Chlorine Dioxide
Final Risk Assessment

Case 4023

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EXECUTIVE SUMMARY

Chlorine dioxide and sodium chlorite are active ingredients in numerous products used in the control of bacteria, fungi, and algal slimes. In addition, chlorine dioxide and sodium chlorite are used as material preservatives and as disinfectants. At this time, products containing chlorine dioxide and sodium chlorite are intended for agricultural, commercial, industrial, medical and residential use. The agricultural premises and equipment uses include the disinfection of hard surfaces and equipment (such as hatching facilities and mushroom houses) and water systems (such as chiller water and humidification water in poultry houses). Commercial, industrial, and medical uses include disinfection of ventilation systems, hard surfaces (e.g., floors, walls, and laboratory equipment), water systems, pulp/paper mills, and food rinses. Residential uses include disinfection of hard surfaces (e.g., floors, bathrooms), heating ventilating and air-conditioning (HVAC) systems, and pool & spa water circulation system treatments. In addition, there is a continuous release gas product (sachet) for the home to control odors.

Environmental Fate: Chlorine dioxide and sodium chlorite are assessed together because chlorine dioxide is produced by a reaction of sodium chlorite (and sometimes sodium chlorate) with hypochlorite /acid. In addition, chlorite is a breakdown product of chlorine dioxide. A major route of exposure is through drinking water.

Chlorine dioxide has a short half life and in the presence of sunlight and will break down into chloride and chlorate ions, and ultimately, oxygen is formed. Sodium chlorite dissolves in water, breaking down into chloride and chlorate ions under similar conditions as chlorine dioxide. Chlorate and chlorite ions tend to only undergo biodegradation under anaerobic conditions degrading to chloride and oxygen. Biodegradation of chlorate and chlorite have been observed in anoxic groundwater, sediments and some soils. No adsorption/desorption constants (K_ds) have been measured or reported in published literature for either chlorite or chlorate. These ions are likely to be mobile and may travel from surface to groundwater easily. The estimated log K_{ow} of chlorine dioxide is -3.22 and for sodium chlorite is -7.17. It is not expected that either would bioaccumulate in aquatic organisms.

Hazard: The acute toxicity of chlorine dioxide (79% a.i.) is moderate by the oral route (LD_{50} = 292 mg/kg [males]; 340 mg/kg [females]; Toxicity Category II). The acute toxicity of chlorine dioxide using sodium chlorite as the test material (80% a.i.) is considered minimal by the dermal route (LD_{50} > 2000 mg/kg; Toxicity Category III). By the inhalation route, using sodium chlorite as the test material (80.6%), chlorine dioxide was moderately toxic (LC_{50} = 0.29 mg/L, Toxicity Category II). For primary eye irritation, chlorine dioxide (2% a.i.) was a mild irritant (Toxicity Category III), but the technical test material was not used. For primary dermal irritation, sodium chlorite (80% a.i.) was a primary irritant (Toxicity Category II). For dermal sensitization, there are no acceptable animal studies for chlorine dioxide or sodium chlorite.

The subchronic toxicity database is considered adequate for characterizing the

subchronic oral and inhalation toxicity of chlorine dioxide/chlorite. Daniel et al. (1990) exposed groups of 10 male and 10 female Sprague-Dawley rats to chlorine dioxide in drinking water for 90 days at concentrations of 0, 25, 50, 100, or 200 mg/L (0, 2, 4, 6, or 12 mg/kg-day chlorine dioxide for males and 0, 2, 5, 8, or 15 mg/kg-day chlorine dioxide for females). The LOAEL for this study is 25 mg/L (2 mg/kg-day) based on a significant increase in incidence of nasal lesions. In a study by Harrington et al. (1995), rats (15/sex/group) were administered doses of 0, 10, 25, or 80 mg/kg-day sodium chlorite (equivalent to 0, 7.4, 19, or 60 mg chlorite/kg-day, respectively) via gavage for 13 weeks. The NOAEL for this study is 7.4 mg/kg-day, and the LOAEL is 19 mg/kg-day, based on stomach lesions and increases in spleen and adrenal weights. Dalhamn (1957) and Paulet and Desbrousses (1970, 1972, and 1974) are co-critical inhalation toxicity studies included in the subchronic toxicity database for chlorine dioxide/chlorite. A NOAEL of 0.1 ppm (~ 0.28 mg/m^3) was selected from Dalhamn (1957) and a LOAEL of 1.0 ppm (~2.8 mg/m^3) was selected from Paulet and Desbrousses (1970, 1972, and 1974), based on respiratory distress and decreased body weights observed in exposed animals.

In a developmental toxicity study (Orme et al., 1985), a NOAEL of 20 mg/L (3 mg/kg/day) was established based on neurodevelopmental effects in the offspring of rats exposed to chlorine dioxide in drinking water. A developmental toxicity study (MRID 41715701) conducted in rabbits using sodium chlorite (purity 80.58%) showed a dose-related increase in incidence of does with reduced fecal output during the dosing period, days 7 to 19, which was considered consistent with decreased food consumption; the NOAEL for developmental and maternal toxicity was 200 ppm (12-14 mg/kg/day). A two-generational reproductive toxicity study (CMA, 1996, MRID 4535890) was conducted with sufficient numbers of animals of both sexes and examined numerous endpoints. The NOAEL for this study is 35 ppm (2.9 mg/kg-day chlorite) and the LOAEL is 70 ppm (5.7 mg/kg-day chlorite) based on lowered auditory startle amplitude and altered liver weights in two generations.

One chronic toxicity study (Haag, 1949) is included in the toxicity database for chlorine dioxide. The study was determined to be of limited use in the assessment of chronic toxicity because an insufficient number of animals were tested per group and pathology was conducted on only a small number of animals. In addition, the study did not provide adequate evaluations of more sensitive parameters, which would have been more useful in the overall assessment of chronic toxicity.

Chlorine dioxide has not been formally assessed for carcinogenic potential. The available dermal carcinogenicity studies do not definitively characterize the carcinogenicity of chlorine dioxide, and additional studies may be required. One subchronic study (Daniel et al., 1990) examined the effects of administration of chlorine dioxide to groups of male and female Sprague-Dawley rats (10/sex/dose) at dose levels of 0, 25, 50, 100, or 200 mg/L for 90 days in drinking water. A significant increase in the incidence of nasal lesions (goblet cell hyperplasia and inflammation of nasal turbinates) was found at all dose levels tested. The significance of these findings is uncertain as they have not been observed in other long-term studies of chlorine dioxide.

Data on the mutagenicity of chlorine dioxide exist in the open scientific literature as well

as within the Agency's database of submitted studies. In Miller et al. (1986) negative effects were reported in Salmonella strains TA98 and TA100 from a 400-fold drinking water concentrate of chlorine dioxide, whereas a 4000-fold concentrate was mutagenic to strain TA98 only in the absence of metabolic activation. In Accession No. 265867, chlorine dioxide was positive for forward mutations under non-activated conditions (dose-related from 3.2-24.3 µg/ml) and activated conditions (48.3µg/mL) in L5178Y/TK cells, positive for structural chromosome aberrations under non-activated and activated conditions (10, 15, and 50 µg/ml), and negative for increased transformed foci up to cytotoxic levels. *In vivo* micronucleus and bone marrow chromosomal aberration assays in Swiss CD-1 mice administered 0.1–0.4 mg chlorine dioxide via gavage for 5 consecutive days were negative, as was a sperm-head abnormality assay in B6C3F1 mice administered 0.1–0.4 mg via gavage for 5 consecutive days (0, 3.2, 8, and 16 mg/kg-day) (Meier et al., 1985).

Neurotoxicity of chlorine dioxide has been observed. In the two-generation reproduction toxicity study (CMA, 1996), significant changes were observed in maximum response in startle amplitude and absolute brain weight in F1 rat pups at a dose of 3 mg/kg/day. In the Orme et al. (1985) developmental toxicity study, neurobehavioral deficits consisting of decreased exploratory and locomotor activities were observed in offspring at a maternal dose of 14 mg/kg/day.

Toxicity Endpoints: The toxicity endpoints used in this document to assess potential risks include acute and chronic dietary reference doses, and short-, intermediate- and/or long-term incidental oral, dermal, and inhalation doses.

Dietary/Oral Endpoints: The chronic NOAEL is 3 mg/kg/day. This endpoint is based on a two-generation reproduction toxicity study (CMA, 1996) and a developmental toxicity study in rats (Orme et al., 1985). An uncertainty factor of 100 (10x for interspecies extrapolation and 10x for intraspecies variability) was applied. An acute dietary endpoint was not identified in the data base for chlorine dioxide.

Dermal Absorption: There is one published report on the kinetics of chlorine dioxide following dermal administration (Scatina et al., Fund. Appl. Toxicol. 4: 479-484). This study measured kinetics of elimination and was not specifically designed to measure the extent of absorption. Based on the results of this study, it is apparent that absorption of chlorine dioxide is fairly rapid, even after repeated dermal administration. However a dermal absorption study, with chlorine dioxide conducted in accordance with the OPPTS 870.7600 guideline, would provide definitive data on the percent dermal absorption of chlorine dioxide. Until more definitive data are available, a default value of 100% will be employed for chlorine dioxide.

Dermal Endpoints: The short-, intermediate-, and chronic-term dermal endpoint is 3 mg/kg/day and is based on a two-generation reproduction toxicity study and a developmental toxicity study in rats (CMA, 1996; Orme et al.,1985). The target MOE is 100 for residential and occupational exposure.

Inhalation Endpoints: The inhalation route of exposure to chlorine dioxide is assessed for three distinct subpopulations: (1) occupational exposures (8 hours/day, 5 days/week), (2) one-

time exposures for residential uses (e.g., HVAC systems, mopping floors, etc), and (3) long-term exposure for continuous release products in the home (24 hours/day, 7 days/week). Several animal studies were used to develop reference concentrations (RfCs). The effects seen at various concentrations include rhinorrhea, altered respiration, respiratory infection, bronchial inflammation, alveolar congestion and hemorrhage, vascular congestion, and peribronchiolar edema. Readers are referred to USEPA (2000a) for a detailed review of the effects seen at specific concentrations and exposure durations along with the derivation of the RfC. In summary, the occupational RfC is determined to be 0.003 ppm and represents an 8-hour time weighted average (TWA). The one-time residential exposure scenario is represented by the RfC of 0.05 ppm and the RfC for long-term, continuous exposure is 0.00007 ppm. The RfC methodology incorporates the uncertainty factors into the concentration. For inhalation, the RfC is compared directly to the air concentration of interest. Inhalation risks are of concern if the air concentrations people are exposed to exceed the RfC.

FQPA Safety Factor: When the original toxicity endpoint assessment was conducted, the Hazard Identification Assessment Review Committee (HIARC) concluded that an extra 10x uncertainty factor under the Food Quality Protection Act should be considered in risk assessments conducted for chlorine dioxide. This recommendation was based upon evidence of susceptibility in a two-generation reproduction toxicity study in rats and evidence of susceptibility from scientific literature reports.

Since that time, the Health Effects Division of the Office of Pesticide Programs issued policy guidance September of 2001 regarding the determination of the appropriate FQPA safety factor in tolerance assessment. This guidance states that whereas in the past "...OPP has routinely applied an additional FQPA safety factor where data on a pesticide shows increased susceptibility or sensitivity (either qualitative or quantitative) in the developing organism," It is the intent that "...OPP will now put greater emphasis on analyzing the degree of concern and, rather than apply an additional safety factor based solely on the identification of heightened sensitivity or susceptibility, will conduct a case-by-case weight of evidence approach that qualitatively examines the level of concern for sensitivity / susceptibility and assess whether traditional uncertainty factors already incorporated into the risk assessment are adequate to protect the safety of infants and children. Using this approach, in many cases the concerns regarding pre- and postnatal toxicity can be addressed when a Reference Dose (RfD) or Margin of Exposure (MOE) is based on the pre- or postnatal endpoints in the offspring."

The endpoint selected for both dietary and non-dietary exposures to chlorine dioxide was based upon adverse effects observed in offspring from developmental and reproductive toxicity data. Consistent with the approach used by the EPA's Office of Water for use of chlorine dioxide as a drinking water disinfectant and the updated guidance on selection of a safety factor under FQPA, the endpoint selected for assessment of risk from dietary and non-dietary exposure to chlorine dioxide was felt to be protective of potentially susceptible populations including children, based upon the selection of an endpoint and effects observed in offspring and the use of an NOAEL value based on those effects. Therefore, it was concluded that an additional safety factor under FQPA was not necessary.

Dietary Exposure: The Agency has conducted a dietary exposure and risk assessment

for use of chlorine dioxide in products used in the control of bacteria, fungi, and algal slimes; as well as its use as a material preservative and disinfectant all of which may end in indirect food contact scenarios. For chronic dietary exposure, the risk from indirect food contact is highest for children (61% of the chronic PAD). For an adult, the chronic dietary exposure is 16% of the chronic PAD.

For direct food contact, AD conducted a chronic risk assessment for the fruit and vegetable washes which were applied post-harvest. The chronic risks appear to be below the levels of concern (7.5% of cPAD for adults and 42% of the cPAD for children between the ages of 1 and 2 years of age).

Total dietary risks (from direct and indirect food contact) are slightly above the Agency's level of concern for children (103% of the cPAD). However, the chronic risks appear to be below the level of concern for adults (23% of the cPAD).

