APPENDIX IX F: GREEN SCREEN FOR MAGNESIUM HYDROXIDE  
(CAS #1309-42-8)\textsuperscript{15}


Chemical Structure of Magnesium Hydroxide:

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\text{Mg(OH)}_2
\]

*Note: Data gaps for this chemical were addressed by using other structurally similar magnesium salts such as magnesium chloride, magnesium lactate, and magnesium citrate. These chemicals in particular were selected due to the fact they are expected to dissociate in stomach acid and because they have been used in other risk assessments as surrogates for magnesium hydroxide (NAS 2000, U.S. EPA 2008).

For Inorganic Chemicals:

**Define Form & Physiochemical Properties**

7. Particle size (e.g. silica of respirable size) – n/a
8. Structure (e.g. amorphous vs. crystalline) – n/a
9. Mobility (e.g. Water solubility, volatility) – 0.009 g/L at 18°C (Hodgman 1959); 0.04 g/L at 100°C (Hodgman 1959)

Identify Applications/Functional Uses: Flame retardant

**Green Screen Rating\textsuperscript{16}:** Magnesium hydroxide was assigned a Benchmark Score of 2 based on a very High persistence (P) rating and a Moderate corrosion (Cr) rating (2c).

<table>
<thead>
<tr>
<th>Human – Tier 1</th>
<th>Human – Tier 2</th>
<th>Eco</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>M</td>
<td>R/D</td>
<td>ED</td>
<td>N</td>
</tr>
<tr>
<td>L</td>
<td>L</td>
<td>L</td>
<td>nd</td>
<td>L</td>
</tr>
</tbody>
</table>

*Endpoints in italics were assigned using estimated values and professional judgment (Structure Activity Relationships).*

\textsuperscript{15} CPA recommends independent third-party validation of all Green Screen assessments. No independent third-party validation has been done for this assessment. Companies may not make marketing claims based on a Green Screen assessment that has not undergone an independent validation.

\textsuperscript{16} For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
Transformation Products and Ratings:
Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) and/or moieties of concern17

<table>
<thead>
<tr>
<th>Life Cycle Stage</th>
<th>Transformation Pathway</th>
<th>Transformation Products</th>
<th>CAS #</th>
<th>Green Screen Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Life</td>
<td>Hydrolysis</td>
<td>Water</td>
<td>7732-18-5</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not present on the Red List of Chemicals (CPA 2009)</td>
</tr>
<tr>
<td>End of Life</td>
<td>Hydrolysis</td>
<td>Magnesium</td>
<td>7439-95-4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not present on the Red List of Chemicals (CPA 2009)</td>
</tr>
<tr>
<td>End of Life</td>
<td>Hydrolysis</td>
<td>Hydrogen peroxide</td>
<td>7722-84-1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

*The above transformation products were screened against the CPA’s table of Red List chemicals; none were found.

Introduction

Magnesium hydroxide is commonly used as an antacid and is the active ingredient in the laxative, milk of magnesia (NAS 2000). Additionally, it is used as a residual fuel-oil additive, an alkali drying agent in food, a color-retention agent, and is an ingredient of tooth (NAS 2000). Mg(OH)₂ is used as a flame retardant (FR) in commercial furniture applications in the United States and in commercial and residential furniture in the United Kingdom (Fire Retardant Chemicals Association 1998). The stability of Mg (OH)₂ at temperatures above 300°C allows it to be incorporated into several polymers (IPCS 1997).

Human Health – Tier 1

Carcinogenicity (C) Score (H, M or L): L
Magnesium hydroxide was assigned a score of Low for carcinogenicity due to findings from several animal studies.

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- Oncologic results predict the hazard rating for carcinogenicity for magnesium hydroxide to be low (OncoLogic 2005).
- The incidence of all cancers among 2,391 Norwegian males who worked between 1951 and 1974 in a factory producing magnesium metal was not significantly increased when compared with cancer incidence for the Norwegian nation population of the same age. The number of cases of lip as well as stomach and lung cancers was significantly increased. Workers in this study were also

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17 A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.
exposed to magnesium oxide dust, coal dust, chlorine gas, hydrochlorine aerosols, chlorinated aromatics, and sulphur dioxide. Therefore, it is not possible to determine whether exposure to magnesium dust alone is responsible for the observed elevations in cancer incidence (Heldaas 1989).

