 days. All rats survived to study termination. There were no clinical signs of toxicity and body weights and food consumption were not statistically different from the control group. White blood cell count, lymphocyte count and % monocytes were statistically lower in female rats in the 500 mg/kg bw/day group. These effects were not considered toxicologically significant because they were within in the normal range and occurred without a dose response. Calcium levels were statistically increased in females at the

high dose; however, the level remained within the normal range and therefore was not considered toxicologically relevant. Upon urinalysis, pH was statistically increased in males at all dose levels. The effect on pH was not considered treatment related because it was seen in males only and there were no effects on the kidney seen macro- or microscopically or on BUN or creatinine levels. The pH of the urine was ~7.5 in controls, 8.0 in the low dose group and 8.5 in the mid and high dose groups. No treatment-related effects were observed on organ weights nor on the incidence of macroscopic or microscopic findings. The NOAEL was the highest dose tested or 1000 mg/kg bw/day and the limit dose for studies of this type.

b) Columbia River Carbonates provided a rationale to satisfy the requirement for 90-day dermal toxicity data in the rat with calcium carbonate based on existing toxicology data and other information as follows: Low acute dermal toxicity (LD50>2,000 mg/kg bw) and low acute oral toxicity (LD50>2,000 mg/kg bw) of micro and/or nanocalcium carbonate; the 90-day oral toxicity study in the rat demonstrates that there are no concerns regarding repeated dose oral toxicity of nanocalcium carbonate with a NOAEL of 1,000 mg/kg bw/day (highest dose tested); and a weight of the evidence evaluation on strength of the evidence for waiving the requirement of a 90-day dermal toxicity study.

c) A 90-day inhalation toxicity study was conducted on nanocalcium carbonate. Male and female Wistar Hannover (RccHan®:WIST) rats (10/sex/group) were exposed nose only to target concentrations of 0, 0.025,0.125, 0.210 or 0.400 mg/L nanocalcium carbonate (98/99% purity) for 13 weeks. The rats were exposed for 6 hours/day, 5 days/week over a 13-week period. Two additional groups (control and high dose group; 10/sex/group) were continued on study for an additional 4 weeks as recovery groups. The actual achieved concentrations of nanocalcium carbonate were determined to be 0, 0.026, 0.123, 0.212 and 0.399 mg/L for the control, low, low mid, high mid and high dose, respectively. No mortality occurred during the study and no treatment-related clinical signs were observed. Ophthalmoscopic examination did not reveal any treatment-related findings. Body weights were not affected by treatment in males; however, in females body weight was slightly but statistically significantly decreased during the first month of treatment which resolved after the first month. Food consumption was comparable across groups. No treatment-related or biologically significant changes in hematology, coagulation or clinical chemistry values were observed in the treated groups compared to controls. Absolute left lung weight and lung weight relative to body weight were statistically increased in males at the high dose and in females at the low mid dose and high dose. No treatment-related macroscopic findings were observed nor were there any microscopic findings that were considered to be treatment related. Slight increases in BAL-derived inflammation and cytotoxicity biomarkers, indicating a minimal inflammatory response in the lungs were observed. Given the convergence of changes in pulmonary toxicological endpoints at 0.400 mg/L—increased lung weights accompanied by increases in BAL-derived inflammation and by toxicity biomarkers, which (in females only) were not fully reversible within a 4-week recovery period—exposure to 0.400 mg/L [measured concentration] nanocalcium carbonate was considered to have resulted in an adverse response in the lower airways. The findings at 0.210 mg/L to be limited and non-adverse since they were not

substantiated by any effects on lung weights or histopathology of the lung. The systemic NOAEC was considered to be the highest dose tested or 0.400 mg/L (measured concentration 0.399 mg/L). The NOAEC for local respiratory effects was considered to be 0.210 mg/L (measured concentration 0.212 mg/L) based on effects on BAL parameters at 0.400 mg/L which were seen along with an increase in lung weights.