Water Exposure and Risk: Chlorine dioxide and sodium chlorite are used as disinfectants in many water treatment plants. Office of water conducted an eighteen month monitoring study for the determination of maximum contaminant levels (MCL) and maximum contaminant level goals (MCLG) of chlorite in the drinking water that reached consumers. AD used the results from this study and determined for all infants less than one year of age, the cPAD (145%) exceeds the level of concern.

Residential Exposure and Risk: Residential uses of chlorine dioxide and/or sodium chlorite products that are applied by homeowners include the control of mold and mildew. For the exposure assessment, household cleaning products were grouped together to be represented by a higher application rate from a sodium chlorite product. The post application scenario is based on a product that applies chlorine dioxide to floors that have the potential for children playing. Three scenarios (mopping, spraying, and placing tablets into pools/spas) were examined for residential uses in the risk assessment. The scenarios were evaluated based on the Residential Exposure Assessment Standard Operating Procedures (SOPs), product label maximum application rates, related use information, Agency standard assumptions, Pesticide Handlers Exposure Database (PHED) unit exposure data, and Chemical Manufacturing Association (CMA) unit exposure data. The calculated dermal MOE is less than the target MOE of 100 for only the application of tablets to pool water circulation systems. The dermal MOE for applications to pool water systems is 46. This risk can be mitigated with the use of gloves (MOE= 500).

Residential post application exposures result when bystanders (adults and children) come in contact with chlorine dioxide in areas where pesticide-treated end-use products have recently been applied (e.g., treated hard surfaces/floors), or when children incidentally ingest the pesticide residues through mouthing the treated end products/treated articles (i.e., hand-to-mouth or object-to-mouth contact). For the purposes of this screening-level assessment, four post application scenarios have been considered: (1) exposure to residue from hard floors that have been cleaned/mopped with a generic cleaner containing chlorine dioxide, (2) exposure to chlorine dioxide used by commercial applicators to clean residential HVAC systems, (3) exposure to a continuous release (gas) deodorizer, and (4) pool & spa treatments.

The child short- and intermediate-term dermal MOE for contact following hard surface disinfection is above the target MOE of 100 for residential and daycare settings (MOE = 280). The short- and intermediate-term incidental oral MOE following hard surface disinfection are above the target MOE of 100 for residential and daycare settings (MOE = 2,300), and thus are not of concern.

Inhalation exposures due to post application activities could occur for children and adults after the treatment of floors; adults and children after the treatment of HVAC systems; and adults and children during the use of continuous release (gas) deodorizers. Chlorine dioxide and/or sodium chlorite can be applied as an aqueous solution to hard surfaces such as floors and as a dust to carpets. For the floor treatments, a theoretical approach to estimating chlorine dioxide air concentrations indicates an 8-hour time weighted average (TWA)air concentration of 0.02 ppm after a 1-hour restricted entry interval (REI). If one could assume that residents would stay out of the house for the first hour, the 8-hour TWA is 0.02 ppm which is below the RfC of 0.05 ppm.

For HVAC treatments, monitoring data are available. The air concentrations monitored indicated the highest peak concentration of 0.02 ppm and the average of the peak concentrations was below the detection limit of 0.01 ppm. The short-term inhalation RfC for chlorine dioxide is 0.05 ppm. Therefore, inhalation exposures from HVAC treatments are not expected to be a concern.

For the continuous release deodorizers, a bounding estimate of air concentration is presented based on the application rate and the label-referenced longevity of the pouches/sachets. The theoretical constant air concentration would be 0.52 ppm assuming no air exchange and no build up of chlorine dioxide over time because of the short half life. The RfC for long-term continuous exposure is 0.00007 ppm. Therefore, the theoretical concentration from the product's release is of concern.

Aggregate Exposure and Risk: In order for a pesticide registration to continue, it must be shown that the use does not result in "unreasonable adverse effects on the environment". Aggregate exposure is the total exposure to a single chemical (or its residues) that may occur from dietary (i.e., food and drinking water), residential, and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal, and inhalation). Aggregate risk assessment were conducted for acute (1 day), short-term (1-30 days), intermediate-term (1-6 months) and chronic (several months to lifetime) exposures.

The acute and chronic aggregate risk assessments are based on dietary and drinking water exposures. For chlorine dioxide acute dietary risks were not assessed based on the lack of acute endpoints. Dietary exposures from indirect food uses (e.g., use in food-contact packaging) and from direct food uses were aggregated together along with the drinking water exposures for a total dietary exposure. The chronic aggregate risk estimates associated with chlorine dioxide from dietary uses are below the Agency's level of concern for adults at 67% of the cPAD. However the dietary risks are above the level of concern for children (165% of the cPAD).

The short- and intermediate-term aggregate assessments were conducted for adults and

children. The following representative scenarios were included in the aggregate assessments:
Short-term, Adults:

- dietary, chronic direct and indirect
- handling cleaning products via spray (dermal only)
- handling cleaning products via mopping (dermal only)
- drinking water, chronic

Short-and intermediate term, Children:

- dietary, chronic direct and indirect
- post application exposure to cleaning product residues (dermal and oral)
- drinking water, chronic

Since the toxicity endpoints for the oral and dermal routes of exposure are based on the same study and same toxic effect, these two routes are aggregated together. The inhalation route is based on a different effect and therefore that route is not included in the aggregate. For the aggregate of the inhalation route, only the continuous release product may co-occur with the other uses and the inhalation risk for the continuous release is of concern by itself. The aggregate risks (oral + dermal) are not of concern for adults, as the total aggregate MOE is 130, which is above the target of 100. For children, the aggregate risk estimates are again below the target MOE of 100 (MOE=44) and thus are of concern. It should be noted that several conservative assumptions were used in this assessment.

Occupational Exposure and Risk: Potential occupational handler exposure from the use of chlorine dioxide products can occur in various use sites, including agricultural premises, food handling, commercial and institutional premises, medical premises, human drinking water systems, industrial processes and water systems, application to material preservatives, and swimming pools and other aquatic areas.

For the occupational handler dermal risk assessment, the short- and intermediate-term risks calculated at baseline exposure (no gloves and no respirators) were above target MOEs for all scenarios (i.e., dermal MOEs were >100), except for the following:

Agricultural premises and equipment:

- application to hard surfaces: low pressure handwand (MOE=31),
- application to hard surfaces: mopping (MOE=70), and
- application to hard surfaces: foam applicator equipment (MOE=52).

Food Handling, Commercial/Institutional, and Medical Premises and Equipment:

- application to hard surfaces: mopping (MOE=66 for commercial and 3 for medical facilities).

There is the potential for the off gassing of chlorine dioxide during some applications that are not totally enclosed (e.g., spray aqueous solution, mopping, pouring, etc). Although no occupational air monitoring data have been submitted to assess the inhalation route, EPA has obtained air concentration measurements from OSHA. OSHA maintains a data base known as the Integrated Management Information System (IMIS). The IMIS entries for chlorine dioxide

are available for 7 industry Standard Industrial Classification (SIC) codes. The summary results of the 33 observations taken from 8-hour TWA personal air samplers for chlorine dioxide indicate that 21 of those measurements were below the LOD of 0.004 ppm. In addition, of the 33 TWA measurements, only 3 were at or above 0.1 ppm. It is also important to note that the OSHA PEL for chlorine dioxide is 0.1 ppm. Facilities using chlorine dioxide are not required to mitigate inhalation exposures until the air concentration reaches 0.1 ppm. Based on the occupational inhalation toxicological endpoint selected for chlorine dioxide (i.e., RfC of 0.003 ppm), levels at or near the PEL are of concern. In fact, the capability (i.e., LOD) of the OSHA sampling method is insufficient for the occupational RfC presented in this document. Reconciliation of the EPA risk-based RfC and the current OSHA standards will be made during the regulatory decision phase of the Reregistration Eligibility Decision (RED) for chlorine dioxide.

Incident Reports: There are some reported incidents associated with exposure to end-use products containing chlorine dioxide. Inhalation is the primary route of exposure. Most of the incidents are related to irritation reaction.

Ecological Hazard and Risk: For terrestrial animals, the results of studies to examine the toxicity of chlorine dioxide/sodium chlorite to birds indicate these chemicals range from slightly to highly toxic to birds on an acute oral basis and from slightly toxic to practically non-toxic on a subacute dietary basis. For freshwater aquatic animals, the results of studies examining the toxicity of chlorine dioxide/sodium chlorite to freshwater fish indicate these chemicals range from slightly toxic to practically non-toxic on an acute basis. For aquatic invertebrates, the studies indicate that chlorine dioxide and sodium chlorite range from very highly toxic for technical grade sodium chlorite a.i. to practically non-toxic for the formulated product on an acute basis. Results of toxicity studies indicate that chlorine dioxide/sodium chlorite are slightly toxic to estuarine/marine fish on an acute basis and range from highly toxic to slightly toxic to estuarine/marine invertebrates on an acute basis.

For terrestrial plants, results of toxicity studies indicate that chlorine dioxide/sodium chlorite are moderately toxic to terrestrial plants. However, since the maximum label rate for many of the chlorine dioxide/sodium chlorite once-through cooling labels was not used in these tests, it is necessary to conduct Tier II testing with rice. For aquatic plants, toxicity study results indicate chlorine dioxide/sodium chlorite are moderately toxic to aquatic plants. The once-through cooling tower use of chlorine dioxide/sodium chlorite requires that 5 aquatic plant tests be conducted due to the algaecidal nature of the chemical and the likelihood of exposure to aquatic plants in surface waters receiving industrial facility outfall from the cooling system; however, only one study (1 species) under this topic has been submitted and 5 are required. The following aquatic plant studies are still required: blue-green cyanobacteria (*Anabaena flos-aquae*), freshwater diatom (*Navicula pelliculosa*), marine diatom (*Skeletonema costatum*) and floating macrophyte (*Lemna gibba*).

Acute risk to aquatic organisms may occur from the use of chlorine dioxide/sodium chlorite in once-through cooling towers based on the screening level assessment conducted. At the highest doses, the model shows risk to freshwater and marine/estuarine fish and invertebrates and aquatic plants, and at the lowest doses the model shows risk only to freshwater invertebrates. Chronic risk to aquatic organisms cannot be assessed at this time due to the lack of chronic toxicity

endpoints for fish and aquatic invertebrates. When the required aquatic chronic toxicity testing described above is submitted, chronic risk to these organisms will be assessed.

Listed Species: Acute risks to listed birds and mammals are not anticipated from the use of chlorine dioxide and sodium chlorite products due to low exposure and low toxicity. The screening level model used in this assessment indicates that there may be acute risks to listed aquatic organisms from the once through cooling tower use of chlorine dioxide/sodium chlorite. Further, potential indirect effects on any species dependent upon a species that experiences effects from use of chlorine dioxide/sodium chlorite cannot be precluded based on the screening level ecological risk assessment. These findings are based solely on EPA's screening level assessment and do not constitute "may effect" findings under the Endangered Species Act. Chronic risks to listed aquatic organisms cannot be assessed at this time; this risk will be assessed when required chronic toxicity data are submitted to and evaluated by the Agency.

1.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

1.1 Chemical Identification

Chemical identification parameters, including CAS Number and molecular formula are provided in Table 1.

Table 1. Chemical Identification Information for Chlorine Dioxide and Sodium Chlorite

Property	Chlorine Dioxide	Sodium Chlorite
OPP Chemical Code	020503	020502
CAS Number	10049-04-4	7758-19-2
Molecular Formula	ClO_2	$NaClO_2$

1.2 Physical/Chemical Properties

The physical and chemical properties of chlorine dioxide and sodium chlorite are shown in Table 2.

Table 2. Physical/Chemical Properties of Chlorine Dioxide and Sodium Chlorite

Property	Chlorine Dioxide	Sodium Chlorite
Molecular Weight	67.45 g/mol	90.45 g/mol
Color	Yellow to Reddish Yellow	White
Melting Point	-59°C	180-200°C (decomposes)
Boiling Point	11°C	n/a
Odor	Strongly pungent, chlorine-like	n/a
Physical State	Gas at room temperature	Solid
Density	1.64 g/ml at 0°C (liquid) 1.614 g/ml at 10° C (liquid)	2.468 g/ml (as a solid)
Vapor Pressure	490 mm Hg (0°C) >760 mm Hg (25°C)	n/a
Stability	Dilute solutions are stable if kept cool and in the dark. Unstable when exposed to sunlight	n/a
Solubility (water)	3.01 g/L at 25°C and 34.5 mmHg	390 g/L at 30°C

2.0 ENVIRONMENTAL FATE ASSESSMENT

A detailed environmental fate assessment for chlorine dioxide and sodium chlorite is presented in the attached appendix.

Chlorine dioxide and sodium chlorite are assessed together because chlorine dioxide is produced by a reaction of sodium chlorite (and sometime sodium chlorate) and hypochlorite/acid. In addition, chlorite is a breakdown product of chlorine dioxide. Major antimicrobial uses of chlorine dioxide and/or sodium chlorite are as water disinfectants and pulp/paper industry disinfectants. The major route of exposure, therefore, is through drinking water.