- Exposure of male Wistar rats to short (4.9x0.31 mm) or long (12x0.44) MgSO₄·3H₂O filaments by inhalation (6 hours per day, 5 days per week for 1 year) was not associated with an increase in the incidence of any tumor types in animals sacrificed 1 day or 1 year after cessation of exposure. One year after exposure, one pulmonary adenoma was observed in animals that had been exposed to long filaments for 3 weeks and none in controls. One year after exposure, neoplastic lesions were observed in control animals and short- and long-filament treated rats that had been exposed for 1 year. Two pulmonary adenomas were observed in the exposed animals and one in control animals. No hepatocellular adenomas or carcinomas occurred in controls, one hepatocellular adenoma was found in the long-filament group, and one hepatocellular carcinoma was found in the short-filament group, respectively (Hori 1994).

- Mice fed 0.5% or 2% of aqueous MgCl₂ in their diet for 96 weeks (68, or 336 mg/kg-day for males; 87 or 470 mg/kg-day for females) showed no significant change in the incidence of malignant lymphoma and leukemia. Dose-related increases in incidence of malignant lymphoma and leukemia occurred in male mice (controls, five of 50; low dose, seven of 50; high dose, eleven of 50), but not in females (controls, nine of 49; low dose, 17 of 50; high dose, 11 of 50). The incidence of hepatocellular carcinomas in male mice was decreased in a dose-related manner (controls, 13 of 50; low dose, six of 50; high dose, four of 50) and the incidence in high-dose males was significantly different from that in controls. Toxicity in female mice (i.e., decreased body weight) suggests that the study was conducted at or near the maximum tolerated dose (MTD) for females (Kurata 1989).

- Several studies in rats have shown that dietary Mg(OH)₂ can protect against chemically induced bowel carcinogenesis by suppressing hyperproliferation of the colon epithelium. Dietary levels of 250 ppm Mg(OH)₂ inhibited the incidence of colon adenoma and adenocarcinoma in rats given carcinogens methylazoxymethanol acetate (MAM acetate) or 1, 2-dimethylhydrazine (Tanaka 1989; Morishita 1991; Mori 1993). Administration of Mg(OH)₂ in the diet and the bowel carcinogen cholic acid reduced cell proliferation in bowel tissue (Wang 1993). Dietary Mg(OH)₂ also prevented the expression of c-myc gene in colon mucosa cells of MAM acetate-treated rats (Wang 1993).

- The subcommittee concludes that Mg(OH)₂ is not likely to be carcinogenic to humans by the oral route. No adequate data are available to assess the carcinogenicity of Mg(OH)₂ by the dermal or inhalation or routes of exposure (NAS 2000).

**Mutagenicity (M) and Genotoxicity Score (H, M or L): L**
Magnesium hydroxide was assigned a score of Low for mutagenicity based on negative results from several genotoxicity assays.

- MgCl₂ was judged to be a non-mutagen in the Ames assay when tested with and without metabolic activation and it did not induce chromosomal aberrations in
Chinese hamster fibroblast cells in vitro (Ishidate 1984). Chromatid gaps, breaks, and exchanges were observed in Chinese hamster lung fibroblasts treated with MgCl$_2$ at concentrations of 8.0 and 12.0 mg/ml but not at or below concentrations of 4 mg/mL (Ashby and Ishidate 1986). Since positive results occurred at only high concentrations, the authors suggest that the clastogenic effects observed may be an artifact induced by hypertonic solutions. MgCl$_2$ did not induce mutations in mouse lymphoma L5178/TK$^+$/− cells at concentrations of 5.7–18.1 mg Mg$^{2+}$/ml (Amacher and Paillet 1980). MgSO$_4$ was not mutagenic in Salmonella typhimurium (strains TA100, TA1535) and Escherichia coli WP2 uvrA at concentrations of 313–5,000 mg/plate (Oguma 1998). MgSO$_4$ was not mutagenic in Salmonella strain TA98 tested without metabolic activation and strain TA1537 tested with metabolic activation at a concentration of 156–5,000 mg/plate (Oguma 1998).

**Reproductive (R) and Developmental (D) Toxicity Score (H, M or L): L**
Magnesium hydroxide was assigned a score of Low for reproductive and developmental toxicity based on the results from one animal study and one study in humans.
- No maternal or reproductive effects were observed in a 10 day (GD 6–15) oral reproductive/developmental study on rats using MgCl$_2$. The authors of the study determined the NOAEL to be >96 mg/kg/day for Mg$^{2+}$ (NAS 2000).
- A repeated dose/developmental (3rd trimester) study on humans produced no effect on newborns except slightly increased body weight and hypermagnesiumemia. Cord serum magnesium levels reported to be 70-100% of maternal levels (potentially causing neurological depression in neonate, characterized by respiratory depression, muscle weakness, decreased reflexes). Prolonged magnesium treatment during pregnancy may be associated with maternal and fetal hypocalcemia and adverse effects on fetal bone mineralization (HSDB 2003).