d) The existence of a 90-day inhalation toxicity study on nanocalcium carbonate. Male and female Wistar Hannover (RccHan®:WIST) rats (10/sex/group) were exposed nose only to target concentrations of 0, 0.025,0.125, 0.210 or 0.400 mg/L nanocalcium carbonate (98/99% purity) for 13 weeks. The rats were exposed for 6 hours/day, 5 days/week over a 13-week period. Two additional groups (control and high dose group; 10/sex/group) were continued on study for an additional 4 weeks as recovery groups. Exposure levels were selected based on the results of a 14-day range finding study. Concentration of the test material in the test atmosphere was determined by gravimetric analysis. Test atmosphere samples were also taken for qualitative assessment of particle shape, size and aggregation state using electron microscopy. Animals were observed for signs of toxicity prior to and after exposure. Group-wise observations were made during exposure. Animals were also observed on days they were not exposed. Ophthalmoscopic examinations were conducted prior to study start in all rats and during the last week of exposure in the rats of the control and high dose groups. Examinations were extended to other groups if effects were observed in the high dose rats. Body weights were recorded prior to the first exposure, and twice weekly thereafter. Rats were also weighed the day before sacrifice and on the day of sacrifice after an overnight fast. Food consumption was measured over 7-day period. Hematology and clinical chemistry parameters were evaluated. A gross necropsy was performed on all animals. The following organs were weighed: adrenals, brain, heart, kidneys, liver, spleen, testes, thymus, thyroid, left lung lobe, ovaries, uterus and epididymides, A complete set of organs/tissues were examined microscopically from the control and high dose groups. All gross lesions were examined microscopically. The right lung was used for bronchoalveolar lavage. The following parameters were evaluated: total protein, alkaline phosphatase, lactate dehydrogenase, Nacetylglucosaminidase, gamma-glutamyltrasferase, total white blood cell numbers and the number of viable cells. Differential cells were evaluated by light microscopy. BAL analyses were conducted on all animals on study including the recovery groups. No mortality occurred during the study and no treatment-related clinical signs were observed. Ophthalmoscopic examination did not reveal any treatment-related findings. Body weight decreases in female rats were no longer observed after the first month. Food consumption was comparable across groups. No treatment-related or biologically significant changes in hematology, coagulation or clinical chemistry values were observed in the treated groups compared to controls. Absolute left lung weight and lung weight relative to body weight were statistically increased in males at the high dose and in females at the low mid dose and high dose. No treatment-related macroscopic findings were observed. The increased incidence of diffuse hepatocellular microvacuolation in the periportal areas in males at the high dose was considered to be a chance finding without any toxicological significance. The results of the BAL evaluations at 0.210 mg/L were considered to be limited and non-adverse since they were not substantiated by any effects on lung weights or histopathology of the lung. The study authors determined there were no observed treatment-related systemic effects. The

systemic NOAEC was considered to be the highest dose tested or 0.400 mg/L. The NOAEC for local respiratory effects was considered to be 0.210 mg/L.

The results of the toxicity testing with microcalcium carbonate and nanocalcium carbonate indicate that there should be no concerns regarding repeated dose dermal or inhalation toxicity of the test item. There was no evidence of adverse effects in the 90-day oral study, thus, indicating the low toxicity of calcium carbonate. The 90-day repeated dose oral toxicity study in the rat with nanocalcium carbonate can be used to determine risk of inhalation exposure if necessary.

5. Endocrine disruption. There is no information available that links calcium carbonate to direct effects on the endocrine system. Calcium carbonate is not compatible with direct endocrine activity on the basis of structural activity relationships. In addition, there is no histopathological or behavioral evidence of an endocrine function in any toxicity evaluations of calcium carbonate conducted in laboratory animals. The calcium carbonate combined repeated dose toxicity study with reproduction/developmental toxicity screening test in rats included pre-mating, mating period, gestation, lactational and post-lactation dosing with no effects of endocrine disruption occurring.

6. Hypersensitivity studies. Columbia River Carbonates is not aware of any hypersensitivity incidents with calcium carbonate and based on the nature and structure does not expect that any would occur. In addition, calcium carbonate was negative for inducing sensitization in a local lymph node assay.]