Chlorine dioxide has a short half life and in the presence of sunlight and will break down into chloride and chlorate ions (between pH 4 and 7). At pH lower than 4, its breakdown products are chlorite and chlorate. Chlorite is the dominant breakdown product. Ultimately, oxygen is formed. Sodium chlorite dissolves in water, breaking down into chloride and chlorate ions under similar conditions as chlorine dioxide. Chemical degradation of sodium chlorite commonly occurs in water as well as in the presence of suspended soil particles containing ions, like Fe(II), Mn(II), I^-, and S^{-2}, through redox reactions. The final breakdown products are chloride and oxygen. These same end products are obtained when sodium chlorite is heated.

Chlorate and chlorite ions tend to only undergo biodegradation only under anaerobic conditions. Biodegradation of chlorate and chlorite have been observed in anoxic groundwater, sediments and some soils. The end products are the same as stated above: chloride and oxygen. No adsorption/desorption constants (K_ds) have been measured or reported in published literature for either chlorite or chlorate. These ions are likely to be mobile and may travel from surface to groundwater easily. The estimated log K_{ow} of chlorine dioxide is -3.22 and for sodium chlorite is -7.17. It is not expected that either would bioaccumulate in aquatic organisms.

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

A detailed hazard assessment for chlorine dioxide is presented in the attached appendix.

Acute Toxicity. The acute toxicity of chlorine dioxide (79% a.i.) is considered moderate by the oral route (Toxicity Category II) and minimal by the dermal route using sodium chlorite as the test material (80% a.i.) (Toxicity Category III). By the inhalation route, chlorine dioxide was moderately toxic (Toxicity Category II) using sodium chlorite as the test material (80.6%). For primary eye irritation, chlorine dioxide (2% a.i.) was a mild irritant (Toxicity Category III), but the technical test material was not used. For primary dermal irritation, sodium chlorite (80% a.i.) was a primary irritant (Toxicity Category II). There are no acceptable animal studies for chlorine dioxide or sodium chlorite for dermal sensitization. Table 3 presents the acute toxicity data for chlorine dioxide/sodium chlorite and Table 4 highlights the key toxicological studies for chlorine dioxide.

Subchronic Toxicity.

Chlorine dioxide: A subchronic oral toxicity study (Daniel et al., 1990) conducted in the rat showed systemic effects after repeated oral administration of chlorine dioxide in the drinking water at doses of 0, 25, 50, 100 or 200mg/L. A significant decrease in body weights and body weight gain was evident (26-29% lower than controls) in males at the 200 mg/L treatment level. Significant reductions were also observed in water (in the ≥50 mg/L treatment for males and ≥25 mg/L treatment for females) and food consumption (in the 200 mg/L treatment for males). Both absolute liver (for males; ≥50 mg/L) and spleen weights (for females; ≥25 mg/L) decreased. In males exposed to 100 or 200 mg/L, serum lactate dehydrogenase and aspartate aminotransferase levels decreased and serum creatinine levels increased. A significant increase in incidence of nasal lesions (goblet cell hyperplasia and inflammation of nasal turbinates) was found in males (ǂ 25 mg/L) and females (ǂ 100 mg/L).

Subchronic inhalation toxicity studies (Dalhamn, 1957; Paulet and Desbrousses, 1970, 1972, and 1974) conducted in the rat have resulted in pulmonary edema and nasal bleeding (at levels of 260 ppm during a single 2-hour exposure) as well as respiratory distress and bronchopneumonia (in rats exposed to 3-minute exposure of decreasing concentrations of chlorine dioxide from 3,400 ppm to 800 ppm once a week for 3 consecutive weeks). At levels of 10 ppm (4 hours/day for 9 days in a 13-day period), rats exhibited rhinorrhea, altered respiration, and respiratory infection.

Sodium chlorite: A subchronic oral toxicity study (Harrington et al., 1995) conducted in the rat showed systemic effects after repeated oral (gavage) administration of sodium chlorite at doses of 0, 10, 25 or 80 mg/L (corresponding to 0, 7.4, 19 or 60 mg/kg/day). Four animals died in the 60 mg/kg/day treatment level and both males and females exhibited salivation, significantly decreased erythrocyte counts, and decreased total serum protein levels. In the 60 mg/kg/day treatment level, males exhibited significantly decreased hematocrit and hemoglobin levels and increased methemoglobin and neutrophil levels, while females exhibited significantly decreased methemoglobin levels. In the 60 mg/kg/day treatment level, the following observations were also noted: morphological changes in erythrocytes in some animals of both sexes, significant increases in relative adrenal and spleen weights in the males, increases in absolute and relative spleen and adrenal weight in females, and increases in relative liver and kidney weights in the females. The 60 mg/kg/day treatment level also exhibited histopathologic alterations such as squamous epithelial hyperplasia, hyperkeratosis, ulceration, chronic inflammation, and edema in the stomachs of seven males and eight females. In the 19 mg/kg/day treatment level, alterations such as occasional salivation in two males, hematologic alterations in males (increased methemoglobin levels and neutrophil count, decreased lymphocyte count), increases in absolute and relative spleen and adrenal weights in females, and histologic alterations in the stomach of two males, similar to those seen in the high-dose group, were reported.

Developmental Toxicity.

Chlorine dioxide: A developmental toxicity study (Orme et al., 1985) was conducted in rats with chlorine dioxide administered in the drinking water at doses of 0, 1, 20 or 100 mg/L. A depression of serum thyroxin (T4) and an increase of serum triiodothyronine (T3) were observed in pups at weaning at the 100 mg/L (14 mg/kg/day) dose level, as well as a decrease in neurobehavioral exploratory and locomotor activities. These effects, however, were not observed in pups at the 20 mg/L dose level (3 mg/kg). Pups administered chlorine dioxide by gavage at 14 mg/kg/day on post-natal days 5-20 showed a larger depression of serum T4 levels and greater delays in development of exploratory and locomotor behavior activity.

Sodium chlorite: A developmental toxicity study (MRID 41715701) was conducted in rabbits using sodium chlorite (purity 80.58%) administered in the drinking water at doses of 0, 200, 600 or 1200 ppm). Mean intake of the test compound via the drinking water was suppressed in a dose-related fashion at the highest levels, especially over the first few days of dosing. The sole treatment-related clinical effect was a dose-related increase in incidence of does with reduced fecal output during the dosing period, days 7 to 19, which was considered consistent with decreased food consumption. Among gross findings in scheduled sacrifices were: pitted kidneys in two mid-dose and one high-dose animal; alopecia in two low-dose, three mid-dose, and two high-dose does; and thoracic fluid in one low-dose animal.

Reproductive Toxicity. A two-generation reproduction study (CMA, 1996) was conducted in which sodium chlorite was administered to rats (F0 generation) in their drinking water at concentrations of 0, 35, 70 or 300 ppm. The F1 generation was given the same treatment as their parents. Because of a reduced number of litters in the 70 ppm F1-F2a generation, the F1 animals were re-mated to produce a F2b generation. All generations, primarily in the 70 and 300 ppm treatment groups, exhibited decreases in water and food consumption, and body weight gain. In the 300 ppm treatment group, there were significant reductions in absolute and relative liver weight in the F0 females and F1 males and females, reduced pup survival, reduced body weight at birth and throughout lactation in F1 and F2 rats, lower thymus and spleen weight in both generations, lowered incidence of pups exhibiting normal righting reflex and with eyes open on postnatal day 15, alteration in clinical condition in F2 animals chosen for neurotoxicity, decrease in absolute brain weight for F1 males and F2 females, delay in sexual development in males (preputial separation) and females (vaginal opening) in F1 and F2 rats, and lower red blood cell parameters in F1 rats. Reduced absolute and relative liver weights were also observed in the 70 ppm treatment groups for F0 females and F1 males.

Chronic Toxicity. A chronic toxicity study (Haag, 1949) was conducted with a group of rats exposed to 0, 1, 2, 4, 8, 100, or 1,000 mg/L chlorite in the drinking water (0, 0.09, 0.18, 0.35, 0.7, 9.3, or 81 mg/kg-day) for 2 years. Animals exposed to chlorite concentrations of 100 or 1,000 mg/L exhibited treatment-related renal pathology. These effects were also observed in a group of animals administered sodium chloride at a concentration equimolar to 1,000 mg sodium chlorite/L. The study was limited because an insufficient number of animals were tested per group, pathology was conducted on a small number of animals, and it did not provide adequate evaluations of more sensitive parameters, which would have been more useful in the overall assessment of chronic toxicity.

Carcinogenicity. Robinson et al. (1986) assessed the potential for chlorine dioxide to induce proliferative epidermal hyperplasia in dorsally shaved female SENCAR mice exposed to

0, 1, 10, 100, 300, or 1,000 ppm liquid chlorine dioxide. The data from this study are considered inadequate for characterizing the carcinogenicity of chlorine dioxide/chlorite. A dermal carcinogenicity study (Kurokawa et al., 1984) evaluated the ability of chlorite to act as a complete carcinogen. In this study, groups of 20 female SENCAR mice were exposed twice weekly for 51 weeks to 20 mg/mL sodium chlorite in acetone. The study was also considered inadequate because the exposure was for less than a lifetime, a high incidence of Sendai virus was found in the rats, and mortality was high in the mouse control group because of excessive fighting.

Mutagenicity. Several studies exist on the mutagenicity of chlorine dioxide both in the open literature and in the Agency's database of submitted studies. In one study (Miller et al., 1986), negative effects in Salmonella strains TA98 and TA100 from a 400-fold drinking water concentrate of chlorine dioxide and positive effects in a 4000-fold concentrate to strain TA98 only in the absence of metabolic activation were reported. Another study indicated chlorine dioxide was positive for forward mutations under non-activated and activation conditions in L5178Y/TK cells (Accession no. 265867). Chlorine dioxide was positive for structural chromosome aberrations under non-activated and activated conditions (Accession no. 265867) and was negative for increased transformed foci up to cytotoxic levels (Accession no. 265867). *In vivo* micronucleus and bone marrow chromosomal aberration assays in Swiss CD-1 mice administered 0.1–0.4 mg chlorine dioxide via gavage for 5 consecutive days were negative, as was a sperm-head abnormality assay in B6C3F1 mice administered 0.1–0.4 mg via gavage for 5 consecutive days (0, 3.2, 8, and 16 mg/kg-day) (Meier et al., 1985).

Metabolism. Oral studies have provided information regarding the pharmacokinetics of both chlorine dioxide and chlorite. Chlorine dioxide rapidly dissociates, predominantly into chlorite (which itself is highly reactive) and chloride ion (Cl-), ultimately the major metabolite of both chlorine dioxide and chlorite in biological systems (Abdel-Rahman et al., 1984). Urine is the primary route of elimination, predominantly in the form of chloride ion (Abdel-Rahman et al., 1984). Chlorite (ClO_2^-) does not persist in the atmosphere either in ionic form or as chlorite salt. The rapid appearance of 36Cl in plasma following oral administration of chlorine dioxide ($^{36}ClO_2$) or chlorite ($^{36}ClO_2^-$) has been shown in laboratory animals (Abdel-Rahman et al., 1984). In rats, absorbed 36Cl (from $^{36}ClO_2$ or $^{36}ClO_2$ sources) is slowly cleared from the blood and is widely distributed throughout the body (Abdel-Rahman et al., 1984).

Neurotoxicity. In a two-generation reproduction toxicity study (CMA, 1996) conducted with sodium chlorite (81.4% purity) administered in the drinking water, significant changes were observed in maximum response in startle amplitude and absolute brain weight in F1 rat pups at a dose of 3 mg/kg/day. In another developmental toxicity study (Orme et al., 1985), neurobehavioral deficits in offspring were observed at a maternal dose of 14 mg/kg/day.

Table 3. Acute Toxicity Profile for Chlorine Dioxide/Sodium chlorite				
Guideline Number	Study Type[a] / Test substance (% a.i.)	MRID Number/ Citation	Results	Toxicity Category
870.1100	Acute oral (79% chlorine dioxide)	43558601	LD_{50} = 292 mg/kg (males) LD_{50} = 340 mg/kg (females)	II
870.1200	Acute dermal (80% sodium chlorite)	40168704	LD_{50} > 2000 mg/kg	III
870.1300	Acute inhalation (80.6% sodium chlorite)	42484101	LC_{50} = 0.29 mg/L	II
870.2400	Primary eye irritation (2% chlorine dioxide)	43441903	Mild irritant	III
870.2500	Primary dermal irritation (80% sodium chlorite)	40168704	Primary irritant	II
870.2600	Dermal sensitization	No acceptable sensitization study available.		

[a] The available acute studies are all graded as acceptable. An acceptable dermal sensitization study is not available in the database.

3.2 FQPA Considerations

Under the Food Quality Protection Act (FQPA), P.L. 104-170, which was promulgated in 1996 as an amendment to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA), the Agency was directed to "ensure that there is a reasonable certainty that no harm will result to infants and children" from aggregate exposure to a pesticide chemical residue. The law further states that in the case of threshold effects, for purposes of providing this reasonable certainty of no harm, "an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. Notwithstanding such requirement for an additional margin of safety, the Administrator may use a different margin of safety for the pesticide residue only if, on the basis of reliable data, such margin will be safe for infants and children."

When the original toxicity endpoint assessment was conducted, the Hazard Identification Assessment Review Committee (HIARC) concluded that an extra 10x uncertainty factor under the Food Quality Protection Act should be considered in risk assessments conducted for chlorine dioxide. This recommendation was based upon evidence of susceptibility in a two-generation reproduction toxicity study in rats and evidence of susceptibility from scientific literature reports.