**Endocrine Disruption (ED) Score (H, M or L): nd**
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- Not listed as a potential endocrine disruptor on the Red List of Chemicals (CPA 2009).
- No other relevant endocrine disruption data could be identified for magnesium hydroxide.

**Neurotoxicity (N) Score (H, M or L): L**
Magnesium hydroxide was assigned a score of Low for neurotoxicity based on professional judgement.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).
- Not listed as a potential neurotoxicant on the Red List of Chemicals (CPA 2009).
- Magnesium hydroxide is expected to be of low hazard for neurotoxicity based on professional judgment (U.S. EPA 2008).
Human Health – Tier 2

Acute Mammalian (AT) Toxicity Score (H, M or L): L
Magnesium hydroxide was assigned a score of Low for acute mammalian toxicity based on oral LD$_{50}$ values greater than 2,000 mg/kg-bw. This score is based on data from one route of exposure in two different species of animals.

- **Oral**: An LD$_{50}$ of 8,500 mg/kg was determined in the rat (Lewis 2000).
- **Oral**: An LD$_{50}$ of 8,500 mg/kg was determined in the mouse (Lewis 2000)

Corrosion/Irritation (Skin/ Eye) (Cr) Score (H, M or L): M
Magnesium hydroxide was assigned a score of Moderate for corrosion/irritation based on the substance being moderately irritating to the eyes of rabbits.

- **Dermal**: No relevant data were identified for magnesium hydroxide.
- **Ocular**: Moderately irritating to rabbit eyes (IUCLID 2000).
- **Ocular**: Administration of milk of magnesia twice a day for 3-4 days caused damage to corneal epithelium of rabbit eyes; however, effects disappeared within 2-3 days. No additional details were provided (HSDB 2003).

Sensitization (Sn) Score (Skin and Respiratory) (H, M or L): L
Magnesium hydroxide was assigned a score of Low for sensitization based on professional judgment.

- Magnesium hydroxide is not expected to cause skin sensitization based on professional judgment. No other details were provided (U.S. EPA 2008).

Systemic/ Organ (ST) Toxicity Score (includes organ effects and immunotoxicity) (H, M or L): M
Magnesium hydroxide was assigned a score of Moderate for systemic/organ toxicity based on suggestive animal studies.

- No human studies were found that investigated the toxic effects of Mg(OH)$_2$ following inhalation exposure. Exposure of male Wistar rats to short (4.9x0.31 mm) or long (12x0.44 mm) MgSO$_4$·5Mg(OH)$_2$·3H$_2$O filaments inhalation, 6 hours per day, 5 days per week for up to a year was associated with a slight increase in the incidence of pulmonary lesions 1 year after cessation of exposure. A year after cessation of exposure, histopathological examination of treated animals revealed a slight increase in segmental calcification of the pulmonary artery and thickening of the lung pleura in rats exposed to either short or long filaments for 4 week or 1 year. Differences between exposed and unexposed animals were statistically significant. No significant differences in body, lung, liver, kidney, or spleen weights were detected between animals sacrificed 1 day or 1 year after a 1 year exposure to short or long filaments. No significant differences in survival were observed between animals sacrificed 1 day or 1 year after a 1 year exposure to short or long filaments (Hori 1994).
- In its review of clinical studies, the Institute of Medicine (IOM 1997) concluded that Mg$^{2+}$ in the diet is never high enough to cause adverse effects. The IOM set a “tolerable upper intake level” (TUL) for the ingestion of magnesium (Mg$^{2+}$) supplements of 5 mg/day for anyone over 1 year old. The TUL was based on the
approximate no-observed-adverse-effects level (NOAEL) for osmotic diarrhea in humans reported by Marken (1989), Fine (1991), Ricci (1991), and Bashir (1993). Five of the six patients reported epigastric burning or distension and two reported diarrhea.

- Decreased body weight was found to be the critical effect in B6C2F1 mice fed diets containing 0%, 0.3%, 0.6%, 1.25%, 2.5%, or 5% MgCl$_2$·6H$_2$O for 13 weeks. Intake of Mg$^{2+}$ added to the diet was calculated to be 73, 146, 322, 650, or 1,368 mg/kg-day in treated males and 92, 190, 391, 817, and 1,660 mg/kg-day in treated females (the amount of magnesium in the basal diet was not provided). The 5% treatment group of both sexes showed a significant decrease in weight gain (15% in males and 10% in females). Males in the 2.5 and 5% group exhibited an increased incidence of renal tubular vacuolation. The authors determined that the LOAEL for this study was 650 mg/kg-day (Tanaka 1994).