D. Aggregate Exposure

1. *Dietary exposure.* [Aggregate pesticide exposures arise from food, drinking water and residential exposures. Aggregate assessments add exposures from relevant sources and are compared to the quantitative estimates of hazard (e.g. a no observed adverse effect level or population-adjusted dose), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, EPA considers both the route and duration of exposure. Dietary risk assessment incorporates both exposure (food and drinking water) and toxicity of a given pesticide. In the case of calcium carbonate, based on the lack of toxicity, a quantitative dietary risk assessment is not required.]

i. *Food.* [Human exposure to calcium carbonate will occur mainly via dietary exposure to foods to which it has been added such as to dairy products as a stabilizer. It is also found in canned sardines, dried fruits, cereals and processed meat and fish products. Baking powder is either calcium carbonate or sodium bicarbonate. It is used as a whitener in food and orally as an antacid, in toothpaste (mild abrasive) and other oral care products and for the treatment of osteoporosis. Exposure to crops treated with MICRONA™ Shield WP is also possible; as the product functions as a barrier crop protectant that can leave a white chalky residue on the crop. However, packing line wash system can effectively remove this residue when using post-harvest wash water with a pH of 5.5 or lower, efficient brushing, approved detergents if needed, and with forced water spray.

According to the EFSA's Re-Evaluation of Calcium Carbonate (E 170) as a Food Additive (2011), calcium carbonate dissociates into its constituent ions in the acid milieu of the stomach. Some of the calcium is absorbed, via active transport or passive diffusion, but a large proportion (up to 80%) is reconverted to calcium carbonate and other insoluble calcium salts and excreted in the feces. Average absorption of calcium from calcium carbonate over a range of studies has been shown to be in the range of 20-40%. After intestinal absorption, calcium and carbonate/bicarbonate ions enter normal metabolic pathways and body pools. The majority of absorbed calcium is stored in the skeleton. Excess calcium is excreted with water via kidneys (and also feces and skin) and excess carbonate is excreted as carbon dioxide via respiration.

Calcium carbonate like other calcium salts can cause constipation if taken in large amounts as an antacid. Hypercalcaemia and alkalosis can occur in individuals taking calcium carbonate (between 2.0 and 16.5 g/day of supplementary calcium) with large amounts of milk or cream for the treatment of peptic ulcer (milk-alkali syndrome), often associated with renal dysfunction, metastatic calcification and other symptomology in the absence of hypercalciuria. Acute hypercalcaemia and recurrent nephrolithiasis were reported in three subjects regularly consuming large quantities (7 to 15 g daily) of calcium carbonate-sodium bicarbonate powders over a period of 10 years.

Based on the low toxicity of calcium carbonate, no toxicological endpoints were identified in subchronic oral, prenatal developmental and reproductive toxicity studies, dietary exposure is not a concern because of the low toxicity of calcium carbonate and history of safe use in food and as an antiacid, abrasive in toothpaste and treatment of osteoporosis.

The proposed use of calcium carbonate on food crops is not likely to result in chronic exposures of workers or the public to calcium carbonate levels above what is expected through its use from dietary or other uses. Additionally, product labeling establishes protections to prevent exposure including PPE requirements for all handlers. Residues of calcium carbonate applied to crops have a low potential for adsorption to soil. Calcium carbonate ions dissociate and are assimilated by species in the water and is necessary to maintain good chemical balance in soils, water, and plants. Carbonate becomes part of the carbon cycle after dissociation. The proposed use of calcium carbonate as a foliar treatment should pose minimal risk to human health.]

ii. *Drinking water.* [Calcium carbonate is found naturally in water. Calcium carbonate is also used in water treatment to reduce acidity and to increase alkalinity of naturally acid waters. Based on the low toxicity of calcium carbonate, no toxicological endpoints were identified in subchronic oral, prenatal developmental and reproductive toxicity studies, drinking water exposure is not a concern because of the low toxicity of calcium carbonate and its natural occurrence in water.

No significant drinking water exposure or residues are expected to result from the pesticidal use of calcium carbonate. MICRONA™ Shield WP is intended for use as a foliar application on food and non-food crops and is not to be applied directly to water.