Since that time, the Health Effects Division of the Office of Pesticide Programs issued policy guidance September of 2001 regarding the determination of the appropriate FQPA safety factor in tolerance assessment. This guidance states that whereas in the past "...OPP has routinely applied an additional FQPA safety factor where data on a pesticide shows increased

susceptibility or sensitivity (either qualitative or quantitative) in the developing organism," It is the intent that "...OPP will now put greater emphasis on analyzing the degree of concern and, rather than apply an additional safety factor based solely on the identification of heightened sensitivity or susceptibility, will conduct a case-by-case weight of evidence approach that qualitatively examines the level of concern for sensitivity / susceptibility and assess whether traditional uncertainty factors already incorporated into the risk assessment are adequate to protect the safety of infants and children. Using this approach, in many cases the concerns regarding pre- and postnatal toxicity can be addressed when a Reference Dose (RfD) or Margin of Exposure (MOE) is based on the pre- or postnatal endpoints in the offspring."

The endpoint selected for both dietary and non-dietary exposures to chlorine dioxide was based upon adverse effects observed in offspring from developmental and reproductive toxicity data. Consistent with the approach used by the EPA's Office of Water for use of chlorine dioxide as a drinking water disinfectant and the updated guidance on selection of a safety factor under FQPA, the endpoint selected for assessment of risk from dietary and non-dietary exposure to chlorine dioxide was felt to be protective of potentially susceptible populations including children, based upon the selection of an endpoint and effects observed in offspring and the use of an NOAEL value based on those effects. Therefore, it was concluded that an additional safety factor under FQPA was not necessary.

3.3 Dose-Response Assessment

The doses and toxicological endpoints selected by ADTC for various exposure scenarios are summarized in Table 4 below.

Table 4. Summary of Toxicological Doses and Endpoint Selection for Chlorine dioxide/ Sodium chlorite

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	UF/MOE for Risk Assessment	Study and Toxicological Effects
Acute Dietary	An acute dietary endpoint was not identified in the data base for chlorine dioxide. This risk assessment is not required.		
Chronic Dietary	NOAEL = 3 mg/kg/day	UF = 100 (10x inter-species extrapolation, 10x intra-species variation) **Chronic PAD =** 0.03 mg/kg/day	Two-generation reproduction toxicity study (CMA, 1996) - decreases in absolute brain and liver weight, and lowered auditory startle amplitude at LOAEL of 6 mg/kg/day Developmental Toxicity - Rat (Orme et al., 1985)- neurobehavioral and exploratory deficits in rat pups at LOAEL of 14 mg/kg/day
Incidental Oral (short and intermediate term)	NOAEL = 3 mg/kg/day	MOE = 100	See summary for chronic dietary assessment

Table 4. Summary of Toxicological Doses and Endpoint Selection for Chlorine dioxide/ Sodium chlorite			
Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	UF/MOE for Risk Assessment	Study and Toxicological Effects
Short-Term Dermal[a] (1-30 days)	NOAEL = 3 mg/kg/day	MOE = 100	See summary for chronic dietary assessment
Intermediate-Term Dermal[a] (30-days-6 months)	NOAEL = 3 mg/kg/day	MOE = 100	See summary for chronic dietary assessment
Long-Term Dermal[a] (> 6 months)	NOAEL = 3 mg/kg/day	MOE = 100	See summary for chronic dietary assessment
Inhalation (occupational and homeowner short-term)	Homeowner short-term: LOAEL = 28 mg/m^3 (10 ppm)[b] Occupational exposure: LOAEL = 2.8 mg/m^3 (1.0 ppm)[b] NOAEL = 0.28 mg/m^3 (0.1 ppm)[b].	Homeowner short-term 'RfC' = **0.14 mg/m^3** (0.05 ppm)[b] Occupational 'RfC' = **0.009 mg/m^3** (0.003 ppm)[b]	Inhalation toxicity studies- Rat Dalhamn, 1957; Paulet and Debrousses, 1970, 1972.
Inhalation (homeowner long-term)	Agency RfC methodology used to derive an RfC value of 2 x 10^{-4} mg/m^3 (USEPA, 2000a)		(Paulet and Desbrousses, 1970, 1972) selected as co-critical studies (USEPA, 2000a)

[a] Based on the use of an oral endpoint for dermal risk assessments and the lack of a dermal absorption study, a dermal absorption value of 100% as a default will be used.
[b] Unit conversion: 1 ppm ClO_2 x 67.46/24.45 = 2.8 mg/m^3

3.4 Endocrine Disruption

The Food Quality Protection Act (FQPA,1996) requires that EPA develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect…." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendations that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, chlorine dioxide may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 EXPOSURE ASSESSMENT AND CHARACTERIZATION

4.1 Summary of Registered Uses

Chlorine dioxide and sodium chlorite are active ingredients in numerous products used in the control of bacteria, fungi, and algal slimes. Chlorine dioxide and sodium chlorite are also used as material preservatives and as disinfectants. At this time, products containing chlorine dioxide and sodium chlorite are intended for agricultural premises, commercial, industrial, medical and residential use. The agricultural uses include the disinfection of hard surfaces and equipment (such as hatching facilities and mushroom houses) and water systems (such as chiller water and humidification water in poultry houses). Commercial, industrial, and medical uses include disinfection of ventilation systems, hard surfaces (e.g., floors, walls, and laboratory equipment), water systems, pulp/paper mills, and food rinses. Residential uses include disinfection of hard surfaces (e.g., floors, bathrooms), HVAC systems, and pool & spa water circulation system treatments.

4.2 Dietary Exposure and Risk

A detailed dietary exposure risk assessment for chlorine dioxide is provided in the Chlorine Dioxide Dietary Risk Assessment, February 24, 2006. The summary of the exposures and risks are presented below.

The Agency has carried out the dietary exposure and risk assessment for use of chlorine dioxide in products used in the control of bacteria, fungi, and algal slimes, as well as its use as a materials preservative and disinfectant, all of which may result in indirect food contact exposures. No residue chemistry data were submitted by the registrants, nor were any asked for by the Agency. To estimate chlorine dioxide residues on food due to migration of this chemical from sanitizing and/or disinfecting hard non-porous surfaces which can come into contact with food, the Agency has used FDA (US Food and Drug Administration) methodology as well as a methodology established for use in the Agency's Reregistration Eligibility Decision (RED) documents. Potential use sites include: (1) mushroom houses, (2) poultry hatcheries, (3) food handling establishments, (4) post-harvest potato treatments, (5) poultry house disinfection, poultry chiller water/carcass spray or dip, (6) food processing plants (meat and fish), (7) dairies, breweries, and bottling plants, and (8) pulp/paper, polymer slurries, paper adhesive, and paper coating.

In the absence of residue data for residues of chlorine dioxide on treated food contact surfaces, the Agency estimated residue levels that may occur in food from the application rates on food contact surfaces. To estimate the Estimated Daily Intake (EDI), the Agency has used an FDA model. The maximum application rate for chlorine dioxide from the various labeled products is used along with the assumptions that food can contact 2000 cm^2 of treated surfaces and an assumption that 10% of the pesticide migrates to food.

The dietary risks for adult and children are shown in Table 6. As there is no acute dietary endpoint for chlorine dioxide, only chronic dietary risk is presented. For adults, the dietary risk is 23% of the PAD. For children, the dietary exposure is 103% of the PAD, above the Agency's level of concern (100%).

Label changes similar to the following might help reduce the exposure concerns for fruit and vegetable washes: "Water containing up to 3 ppm residual chlorine dioxide may be used for washing fruits and vegetables that are not raw agricultural commodities in accordance with 21 CFR 173.300. Treatment of fruits and vegetables with chlorine dioxide must be followed by blanching, cooking or canning."

If the suggested label changes as stipulated above are made, it is likely the levels of concern (% cPAD) for all populations, including one to two year old children, would be drastically reduced.

Table 6. Summary of Dietary Exposure and Risk for Chlorine Dioxide					
Use Site	**Food Type**	**Population Subgroup**	**EDI (mg/person/day)**	**Chronic Dietary**	
				Dietary Exposure[a] (mg/kg/day)	**% cPAD [b]**
Indirect Food Use					
Food handling establishments/ kitchens	NA	Adult	2.00×10^{-1}	9.5E-07	0.00316
		Child		8.8E-06	0.0293
Dairies, Breweries, Bottling Plants, Food Contact Surfaces/Food Processing Plants for Meats and Fish[d]	Beverages, alcoholic, beer	Adult	1.2×10^{-3}	1.70E-05	0.56
	Beverages, non-alcoholic	Adult	1.6×10^{-3}	2.40E-05	0.08
		Child		1.00E-04	0.33
	Egg Products, Mayonnaise	Adult	1.4×10^{-4}	2.00E-06	0.0086
		Child		9.33E-06	0.031
	Milk	Adult	1.9×10^{-2}	2.70E-04	0.66
		Child		1.30E-03	4.2
Pulp/Paper, Polymer Slurries, Paper Adhesive, Paper Coating	NA	Adult	1.1×10^{-1}	9.8E-05	0.326
		Child		2.3E-04	0.766
Total Indirect Food-Contact Exposure		**Adult**	**3.3×10^{-1}**	**4.12E-04**	**1.64**
		Child 1-2 years	**2.7×10^{-1}**	**1.65E-03**	**5.35**
		Infant <1			**<5.35 [f]**
Direct Food Use					
Post Harvest Application	Fruit and Vegetable Wash	Adult		2.24E-03[c, e]	7.5
		Child		1.27E-02 [c, e]	42.3
Total Direct Food-Contact Exposure		**Adult**		**2.24E-03**	**7.5**
		Child 1-2 years		**1.27E-02**	**42.3[g]**
		Infant <1		**3.49E-03**	**11.6 [f]**
Inorganic Chlorate Use					
Highest Exposure from Agricultural Use		**Child 1 – 2 years**		**8.38E-03[c]**	**28**
		Infant <1 year		4.511E-03	**15 [f]**
Total Dietary Exposure					
Total Direct and Indirect Food-Contact Exposure		**Adult**		**2.65E-03**	**9.1**
		Child 1-2 years		**2.27E-02**	**75.7**
		Infant <1 year			**<31.95 [f]**

a-- For adults, acute and chronic exposure analysis is based on a body weight of 70 kg. For adult females, the body weight is 60 kg. For children, exposure is based on a body weight of 15 kg.

*b--%PAD = dietary exposure (mg/kg/day) * 100 / cPAD, where cPAD for adults and children = 0.03 mg/kg/day;*

c--children 1-2 years of age, adults 20-49 years of age
d--food processing plants for meats/fish have exposures which are similar to other food contact surfaces, exposure numbers not included for this scenario.
e-- includes all fruits and vegetables and apple and orange juices; assumes 100% of fruit is washed with chlorine dioxide.
f--Infants (<1 year) are included in this table for comparison purposes and were not added to the total dietary exposure as it was not the most highly exposed subpopulation.
g--Assuming 50% of fruits/vegetables are treated, the dietary risk for children (1 – 6) would represent 21% of the cPAD.

In the poultry hatcheries, eggs are produced for the production of chicks and not for human consumption. Although it is likely some sanitizer/disinfectant chemicals may penetrate the egg shells and bioaccummulate in the developing chicks, at this time the Agency believes that the amount of the chemical transferred to the developing chicks is not likely to adversely affect the development of chicks and will have an even smaller transfer into humans. The Agency has no dietary risk concerns at this time for this use.

Similarly, the Agency has no concerns at this time for use of chlorine dioxide and sodium chlorite for stored potato treatment and subsequent interstate commerce of this commodity. EPA's Antimicrobials Division had asked the States of Idaho and Washington to collect analytical data on the residues on chlorine dioxide treated post-harvest potatoes (USEPA, 1998). Two breakdown products of chlorine dioxide were measured, chlorite and chlorate. Chlorite was found to be non-detect in the samples and only small quantities of chlorate (0.97 to 1.1 µg/g) were found in only three samples. The Agency did not see any concerns for the presence of chlorate at the levels reported in the samples.

For poultry house disinfection and poultry chiller water/carcass spray or dip, the application and method of application is exactly the same as was submitted to FDA for their risk assessment. FDA assessed the risks involved for this use (FDA Memo: FAP: 4A4433, 1994). FDA extensively reviewed the efficacy and analytical chemistry data on the residues of chlorate/chlorite or possibly chlorine dioxide for the scenarios listed. Residues of chlorite and chlorates were measured on poultry carcasses after pre-chiller and chiller water treatments. After the pre-chiller, neither chlorite nor chlorate was detected between 0.009 ppm to 0.011 ppm levels of detection. In the chiller water treatment, chlorite detection was at 0.54 ppm at time zero, 0.09 ppm at 10 minutes and at 0.021 ppm after one hour. The level of detection (LOD) was set at 0.016 ppm. Chlorite was non-detect after 2 hours. Chlorate was non-detect even at time zero. It is likely that the residual chlorate/chlorite associated with the poultry may be going through oxidative processes to form chlorinated organics. FDA asked the industry to conduct studies on the formation of chlorinated organics, and no evidence was found for the formation of chlorinated organics. However, some PCBs were detected at the background levels. Open literature studies support the results that with acidified sodium chlorate treatment of poultry no chlorinated organics are formed. FDA accepted the studies and concurred with the results. At this time, the Agency does not have any concerns with the use of acidified sodium chlorite solution on carcasses.

For food processing plants (meat and fish), the application rates are similar to those used for food handling establishments, and therefore, the exposure would also be similar. At this time, the Agency does not have any dietary concerns for this application.