- Decreased body weight and increased renal vacuolation were observed in male, but not female B6C3F1 mice fed a diet that contained 5% MgCl$_2$·6H$_2$O (Mg$^{2+}$ at 840 mg/kg/day) for 13 weeks. No treatment-related effects were reported for male and female mice fed a diet containing 0, 0.3, 0.6, 1.25 or 2.5% MgCl$_2$·6H$_2$O for 13 weeks. The NOAEL for Mg$^{2+}$ in this study was determined to be 587 mg/kg-day for females and 420 mg/kg-day for males (Kurata 1989).

- Decreased body weight gain (about 25% at termination of the exposure) and increases in relative brain, heart, and kidney weights compared with controls were observed in female B6C3F1 mice fed diets for 96 weeks that contained 2% MgCl$_2$·6H$_2$O (470 mg Mg$^{2+}$/kg-day). No treatment-related effects were observed in male mice fed diets that contained 0.5% or 2% of MgCl$_2$·6H$_2$O (68 or 336 mg/kg/day) or female mice fed diets that contained 0.5% of MgCl$_2$·6H$_2$O (87 mg/kg-day) for 96 weeks. Histopathological examination after 104 weeks of exposure revealed no treatment-related changes. Urinary, hematological, and clinical chemistry parameters and histopathological measures were not affected by treatment, except for a significant increase in serum albumin in high-dose females. Survival rates were comparable between treated and control animals. The LOAEL for this study is 470 mg/kg-d based on the treatment-related effects in high-dose female mice (Kurata 1989).

**Ecotoxicity**

**Acute Aquatic (AA) Toxicity Score (H, M or L): L**

Magnesium hydroxide was assigned a score of Low for acute aquatic toxicity based on LC$_{50}$ values greater than 100 mg/L.

- An LC$_{50}$ of 1,110 mg/L was estimated in fish (species not specified) (fish, 96 hour) from the measured LC$_{50}$s for MgCl$_2$ and MgSO$_4$, modified by a molecular weight adjustment for Mg(OH)$_2$ (Mount 1997).

- An LC$_{50}$ of 648 mg/L was estimated in daphnia (species not identified) (daphnid, 48 hour) from the measured LC$_{50}$s for MgCl$_2$ and MgSO$_4$, modified by a molecular weight adjustment for Mg(OH)$_2$ (Mount 1997; Biesinger and Christensen 1972).
An EC$_{50}$ of 2,111 mg/L was estimated in green algae (species not identified) (green algae, 96 hour) by using an acute to chronic ratio of 4 (U.S. EPA 2008).

**Chronic Aquatic (CA) Toxicity Score (H, M or L): L**
Magnesium hydroxide was assigned a score of Low for chronic aquatic toxicity based on ChV values greater than 10 mg/L.

- A ChV of 403 mg/L was estimated in fish (species not identified) (fish, time not identified) using an acute to chronic ratio of 3.3. This ratio is for daphnids and has not been validated for use with fish (U.S. EPA 2008).
- A ChV of 197 mg/L was estimated in daphnia (species not identified, length of time not identified) from the measured ChV for Mg$^{2+}$ ion, modified by a molecular weight adjustment for Mg(OH)$_2$ (Suter 1996).
- A ChV of 528 mg/L was estimated in green algae (species not identified, length of time not identified) from the measured NOEC and LOEC for MgSO$_4$, modified by a molecular weight adjustment for Mg(OH)$_2$ (ECOTOX Database undated).

**Environmental Fate**

**Persistence (P) Score (vH, H, M, or L): vH**
Magnesium hydroxide was assigned a score of very High for persistence based on its inability to biodegrade in the environment.

- As a fully oxidized inorganic material, magnesium hydroxide is not expected to biodegrade, oxidize in air, or undergo hydrolysis under environmental conditions. Magnesium hydroxide does not absorb light at environmentally relevant wavelengths and is not expected to photolyze. No degradation processes for magnesium hydroxide under typical environmental conditions were identified. Chemical is identified as recalcitrant (U.S. EPA 2008).

**Bioaccumulation (B) Score (vH, H, M, or L): L**
Magnesium hydroxide was assigned a score of Low for bioaccumulation based on a BCF value less than 500.

- Magnesium hydroxide is not expected to be bioaccumulative based on an estimated BCF of <500 (U.S. EPA 2008).

**Physical Properties**

**Explosivity (Ex) Hazard Rating (H, M or L): L**
Magnesium hydroxide was assigned a score of Low for explosivity because no basis for concern was identified.

- Magnesium hydroxide is not explosive (IUCLID 2000).

**Flammability (F) Hazard Rating (H, M or L): L**
Magnesium hydroxide was assigned a score of Low for flammability because no basis for concern was identified.

- Magnesium hydroxide is not flammable (IUCLID 2000).
REFERENCES


Magnesium Hydroxide Green Screen Evaluation Prepared By:

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