Calcium carbonate has a propensity to leach through soil if water is applied. As calcium carbonate moves to where water content is low, the leaching stops. If exposure via drinking water did occur from accidental spraying or leaching, the risk would be expected to be minimal based on the low acute and subchronic oral toxicity and the long history of human exposure to calcium carbonate without adverse effects.

Calcium carbonate is ubiquitous in groundwater and most soils. Following normal application scenarios of the MICRONA™ Shield WP, under typical environmental conditions, the active substance is expected to ultimately wash off foliar surfaces during rainfall and irrigation events and enter the soil compartment where it is naturally incorporated.

Calcium carbonate is an inorganic ionic solid for which an octanol/water partition coefficient cannot be reliably determined. Calcium carbonate dissociates into the calcium Ca^{2+} and carbonate CO_3^{2-} ions at environmental pH. These ions are essential to all living organisms (flora and fauna) and their intracellular and extra-cellular concentrations are actively regulated. Calcium carbonate and water form calcium bicarbonate; and with acid, such as hydrochloric acid, forms calcium chloride, water, and carbon dioxide. Bioaccumulation is therefore not expected.]

2. *Non-dietary exposure.* [There are no proposed residential (non-occupational) uses for calcium carbonate. The potential for non-occupational exposures to calcium carbonate from the proposed uses by the general population including infants and children is unlikely.

Calcium carbonate has a number of non-dietary uses including but not limited to:

a) Blackboard chalk;
b) For refining and separating iron from iron ore in mining;
c) For making glossy paper and acid free paper;
d) As a filler and whitener in many cosmetic products including mouth washes, creams, pastes, powders and lotions; and
e) In arts and crafts supplies and office supplies.

Humans are exposed to non-dietary calcium carbonate via dermal exposure when using blackboard chalk, arts and crafts supplies, cosmetics and occupationally for the above listed uses as well as other uses with no reported adverse effects,]

E. Cumulative Effects

[Data have not been identified to suggest that calcium carbonate has a common mechanism of toxicity with other substances.]

F. Safety Determination

1. *U.S. population.* [There is reasonable certainty that no harm will result from aggregate exposure to residues of calcium carbonate to the U.S. population, infants, and children. This includes all anticipated dietary exposures and all other exposures for which

there is reliable information. This conclusion is based on the low level of toxicity of calcium carbonate Toxicity data show that calcium carbonate is of low toxicity through all routes of exposure and no toxicological end points have been identified. The risks from aggregate exposure via oral, dermal and inhalation exposure are expected to be negligible.]

2. *Infants and children*. [FFDCA section 408 provides that EPA shall apply an additional tenfold margin of exposure (also referred to as a margin of safety) for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database unless EPA determines that a different margin of exposure will be safe for infants and children. EPA has sufficient data to consider the potential additional sensitivity of infants and children to pesticidal uses of calcium carbonate residues. Based on these data, the use of calcium carbonate will not pose a risk in infants and children. Because no toxicological end points have been identified, the provision requiring an additional margin of safety does not apply.]

G. Effects on the Immune and Endocrine Systems

[Parameters that are indicative of potential immunotoxicity were examined in the 90-day oral toxicity study on nanocalcium carbonate and were unaffected by treatment. No other information is available to suggest that calcium carbonate will affect the immune system. There is no information available that links calcium carbonate to direct effects on the endocrine system. Calcium carbonate is not compatible with direct endocrine activity on the basis of structural activity relationships. In addition, there is no histopathological or behavioral evidence of an endocrine function in any toxicity evaluations of calcium carbonate conducted in laboratory animals. The calcium carbonate combined repeated dose toxicity study with reproduction/developmental toxicity screening test in rats included pre-mating, mating period, gestation, lactational and post-lactation dosing with no effects of endocrine disruption occurring.]

H. Existing Tolerances

[There are no current tolerances or tolerance exemptions established for calcium carbonate.]

I. International Tolerances

[There are no known CODEX or international tolerances or tolerance exemptions established for calcium carbonate.]