The Agency, at this time, has not established any tolerances or exemptions from the requirement of tolerance for chlorine dioxide as a sanitizer in mushroom facilities. Chlorine

dioxide is applied to equipment at rates that vary between 100 -200 ppm; however transfer of residue levels on mushrooms is not indicated. The Agency is not requiring any tolerances any tolerances of chlorine dioxide on mushroom uses. The Agency has not conducted any dietary risk assessment for mushroom use, as no dietary risks are indicated.

FDA assumptions were used to calculate the dietary exposure from sanitizing food-contact surfaces; processing equipments; and utensils in dairies, breweries, canning operations, and meat and vegetable processing plants. Based on these assumptions and data on alcoholic beverages/beer, non-alcoholic beverages, egg products, and salad dressing/mayonnaise, the highest %cPAD calculated is 4.2% for children's consumption of milk.

According to the Agency's memo of may 9, 2006, the Agency has accepted the label change from the label for SLIME-TROL RX33 (USEPA reg # 74655-2) which allowed for the deletion of the label statement which referred to the use of the product in pulp and paper as a slimicide. Based on this information, the Agency has decided to exclude the dietary assessment which covers uses of chlorine dioxide and sodium chlorite as a polymer slurry as filler paper, as a paper adhesive preservative and as a paper coating preservative.

For direct food uses, AD conducted a chronic risk assessment for the fruit and vegetable washes (post-harvest) and the chronic risk from these uses appear to be below the Agency's level of concern.

Table 7. Exposure by Population Group

Population Subgroup	Total exposure (mg/kg body wt./day)	% cPAD
U.S. Population	0.003292	11
Infants <1 year	0.003493	12
Children 1-6 years	0.009933	33
Children 7-12 years	0.004208	14
Females 13-50	0.002689	9

4.3 Drinking Water Exposures and Risks

In a memo from Pat Fair of the EPA's Office of Water, exposure to chlorine dioxide from drinking water was characterized. Chlorine dioxide is used as a disinfectant in water treatment plants in the USA. Chlorite ions (ClO_2) are present in drinking water as a result of reactions involving chlorine dioxide. Because of the health concerns resulting from the presence of the chlorite ions and their subsequent conversion to chlorate ions, the Agency wanted to make sure that the level of chlorite ions did not exceed certain specified limits. The EPA instituted a system for monitoring the occurrence of chlorite in drinking water and collected data from July 1997 to December 1998.

Based on the results of this monitoring data, the Agency established a Stage I Disinfectants and Disinfection Byproduct Rule, which established a maximum contaminant level goal (MCLG) and a maximum contaminant level (MCL) for chlorite ions. The MCLG and MCL are 0.8mg/L and 1.0 mg/L, respectively. Based on the values obtained from the monitoring data,

the Agency conducted a drinking water assessment using chlorite concentrations at the maximum, 90th percentile, and median annual averages of chlorite concentrations of 0.700, 0.630, and 0.390 mg/L, respectively. The DEEM-FCID™, Version 2.0 software (EPA, 2000) was used to determine the exposure values (Memo from David Hrdy, HED, to Jennifer Slotnick, AD). Table 8 presents the exposures and corresponding risks. The 90th percentile exposure values will be used in the aggregate risk assessments, with children represented by the 1-6 year old age category. The only subpopulation that the Agency has concerns for is infants (less than one year old) when exposed to chlorine dioxide treated water. All other subpopulations and the general population have risks below the Agency's level of concern.

In addition to the information above, the Agency has reviewed an additional study on the determination of chlorite in baby formula prepared from water containing residual chlorite (report by T.V. Tran, report # TR05-01). The Agency agrees that there is evidence that the components of the baby formula react with chlorite in the drinking water; however, the Agency has no quantitative tool to assess the extent of reduction in exposure to chlorite if specific chemicals are present in the baby formula. Due to these uncertainties, the Agency believes that for all infants (< 1 year old) as well as non-nursing infants (<1 year old), the % cPAD may likely be less than 100.

Table 8. Chlorite Exposure by Population Group

Population subgroup	Maximum Concentration		90th Percentile Concentration		Median Concentration	
	Total exposure (mg/kg/day)	% cPAD	Total exposure (mg/kg/day)	% cPAD	Total exposure (mg/kg/day)	% cPAD
U.S. Population	0.014754	49	0.013279	44	0.008220	27
Infants < 1 year	0.048372	161	0.043535	145	0.026950	90
Children 1-6 years	0.020613	69	0.018552	62	0.011485	38
Children 7 -12 years	0.013402	45	0.012062	40	0.007467	25
Females 13-50	0.014274	48	0.012846	43	0.007952	27

4.4 Residential Exposure/Risk Pathway

A detailed human exposure risk assessment for chlorine dioxide is provided in the attached Appendix. The summary of the exposures and risks to the residential population are presented below.

4.4.1 Residential Handler Scenarios

Exposure Scenarios

Chlorine dioxide and sodium chlorite are active ingredients in numerous products used in the control of bacteria, fungi, and algal slimes. In addition, chlorine dioxide and sodium chlorite are used as material preservatives and as disinfectants. Residential uses of chlorine dioxide and/or sodium chlorite products that are applied by homeowners include the control of mold and

mildew (i.e., EPA Reg. No. 21164-3). For the exposure assessment, household cleaning products were grouped together to be represented by a higher application rate from a sodium chlorite product (i.e., EPA Reg. No. 21164-3). The post application scenario is based on a product that applies chlorine dioxide to floors that have the potential for children playing. Three scenarios, mopping, spraying, and placing tablets in pools/spas, were examined to represent the residential uses in the risk assessment.

Exposure Data and Assumptions

There are no chemical-specific exposure data to assess applications to hard surfaces with a mop or trigger-pump sprayer or to pools/spas. However, surrogate data are available. Dermal exposures were assessed using the proprietary Chemical Manufacturers Association (CMA) data (MRID 42587501) for mopping as well as placing tablets in pools/spas and the Pesticide Handler Exposure Database (PHED, 1998) for spraying. The CMA data for mopping are based on individuals mopping floors and receiving exposure via contact with the mop or with the bucket. Dermal exposures were assessed for trigger pump spray application methods using *PHED Version 1.1* values found in the *Residential Exposure SOPs* (USEPA, 2000b). The surrogate exposure data in PHED are based on test subjects applying an insecticide from an aerosol can to baseboards in kitchens. The dermal exposures from these techniques have been normalized by the amount of active ingredient handled and reported as unit exposures (UE) expressed as mg/lb ai handled.

In addition, product label maximum application rates, related use information, and Agency standard values were used to assess residential handler exposures. For example, it was assumed that one gallon of diluted solution is used for mopping floors, while 0.5 liters (0.13 gallons) are used in the trigger pump spray scenario. The residential handler scenarios are assumed to be of short-term duration (1-30 consecutive days).

Risk Characterization

A summary of the dermal residential handler exposures and risks are presented in Table 9. Although the dermal endpoint represents short-, intermediate-, and long-term durations, the exposure duration of most homeowner applications of cleaning products is believed to be best represented by the short-term duration. The toxicological endpoint is based on an oral study and no dermal absorption value is available. Therefore 100% dermal absorption was assumed. The calculated dermal MOEs are above the target MOE of 100 for both of the cleaning scenarios. The dermal MOE for applications to hard surfaces via trigger-pump sprayer is 3,200 and the dermal MOE for application of liquid formulations via mopping is 1,300. However, the dermal MOE for the placement of tablets into pools is 46, and therefore, of concern. This risk can be mitigated with the use of gloves (MOE=500).

Table 9. Estimates of Short-term Dermal Exposures and Risks to Residential Handlers of Chlorine Dioxide

Product	Exposure Scenario	Potential Dermal Dose[a] (mg/kg/day)	Dermal MOE[b] (Target MOE = 100)

Cleaning	Mopping - hard surfaces	0.095	1300
	Trigger-pump sprayer - hard surfaces	0.038	3200
Swimming Pools	Solid Place (tablets)	0.065 (no gloves) 0.006 (gloves)	46 (no gloves) 500 (gloves)

a Potential Dermal Dose (mg/kg/day) = Application Rate (lb ai/gallon) * gallons used * Dermal Unit Exposure (mg/lb ai))/ Body Weight (60 kg), where dermal absorption is 100 percent.

b Dermal MOE= Dermal NOAEL (3 mg/kg/day)/Absorbed Dermal Dose (mg/kg/day).

The potential inhalation of chlorine dioxide may occur from off gassing during application of the aqueous solution. Chlorine dioxide has the potential to generate a gas during the residential uses of mopping and spraying. However, it is unlikely that levels of concern for chlorine dioxide would be generated outdoors while treating swimming pools & spas with tablets placed into water.

EFAST (Exposure and Fate Assessment Screening Tool) was used to model the air concentration from general purpose cleaners (http://www.epa.gov/opptintr/exposure/). The peak instantaneous air concentration is 0.265 mg/m^3 (0.09 ppm) and the average daily TWA (time-weighted average) air concentration is determined to be 0.00794 mg/m^3 (0.003 ppm). The residential short-term inhalation endpoint (RfC) is 0.05 ppm. Based on the average daily air concentration (representing both application and post application), the handler inhalation exposures of chlorine dioxide are not of concern (i.e., the average air concentration estimated by EFAST of 0.003 ppm is below the RfC of 0.05 ppm).

4.4.2 Residential Post Application Exposure

Residential post application exposures result when bystanders (adults and children) come in contact with chlorine dioxide in areas where pesticide-treated end-use products have recently been applied (e.g., treated hard surfaces/floors), or when children incidentally ingest the pesticide residues through mouthing the treated end products/treated articles (i.e., hand-to-mouth or object-to-mouth contact). Because of the high vapor pressure of chlorine dioxide, inhalation exposure to chlorine dioxide off gassing is also a potential route of exposure.

For the purposes of this screening-level assessment, four scenarios have been considered. These include: (1) exposure to residue from hard floors that have been cleaned/mopped with a generic cleaner containing chlorine dioxide, (2) exposure to chlorine dioxide used to clean residential HVAC systems, (3) exposure to a continuous release (gas) deodorizer, and (4) swimming.

Exposure Data and Assumptions

Typically, most products used in a residential setting result in exposures occurring over short-term time duration (1 – 30 days). If the products are used on a routine basis (i.e., once a week) and the active ingredient has a long indoor half-life, exposures may occur over an intermediate-term time duration (30 days – 6 months). At this time, AD does not have residue

dissipation data or reliable use pattern data, including the frequency and duration of use of antimicrobial products in the residential setting. Even though AD does not believe that the use patterns of many residential products result in intermediate-term exposure, they are assessed to provide an upper bound estimate of exposure. AD does believe, however, that intermediate-term exposure to children may occur in day care centers where disinfecting products are used more frequently.

A number of conservative assumptions were used in assessing post application risks including maximum application rates from the label. In addition, quantities handled/treated were estimated based on information from various sources, including the Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments (USEPA 2000b). In certain cases, no standard values were available for some scenarios. Assumptions for these scenarios were based on AD estimates and could be further refined from input from affected sectors.

Risk Characterization

A summary of the residential dermal and oral post application exposures and risks are presented in Table 10. The child short- and intermediate-term dermal MOE for contact following hard surface disinfection is above the target MOE of 100 for residential and daycare settings (MOE = 280). The short- and intermediate-term incidental oral MOE following hard surface disinfection is above the target MOE of 100 for residential and daycare settings (MOE = 2,300), and thus is not of concern.

Inhalation exposures due to post application activities could occur for children after the treatment of floors; adults and children after the treatment of HVAC systems; and adults and children after the use of continuous release (gas) deodorizers. Chlorine dioxide and/or sodium chlorite can be applied as an aqueous solution to hard surfaces such as floors (as well as dust applications to carpets). Based on the use label, which contains the highest rate of application of chlorine dioxide to disinfect a room, and using several assumptions, the maximum air concentration of chlorine dioxide can be estimated. Two methods were used to assess the inhalation risks to residents. First, there are air concentration measurements available after the application of chlorine dioxide as a dust treatment on carpets (Speronello 2005). Although there are limitations to this study (e.g., not conducted under Good Laboratory Practices (GLPs), minimal information is available in the study report), it is the only data source available at this time. Secondly, a theoretical approach to estimating chlorine dioxide air concentration is also presented based on dilution and ventilation along with the half-life of chlorine dioxide. Based on these estimates, an 8-hour TWA air concentration starting immediately after application has been determined to be 0.08 ppm which is above the short-term RfC of 0.05 ppm. To mitigate this risk concern, a second 8-hour TWA air concentration was calculated assuming a 1-hour restricted entry interval (REI). If one could assume that residents would stay out of the house for the first hour, the 8-hour TWA is 0.02 ppm which is below the RfC of 0.05 ppm. To accurately determine the initial concentration of chlorine dioxide in the air after mopping, air monitoring data would be needed.

For HVAC systems, BCI (2002) monitored a chlorine dioxide treatment of a HVAC

system in a residence. The air concentrations monitored indicated a maximum value of 0.02 ppm and the average value was below the detection limit of 0.01 ppm. The short-term inhalation RfC for chlorine dioxide is 0.05 ppm. According to the label, the frequency of HVAC system treatments is to *"treat as required."* The frequency of residential (and/or commercial/intuitional) HVAC treatments is expected to be minimal (most likely less than once per year). In addition, the half-life of chlorine dioxide is rapid. Therefore, inhalation exposure is expected to be limited to short-term durations and inhalation risks are not expected to be a concern.

For the continuous release deodorizers, a bounding estimate of air concentration is presented based on the application rate and the label-referenced longevity of the pouches/sachets. The theoretical constant air concentration would be 0.52 ppm assuming no air exchange and no build up of chlorine dioxide over time because of the short half-life. The RfC for long-term continuous exposure is 0.00007 ppm. Therefore, the theoretical concentration from the product's release is of concern. This bounding estimate can be refined by determining residential (and commercial/institutional) ventilation rates, identifying sensitive analytical detection methods and collecting monitoring data, and determining the number of hours an individual is exposed in treatment areas. However, before any refinements to these air concentration estimates are attempted, it should be determined if the product's efficacy can be maintained at the RfC of ~0.00007 ppm.

Table 10. Summary of Short- and Intermediate-Term Residential Postapplication Exposures and Risks

Scenario		Dose [a] (mg/kg/day)	MOE[b] (Target MOE>100 dermal and oral)
Dermal Exposure			
Hard surface Disinfection	Residential Setting and Daycare center	0.017	280
Incidental Oral Exposure			
Hard surface Disinfection	Residential Setting and Daycare center	0.0013	2,300

[a] Dose calculations for each scenario above are outlined in the attached Occupational/Residential Assessment.
[b] MOE= NOAEL (mg/kg/day) / Dose (mg/kg/day). Oral and dermal NOAEL is 3 mg/kg/day.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATIONS

In order for a pesticide registration to continue, it must be shown that the use does not result in "unreasonable adverse effects on the environment". Section 2 (bb) of FIFRA defines this term to include "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with standard under section 408..." of FFDCA. Consequently, even though no pesticide tolerances have been established for chlorine dioxide, the standards of FQPA must still be met, including "that there is reasonable certainty that no harm will result from

aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there are reliable information." Aggregate exposure is the total exposure to a single chemical (or its residues) that may occur from dietary (i.e., food and drinking water), residential, and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal, and inhalation). Aggregate risk assessment were conducted for acute (1 day), short-term (1-30 days), intermediate-term (1-6 months) and chronic (several months to lifetime) exposures.

In performing aggregate exposure and risk assessments, the Office of Pesticide Programs has published guidance outlining the necessary steps to perform such assessments (General Principles for Performing Aggregate Exposure and Risk Assessments, November 28, 2001; available at http://www.epa.gov/pesticides/trac/science/aggregate.pdf). Steps for deciding whether to perform aggregate exposure and risk assessments are listed, which include: identification of toxicological endpoints for each exposure route and duration; identification of potential exposures for each pathway (food, water, and/or residential); reconciliation of durations and pathways of exposure with durations and pathways of health effects; determination of which possible residential exposure scenarios are likely to occur together within a given time frame; determination of magnitude and duration of exposure for all exposure combinations; determination of the appropriate technique (deterministic or probabilistic) for exposure assessment; and determination of the appropriate risk metric to estimate aggregate risk.

5.1 Acute and Chronic Aggregate Risks

The acute and chronic aggregate risk assessments include only dietary and drinking water exposures. An acute risk assessment was not conducted for chlorine dioxide because there were no acute dietary endpoints of concern. Drinking water exposure estimates are presented in Section 4.3. Acute and chronic dietary risk estimates from direct and indirect food uses are presented in Table 6 of Section 4.2. Table 11 presents a summary of these exposures, including the aggregate dietary exposure (all direct and indirect food contact exposures) as well as a total dietary aggregate exposure value (drinking water plus direct/indirect dietary exposures).

Table 11. Chlorine Dioxide Chronic Aggregate Exposures and Risks

Exposure Routes	Chronic Dietary Exposures (mg/kg/day)			
	Dietary (indirect + direct food contact+ chlorate) Exposures[a]	Drinking water exposures	Aggregate Dietary Exposures[b]	Aggregate Dietary Risks (%cPAD)
Adults				
Oral Ingestion	2.65E-03	1.33E-02	1.6E-02	53.3%
Children (age 1 – 6)				
Oral Ingestion	2.27E-02	1.86E-02	4.13e-02	133%

a Dietary (indirect + direct food contact) exposures = sum of dietary exposures presented in Table 6.
b Aggregate Dietary Exposures = sum of both dietary (direct and indirect food contact) exposures and drinking water exposures.

5.2 Short- and Intermediate-Term Aggregate Exposures and Risks

Short- and intermediate-term aggregate exposures and risks were assessed for adults and children that could be exposed to chlorine dioxide residues from the use of products in non-occupational environments. The following list summarizes all of the potential sources of chlorine dioxide exposures for adults and children.

Adult chlorine dioxide exposure sources:

- handling of cleaning products containing chlorine dioxide as an active ingredient during wiping activities;
- handling of cleaning products containing chlorine dioxide as an active ingredient during mopping activities;
- eating food having chlorine dioxide residues from use of product on fruits and vegetables;
- eating food having chlorine dioxide residues from indirect food contact; and
- drinking water containing chlorine dioxide.

Child chlorine dioxide exposure sources:

- post-application exposures to cleaning product residues containing chlorine dioxide as an active used on hard surfaces (i.e., floors);
- eating food having chlorine dioxide residues from use of product on fruits and vegetables;
- eating food having chlorine dioxide residues from indirect food contact; and
- drinking water containing chlorine dioxide.

The use patterns of the products and probability of co-occurrence must be considered when selecting scenarios for incorporation in the aggregate assessment. Table 12 summarizes the scenarios included in the short- and intermediate-term aggregate assessments.

Table 12. Exposure Scenarios Included in the Aggregate Assessments

	Short-term Aggregate	Intermediate-Term Aggregate
Adults	▪ chronic dietary (direct and indirect) ▪ handling cleaning products – spray (dermal only) ▪ handling cleaning products – mopping (dermal only) ▪ chronic drinking water	N/A
Children	▪ chronic dietary – (direct and indirect) ▪ post-app to cleaning product (dermal and oral) ▪ chronic drinking water	▪ chronic dietary – (direct and indirect) ▪ post application to cleaning product (dermal and oral) ▪ chronic drinking water

The chronic dietary exposures were used in both the short- and intermediate-term aggregate assessment because chronic dietary exposures occur nearly every day (as opposed to acute dietary exposures occurring on a one-time basis). Therefore, short- or intermediate-term non-dietary exposures have a much higher probability to co-occur with the chronic dietary intake rather than the acute dietary intake.

Cleaning activities in a residential setting occur on a short-term basis. However, the chlorine dioxide-containing cleaning products are also labeled for use in institutional settings such as day-care facilities where cleaning activities can occur on an intermediate-term basis. Therefore, children could have exposure to cleaning product residues on a more continuous basis in a day care facility, thus, these post application scenarios were included in the intermediate-term aggregate assessment.

Since the toxicity endpoints for the oral and dermal routes of exposure are based on the same study and same toxic effect, these two routes are aggregated together. Aggregate risks were calculated using the total MOE approach outlined in OPP guidance for aggregate risk assessment (August 1, 1999, Updated "Interim Guidance for Incorporating Drinking Water Exposure into Aggregate Risk Assessments"). Table 13 presents a summary of both dietary and dermal exposures. Table 14 presents a summary of the short- and intermediate-term aggregate risk MOEs. The aggregate risks are not of concern for adults, as the total aggregate MOE is 130, which is above the target of 100. For children, the aggregate risk estimates are below the target MOE of 100 (MOE=44) and thus are of concern. It should be noted that several conservative assumptions were used in this assessment.

Table 13. Doses for Short- and Intermediate-term Aggregate Assessment

Exposure Routes	Aggregate Dietary Exposures (mg/kg/day)	Dermal Exposures (mg/kg/day)		
		Hard Surface Cleaning		
		Applicator		Post-Application
		Mop	Spray	
Adults				
Oral Ingestion	2.0E-02	NA	NA	NA
Dermal	NA	0.0024	0.00095	NA
Children				
Oral Ingestion	5.0E-02	NA	NA	0.0013
Dermal	NA	NA	NA	0.017

Table 14. Short- and Intermediate-term Aggregate Risks (MOEs)

Exposure Routes	Aggregate Dietary Risks	Dermal Risks (MOE)			Aggregate Risks (MOE)
		Hard Surface Cleaning			
		Applicator		Post-Application	
		Mop	Spray		
Adults					
Oral Ingestion MOEs	150	NA	NA	NA	150

Table 14. Short- and Intermediate-term Aggregate Risks (MOEs)					
Exposure Routes	Aggregate Dietary Risks	Dermal Risks (MOE)			Aggregate Risks (MOE)
		Hard Surface Cleaning			
		Applicator		Post-Application	
		Mop	Spray		
Dermal MOEs	NA	1300	3200	NA	900
Total MOE	150	1300	3200	NA	130
Children (age 1 – 6)					
Oral Ingestion MOEs	60	NA	NA	2300	58
Dermal MOEs	NA	NA	NA	180	180
Total MOE	60	NA	NA	160	44
Infants < 1					
Oral Ingestion	55	NA	NA	2300	55
Dermal MOEs	NA	NA	NA	180	180
Total MOE	55	NA	NA	160	41

MOE = NOAEL/dose
Aggregate MOE = $1/((1/MOE_{dietary}) + (1/_{MOEdrinking\ water}) + (1/MOE_{dermal})$
All NOAELs = 3 mg/kg/day
Target MOE oral = 100
Target MOE dermal = 100

6.0 CUMULATIVE RISK

Section 408 of the FFDCA stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

EPA has not assumed that chlorine dioxide has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

7.0 OCCUPATIONAL EXPOSURE

A detailed human exposure risk assessment for chlorine dioxide is provided in the attached Appendix. The summary of the exposures and risks to occupational workers are presented below.

7.1 Occupational Handler

Potential occupational handler exposure from the use of chlorine dioxide products can occur in various use sites, including agricultural premises, food handling, commercial and institutional premises, medical premises, human drinking water systems, industrial processes and water systems, application to material preservatives, and swimming pools and other aquatic areas. The occupational exposure scenarios and estimated risks are presented in Table 15. Exposure estimates for the fruits and vegetable wash and the machinists exposed to treated metal working fluids (MWF) are presented separately.

To assess the handler risks, AD used surrogate unit exposure data from both the proprietary Chemical Manufacturers Association (CMA) antimicrobial exposure study and the Pesticide Handlers Exposure Database (PHED). Inhalation handler exposures were combined with post application exposures to represent a "full-day" or 8-hour time weighted average (TWA) to be comparable to the inhalation RfC. Inhalation exposure to the release of chlorine dioxide gas during the mixing/loading/application of products producing chlorine dioxide may occur. Because the inhalation toxicological endpoint is based on an 8-hour TWA, the assessment of handler inhalation exposures is assessed as a combination of activities throughout a work day. The assessment of inhalation exposure is presented in the post application/bystander section

For the occupational handler dermal risk assessment, the short- and intermediate- term risks calculated at baseline exposure (no gloves and no respirators) were above target MOEs for all scenarios (i.e., dermal MOEs were >100), except for the following:

Agricultural premises and equipment:

- application to hard surfaces: low pressure handwand (MOE=31),
- application to hard surfaces: mopping (MOE=70), and
- application to hard surfaces: foam applicator equipment (MOE=52).

Food Handling, Commercial/Institutional, and Medical Premises and Equipment:

- application to hard surfaces: mopping (MOE=66 commercial; 3 medical).

To calculate the dermal exposure for a worker treating fruits and vegetables, the Consumer Exposure Pathway of the Exposure and Fate Assessment Tool (CEM/E-FAST) was used. CEM calculates conservative estimates of inhalation and dermal exposures to consumer products. The estimated dermal MOE for the fruit and vegetable wash is 2,300, and therefore, not of concern.

Finally, there is the potential for exposure to machinists contacting chlorine dioxide when used as a material preservative in metal working fluid (MWF). There is a potential for dermal and inhalation exposure when a worker handles treated metalworking fluids. Because of the high vapor pressure of chlorine dioxide, the inhalation route of exposure is not assessed in the

typical manner (i.e., using the OSHA PEL for oil mist x percent concentration in solution). See below for the discussion of the inhalation route of exposure for occupational workers. The dermal route of exposure to machinists occurs after the chemical has been incorporated into the metalworking fluid and a machinist is using/handling this treated end-product. Short-, intermediate-, and long-term exposure estimates were derived using the 2-hand immersion model from ChemSTEER. The results indicate that the short-, intermediate-, and long-term dermal MOE is 14,000, and therefore, not of concern.

Table 15. Short-, Intermediate-Term Risks for Occupational Handlers

Exposure Scenario	Method of Application	Application Rate (lb ai/ gallon)	Quantity Handled/ Treated per day (gallons)	MOE[c]	
				Baseline Dermal[a] (Target MOE>100)	PPE Gloves Dermal[b] (Target MOE>100)
Agricultural Premises and Equipment					
Application to hard surfaces	Low pressure handwand	0.015	2	**31**	No data
	Liquid Pour		0.188	1,300	6,300
	Trigger-pump sprayer		0.26	240	570
	Mopping	0.018	2	**70**	No data
	Foam applicator equipment	0.06	4	**20**	**52**
Food Handling, Commercial/Institutional, and Medical Premises and Equipment					
Application to hard surfaces	Mopping	0.019	2	**66**	No data
	Trigger-pump sprayer	0.08	0.26	**46**	110
Human Drinking Water Systems					
Water and Storage systems	Metering pump	0.007	34,000	No data	120
Material Preservatives					
MWF	Liquid pour	0.0001	300	No data	33,000
Industrial Processes and Water Systems					
Paper and pulp white water systems	Metering pump	0.0344 lb ai/ton paper	500 tons paper	No data	2,300
Oil systems	Open pour	0.069	2.8	NA	6,900
			5.6		3,500

Table 15. Short-, Intermediate-Term Risks for Occupational Handlers					
Exposure Scenario	Method of Application	Application Rate (lb ai/ gallon)	Quantity Handled/ Treated per day (gallons)	MOE[c]	
				Baseline Dermal[a] (Target MOE>100)	PPE Gloves Dermal[b] (Target MOE>100)
Swimming Pools and Aquatic Areas					
Retention ponds/fountain	Liquid pour	0.00001	10,000	No data	670
Swimming pools (public)	Solid place	1.8E-5	200,000	**5**	120
HVAC Systems					
HVAC	Airless sprayer	0.007	5	140	NA
	Fogger (liquid pour)		0.25	2,000	NA

a Baseline Dermal: Long-sleeve shirt, long pants, no gloves.
b PPE Dermal with gloves: baseline dermal plus chemical-resistant gloves.
c MOE = NOAEL (mg/kg/day) / Daily Dose [Where short-and intermediate-term NOAEL = 3 mg/kg/day for dermal exposure]. Target MOE is 100 for dermal exposure.

7.2 Occupational Post Application Exposure

7.2.1 Dermal Post Application Exposure

No information is available to assess post application/bystander dermal exposure to uses in agricultural premises as well as food handling, commercial/institutional and medical premises; human drinking water facilities; industrial processes; and retention ponds. However, dermal post application exposure to chlorine dioxide is expected to be less than that of the dermal contact of children playing on treated floor surfaces. Therefore, the dermal exposure route is not believed to be of concern in these industries.

7.2.2 Inhalation Post Application Exposure

Non-Fogging Uses

There is the potential for the off gassing of chlorine dioxide during some applications that are not totally enclosed (e.g., spray aqueous solution, mopping, pouring, etc). Although no occupational air monitoring data have been submitted to assess the inhalation route, EPA has obtained air concentration measurements from OSHA. OSHA maintains a data base known as the Integrated Management Information System (IMIS). The IMIS entries for chlorine dioxide are available for 7 industry Standard Industrial Classification (SIC) codes. Specific uses such as applicators, bystanders and the activities involved are not available. The SIC codes representing the chlorine dioxide data in IMIS used in this assessment include:

- SIC 0723 Crop preparation services for market;
- SIC 1629 Heavy construction;
- SIC 2611 Pulp mills;

- SIC 2621 Paper mills;
- SIC 2819 Industrial inorganic chemicals;
- SIC 2836 Biological products; and
- SIC 3999 Manufacturing industries.

The data selected for this analysis include only those samples that are reported as 8-hour TWA measurements from personal air samplers. Other samples, such as peak concentrations and/or area monitors, have been omitted. The chlorine dioxide sampling and analytical procedures used in the collection of the data in IMIS are available at http://www.osha.gov/dts/sltc/methods/inorganic/id202/id202.html. The quantitative LOD from this method is 0.004 ppm for a 4-hour sample (the recommended sampling time). The reported full 8-hour work shift samples are based on two 4-hour samples collected in sequence. The inhalation endpoint selected by EPA is 0.003 ppm, just below the OSHA LOD for an 8-hour TWA air sample [i.e., (0.5 x 0.004 ppm per 4 hrs) + (0.5 x 0.004 ppm per 4 hrs)=0.004 ppm per 8 hours].

The summary results of the 33 observations taken from 8-hour TWA personal air samplers for chlorine dioxide are above the EPA selected inhalation reference concentration (RfC) of 0.003 ppm, and therefore, are of concern. Of the 33 TWA measurements available, 21 of those measurements were below the LOD of 0.004 ppm. In addition, of the 33 TWA measurements, only 3 were at or above the OSHA PEL of 0.1 ppm.

Fogging Uses

The fogging use of chlorine dioxide is unique such that no persons are present during the actual application/fogging. There is also a greater potential for chlorine dioxide gas formation from fogging then an aqueous-based application such as mopping. Therefore, a separate assessment was developed for foggers that indicate potential inhalation exposure and reentry recommendations. The air concentration in a fogged area should be below the occupational RfC of 0.003 ppm before the room is entered by persons not wearing respiratory protection. EPA Reg. No. 74602-2 was used to illustrate potential air concentrations.

Concentrations of chlorine dioxide were estimated for buildings after fogging applications. Air concentrations were calculated using the Multi-Chamber Concentration and Exposure Model (MCCEM v1.2). MCCEM estimates average and peak indoor air concentrations of chemicals released from products or materials in houses, apartments, townhouses, or other residences. Although the data libraries contained in MCCEM are limited to residential settings, the model can be used to assess other indoor environments. MCCEM has the capability to estimate inhalation exposures to chemicals, calculated as single day doses, chronic average daily doses, or lifetime average daily doses.

The product, EPA Reg # 74602-2 (sodium chlorite with a 5% chlorine dioxide equivalent) has a maximum application rate for egg houses of 0.0083 lb ai/gal (1000 ppm chlorine dioxide treatment solution). This particular product specifically lists a Dramm fogger for the application (i.e., ultra low volume (ULV)). According to the registrant, the Dramm fogger for chlorine dioxide applications uses 2.5 ounces of the diluted product per 225,000 cubic feet (USEPA 2006), and the label states to run the fogger for five minutes. **Note: This labeled**

rate should be added to all chlorine dioxide fogger uses. If other registrants require a higher application rate, these rates need to be brought to EPA's attention during the development of the chlorine dioxide RED.

Using an air exchange rate (air changes per hour or ACH) of 0.18, an 8-hr TWA of less than 0.003 ppm (0.0084 mg/m^3) is expected with no REI. Although there appears to be no inhalation risks of concern, a 1-hour REI would be prudent.

In a second fogging example, EPA Reg. No. 21164-3 allows chlorine dioxide fogging and misting applications while workers are in the room if the level of chlorine dioxide does not exceed the TLV-TWA of 0.1 ppm. The use directions are as follows:

> *"…may be added to the plant misting or fogging systems to deodorize and to control odor causing bacteria, mold and mildew in food processing plants, dairies, bottling plants, poultry, meat and fish plants and animal facilities such as poultry houses, swine pens, calf barns and kennels. If the TLV-TWA is to be exceeded, turn off air handlers and vacate people and livestock from the rooms to be fogged or misted. Ventilate for 15 minutes prior to reentry. Note – Be careful not to add concentrated acid solutions to undiluted DURA KLOR as high concentrations of chlorine dioxide gas may evolve. The concentration of chlorine dioxide in the diluted DURA KLOR solution should not be allowed to exceed 0.5 ppm…"*

The occupational RfC of 0.003 ppm could be exceeded based on these use directions (i.e., workers do not need to leave treatment area unless the TLV-TWA of 0.1 ppm is exceeded).

EPA's Risk-based RfC versus OSHA PEL

It is also important to note that the OSHA PEL for chlorine dioxide is 0.1 ppm. Air concentrations above the PEL are assumed to be mitigated at each facility. Facilities using chlorine dioxide are not required to mitigate inhalation exposures until the air concentration reaches 0.1 ppm. Based on the occupational inhalation toxicological endpoint selected for chlorine dioxide (i.e., RfC of 0.003 ppm), levels at or near the PEL are of concern. In fact, the capability (i.e., LOD) of the OSHA sampling method is insufficient for the occupational RfC presented in this document. Reconciliation of the EPA risk-based RfC and the current OSHA standards will be made during the regulatory decision phase of the Reregistration Eligibility Decision (RED) for chlorine dioxide. The various cited chlorine dioxide levels from other organizations are reported below for review by regulatory managers.

Table 16. Chlorine Dioxide Regulatory and/or Recommended Air Concentrations

Organization	Time/Duration	Description	Air Concentration (ppm)
OSHA	8-hour TWA	PEL	0.1
ACGIH	8-hour TWA	TLV	0.1
	15-minutes	STEL	0.3
NIOSH	10-hour TWA	REL	0.1
	30-minutes (escape)	IDLH	5
EPA	8-hour TWA	RfC - Occupational	0.003
	"Short-term"	RfC – Residential for single exposures	0.05

	Continuous (24/7)	RfC – Residential	0.00007

8.0 INCIDENT REPORT ASSESSMENT

A detailed summary of the human incident data is presented in the document "Chlorine Dioxide Incident Reports." Below is a brief summary of this information. The Agency consulted the following databases for poisoning incident data for chlorine dioxide and other similar compounds:

(1) **OPP Incident Data System (IDS)** - The Incident Data System of The Office of Pesticide Programs (OPP) of the Environmental Protection Agency (EPA) contains reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, with enough cases and/or enough documentation, risk mitigation measures may be suggested.

(2) **Poison Control Centers** - as a result of a data purchase by EPA, OPP received Poison Control Center data covering the years 1993 through 2003 for all pesticides. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System, which obtains data from about 65-70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc.

(3) **California Department of Pesticide Regulation** - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.

(4) **National Pesticide Telecommunications Network (NPTN)** - NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive, has been prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others.

(5) **Published Incident Reports** - Some incident reports associated with chlorine dioxide related human health hazards are published in the scientific literature.

There are no significant health effects associated with chlorine dioxide in published scientific literature; however there are some reported incidents associated with exposure to end-use products containing chlorine dioxide. Inhalation is the primary route of exposure. Most of the incidents are related to irritation reaction..

9.0 ECOTOXICOLOGY ASSESSMENT

A detailed ecotoxicology risk assessment for chlorine dioxide is provided in the Environmental Hazard and Risk Assessment Chapter. The summary of the exposures and risks are presented below.

Environmental Modeling/Exposure

The Probabilistic Distribution Model version 4 (PDM4) was used to estimate exposure from once-through cooling tower uses. This screening-level model was used to provide the percentage of days per year various concentrations are exceeded for several different flow, application, and dosing scenarios. The details of this model can be found in the Environmental Modeling Chapter.

Three different flow regimes were considered: high flow [power plants with average stream flow rates of 1000±50 million gallons per day (MGD)]; medium flow (power plants with average stream flow rates of 500±50 MGD); and low flow (power plants with average stream flow rates of 100±10 MGD). Two pesticide application scenarios, continuous feed and intermittent feed, were used in the modeling, based on label instructions. For continuous feed use, the label rates ranged from 0.10 ppm to 2.0 ppm chlorine dioxide/sodium chlorite in the water. For intermittent use, the label rates ranged from 0.10 ppm to 25 ppm chlorine dioxide/sodium chlorite in the water. A single label contained the rate of 800 ppm chlorine dioxide/sodium chlorite and did not specify whether this was for continuous or intermittent use. It is believed that this label with the 800 ppm dose rate will be either cancelled or amended by the registrant to delete this dose. The concentrations (the "concentrations of concern," or COC) used in the model were endpoints from aquatic organism toxicity studies with sodium chlorite.

Exceedance values for average and worst-case situations were modeled. The average values were calculated by averaging all of the values for a given flow category. The worst-case values were calculated by averaging the highest (peak) values for a given flow category. Since the modeling for chlorine dioxide/sodium chlorite provides results as percent days per year a particular concentration is exceeded, Risk Quotients were not used in the usual way to provide numeric estimates of risk. Instead, the endpoints from various toxicity studies were adjusted to determine the numeric Level of Concern (LOC) for each taxa for both acute and chronic effects. The adjustment factor is the same as the one used with the RQ method, e.g. 0.5 * LC_{50} or EC_{50} for acute effects, and 0.05 * LC_{50} or EC_{50} for acute endangered species risks. The chronic LOC needs no adjustment. The modeling results provided the percentage of days concentrations were exceeded for a range encompassing the numeric LOCs. When a specific LOC was not listed in the modeling output tables, the percent days exceeded for the LOC was interpolated from the closest numbers above and below the specific LOC. The percentage of days was then multiplied by 365 to provide the number of days per year the LOC is exceeded.

For terrestrial organisms, there is no model available to estimate exposure and risk from discharge of once-through cooling system effluents into surface waters. The rapid degradation of the chemicals, coupled with the generally low toxicity of chlorine dioxide and sodium chlorite to birds and mammals, make risk to these organisms unlikely. The very limited data available to assess the phytotoxicity of chlorine dioxide/sodium chlorite make it difficult to determine the risk to terrestrial/semi-aquatic plants.

Acute risk to aquatic organisms may occur from the use of chlorine dioxide/sodium chlorite in once-through cooling towers based on the screening level assessment conducted. At the highest doses, the model shows risk to freshwater and marine/estuarine fish and invertebrates and aquatic plants, and at the lowest doses the model shows risk only to freshwater invertebrates. Chronic risk to aquatic organisms cannot be assessed at this time due to the lack of chronic toxicity endpoints for fish and aquatic invertebrates. When the required aquatic chronic toxicity testing described above is submitted, chronic risk to these organisms will be assessed.
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Ecological Hazard and Risk

Studies have been submitted, which fulfill the requirements of several EPA ecotoxicity guidelines. For terrestrial animals, the results of studies to examine the toxicity of chlorine dioxide/sodium chlorite to birds indicate these chemicals range from slightly to highly toxic to birds on an acute oral basis and from slightly toxic to practically non-toxic on a subacute dietary basis. For freshwater aquatic animals, the results of studies examining the toxicity of chlorine dioxide/sodium chlorite to freshwater fish indicate these chemicals range from slightly toxic to practically non-toxic on an acute basis. For aquatic invertebrates, the studies indicate that chlorine dioxide and sodium chlorite range from very highly toxic for technical grade sodium chlorite a.i. to practically non-toxic for the formulated product on an acute basis. Results of toxicity studies indicate that chlorine dioxide/sodium chlorite are slightly toxic to estuarine/marine fish on an acute basis and range from highly toxic to slightly toxic to estuarine/marine invertebrates on an acute basis.

For terrestrial plants, results of toxicity studies indicate that chlorine dioxide/sodium chlorite are moderately toxic to terrestrial plants. However, since the maximum label rate for many of the chlorine dioxide/sodium chlorite once-through cooling labels was not used in these tests, it is necessary to conduct Tier II testing with rice. For aquatic plants, toxicity study results indicate that chlorine dioxide/sodium chlorite are moderately toxic to aquatic plants. The once-through cooling tower use of chlorine dioxide/sodium chlorite requires that 5 aquatic plant tests be conducted due to the algaecidal nature of the chemical and the likelihood of exposure to aquatic plants in surface waters receiving industrial facility outfall from the cooling system; however, only one study (1 species) under this topic has been submitted and 5 are required. The following aquatic plant studies are still required: blue-green cyanobacteria (*Anabaena flos-aquae*), freshwater diatom (*Navicula pelliculosa*), marine diatom (*Skeletonema costatum*) and floating macrophyte (*Lemna gibba*).

Data is still required for the following guideline requirements: (1) a freshwater fish early life-stage test using the technical grade of the active ingredient, (2) a freshwater aquatic invertebrate life-cycle test using the technical grade of the active ingredient, (3) an estuarine/marine invertebrate life-cycle toxicity test is required due to the high acute toxicity of sodium chlorite to estuarine/marine invertebrates; however, freshwater invertebrates tend to be more sensitive than estuarine/marine invertebrates to sodium chlorite on an acute basis, and, therefore, freshwater life-cycle endpoints will suffice for assessing risk to estuarine/marine invertebrate species.

Table 17. Acute Oral Toxicity of Chlorine Dioxide and Sodium Chlorite to Birds				
Substance/% Active Ingredient (AI)	**Organism**	**Endpoints/Results (mg/kg) (95% conf. interval)**	**Reference**	**Study Classification**
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	LD50 = 382 (300-520) NOEL = 175	Robaidek, 1985 ACC # 259373	acceptable
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	LD50 = 390 (310-490) NOEL = N.R.	Robaidek and Johnson, 1985 ACC # 257341	acceptable
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	LD50 = 395 (272-573) NOEL = N.R.	Fletcher, 1984 ACC # 253378	acceptable
Sodium Chlorite/83%	Northern bobwhite (*Colinus virginianus*)	LD50 = 660 (540-810)	Fletcher, 1973 MRID # 31610	acceptable
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	LD50 = 467 (372-585)	Beavers, 1984 ACC # 254177	acceptable
Sodium Chlorite/80%	Mallard Duck (*Anas platyrhynchos*)	LD50 > 31.25	Beavers, 1984 ACC # 254176	supplemental
Sodium Chlorite/25%	Northern bobwhite (*Colinus virginianus*	LD50 = 797(420-2594) NOEL= 125	MBA Laboratories, 1984 ACC# 252854	acceptable

Table 18. Acute Ecotoxicity of Chlorine Dioxide and Sodium Chlorite				
Substance/% Active Ingredient (AI)	**Organism**	**Endpoints/Results (ppm) (95% conf. interval)**	**Reference**	**Study Classification**
Freshwater fish				
Sodium Chlorite/80%	Rainbow trout (*Oncorhynchus mykiss*)	LC50 = 360 (216-600) NOEC = 216	Barrows, 1984 MRID # 94068007	acceptable
Sodium Chlorite/80%	Bluegill (*Lepomis macrochirus*)	LC50 = 244 (196-304) NOEC = 108	Larkin, 1984 ACC # 254181	acceptable
Sodium Chlorite/80%	Rainbow trout (*Oncorhynchus mykiss*)	LC50 = 360 (216-600) NOEC = 216	Larkin, 1984 ACC # 254180	acceptable
Sodium Chlorite/80.25%	Bluegill (*Lepomis macrochirus*)	LC50 = 265 (231-309) NOEC = 130	EG&G, Bionomics, 1978 ACC # 69809	supplemental

Table 18. Acute Ecotoxicity of Chlorine Dioxide and Sodium Chlorite				
Substance/% Active Ingredient (AI)	**Organism**	**Endpoints/Results (ppm) (95% conf. interval)**	**Reference**	**Study Classification**
Sodium Chlorite/79%	Bluegill (*Lepomis macrochirus*)	LC 50 = 208 (165-262) NOEC = N.R.	Sleight III, 1971 MRID # 131351	supplemental
Sodium Chlorite/79%	Rainbow trout (*Oncorhynchus mykiss*)	LC50 = 50.6 (38-65.8) NOEC = 32	Sleight III, 1971 MRID # 131351	supplemental
Sodium Chlorite/80%	Rainbow trout (*Oncorhynchus mykiss*)	LC50 >100 NOEC = N.R.	McMillen, 1984 ACC # 253743	supplemental
Sodium Chlorite/80%	Bluegill (*Lepomis macrochirus*)	LC50 >100 NOEC = N.R.	McMillen, 1984 ACC # 253743	supplemental
Sodium Chlorite/25%	Rainbow trout (*Oncorhynchus mykiss*)	LC50 = 203 (175-236) NOEC = 100	MBA Laboratories, 1984 ACC # 252854	acceptable
Sodium Chlorite/25%	Bluegill (*Lepomis macrochirus*)	LC50 = 222 (207-237) NOEC = 186	MBA Laboratories, 1983 ACC # 252854	supplemental
Sodium Chlorite/81.5%	Bluegill (*Lepomis macrochirus*)	LC50 = 310 (270-350) NOEC = 220	Sousa, 1981 ACC # 245697	acceptable
Sodium Chlorite/80.25%	Rainbow trout (*Oncorhynchus mykiss*)	LC50 = 290 (250-340) NOEC = 70	EG&G, Bionomics, 1979 ACC # 69810	acceptable
Sodium Chlorite/80%	Rainbow trout (*Oncorhynchus mykiss*)	LC50 = 340 (220-600) NOEC = N.R.	Sousa and Surprenant, 1984 ACC # 253379	acceptable
Sodium Chlorite/80%	Bluegill (*Lepomis macrochirus*)	LC50 = 420 (220-600) NOEC = N.R.	Sousa and Surprenant, 1984 MRID # 94068006	acceptable
Freshwater Invertebrates				
Sodium Chlorite/80%	*Daphnia magna*	EC50 = 0.027 (0.021-0.031) NOEC = 0.003	Barrows, 1984 MRID # 146162	acceptable
Sodium Chlorite/80%	*Daphnia magna*	EC50 = 0.39 (0.32-0.54) NOEC =N.R.	Hoberg and Surprenant, 1984 MRID # 141149	acceptable
Sodium Chlorite/79%	*Daphnia magna*	LC50 = 0.29 (0.25-0.33) NOEC = 0.10	Vilkas, 1976 MRID # 131350	acceptable
Sodium Chlorite/80%	*Daphnia magna*	LC50 = 0.08 (0.06-0.10) NOEC = 0.06	Larkin, 1984 ACC # 254182	acceptable
Sodium Chlorite/80%	*Daphnia magna*	LC50 = 0.146 (0.12 - 0.18) NOEC = 0.06	Nachrord, 1984 MRID # 94068009	acceptable
Sodium Chlorite/25%	*Daphnia magna*	LC50 = 1.4 (1.0-1.9) NOEC = 0.4	MBA Laboratories, 1984 ACC # 252854	supplemental
Estuarine/Marine Fish				

Table 18. Acute Ecotoxicity of Chlorine Dioxide and Sodium Chlorite				
Substance/% Active Ingredient (AI)	**Organism**	**Endpoints/Results (ppm) (95% conf. interval)**	**Reference**	**Study Classification**
Sodium Chlorite/79%	Sheepshead minnow *(Cyprinodon variegatus)*	LC50 = 75 (62.6-89.8) NOAEC = 13.9	Yurk and Overman, 1994 MRID # 43259401	acceptable
Estuarine/Marine Invertebrates				
Sodium Chlorite/79%	Eastern oyster *(Crassostrea virginica)*	96 hour LC50/EC50 = 21.4 (14.3-27.1) NOEC = 14.3	Yurk and Overman, 1994 MRID # 43259403	acceptable
Sodium Chlorite/79%	Mysid (*Mysidopsis bahia*)	96 hour LC50/EC50 = 0.576 (0.44-0.75) NOEC= N.R.	Yurk and Overman, 1994 MRID # 43259402	acceptable
Terrestrial/Semi-aquatic Plants				
Sodium Chlorite/80%	Monocots & Dicots (10 Species)	EC25 = >3.5	Backus *et al.*, 1990 MRID # 41843101	acceptable
Sodium Chlorite/80%	Monocots & Dicots (10 Species)	EC25 = >3.5	Backus *et al.*, 1990 MRID # 41843102	acceptable
Sodium Chlorite/80%	Buckwheat (*Polygonum convolvulus*)	EC25 = <3.5	Backus *et al.*, 1990 MRID # 41843102	acceptable
Aquatic Plants				
Sodium Chlorite/80%	Green Algae (*Selenastrum capricornutum*)	EC50 = 1.32 (1.18-1.47) NOEC = < 0.62	Ward and Boeri, 1991 MRID # 41880403	supplemental

Table 19. Avian Subacute Dietary Toxicity of Chlorine Dioxide and Sodium Chlorite					
Substance/% AI	**Organism**	**LC50 (ppm) (95 % c.i.)**	**NOAEC (ppm)**	**Reference**	**Study Classification**
Sodium Chlorite/80%	Mallard Duck (*Anas platyrhynchos*)	>5000	5000	Johnson, 1984 MRID # 94068008	acceptable
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	> 5000	N.R.	Fletcher, 1984 ACC # 253378	acceptable

Table 19. Avian Subacute Dietary Toxicity of Chlorine Dioxide and Sodium Chlorite					
Substance/% AI	**Organism**	**LC50 (ppm) (95 % c.i.)**	**NOAEC (ppm)**	**Reference**	**Study Classification**
Sodium Chlorite/80%	Mallard Duck (*Anas platyrhynchos*)	> 5000	N.R.	Fletcher, 1984 ACC # 253378	acceptable
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	> 5000	N.R.	Johnson, 1984 MRID # 94068005	acceptable
Sodium Chlorite/80%	Mallard Duck (*Anas platyrhynchos*)	> 5620	N.R.	Beavers, 1984 ACC # 254178	acceptable
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	> 5620	N.R.	Beavers, 1984 ACC # 254179	acceptable
Sodium Chlorite/80%	Northern bobwhite (*Colinus virginianus*)	>10,000	N.R.	Fink, 1977 MRID # 130649	acceptable
Sodium Chlorite/80%	Mallard Duck (*Anas platyrhynchos*)	>10,000	N.R.	Fink, 1977 MRID # 130650	acceptable
Sodium Chlorite/25%	Mallard Duck (*Anas platyrhynchos*)	18686 (8186-109184)	1250	MBA Laboratories, 1983 ACC # 252854	acceptable
Sodium Chlorite/25%	Northern bobwhite (*Colinus virginianus*)	2031(1226-3903)	417	MBA Laboratories, 1984 ACC #252854	acceptable

Listed Species Consideration

Section 7 of the Endangered Species Act, 16 U.S.C. Section 1536(a)(2), requires all federal agencies to consult with the National Marine Fisheries Service (NMFS) for marine and anadromous listed species, or the United States Fish and Wildlife Services (FWS) for listed wildlife and freshwater organisms, if they are proposing an "action" that may affect listed species or their designated habitat. Each federal agency is required under the Act to insure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. To jeopardize the continued existence of a listed species means "to engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of the species." 50 C.F.R. § 402.02.

To facilitate compliance with the requirements of the Endangered Species Act subsection (a)(2) the Environmental Protection Agency, Office of Pesticide Programs has established procedures to evaluate whether a proposed registration action may directly or indirectly reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of any listed species (U.S. EPA, 2004). After the Agency's screening-level risk assessment is performed, if any of the Agency's Listed Species LOC Criteria are exceeded for either direct or indirect effects, a determination is made to identify

if any listed or candidate species may co-occur in the area of the proposed pesticide use. If determined that listed or candidate species may be present in the proposed use areas, further biological assessment is undertaken. The extent to which listed species may be at risk then determines the need for the development of a more comprehensive consultation package as required by the Endangered Species Act.

Acute risks to listed birds and mammals are not anticipated from the use of chlorine dioxide and sodium chlorite products due to low exposure and low toxicity. The screening level model used in this assessment indicates that there may be acute risks to listed aquatic organisms from the once through cooling tower use of chlorine dioxide/sodium chlorite. Further, potential indirect effects on any species dependent upon a species that experiences effects from use of chlorine dioxide/sodium chlorite cannot be precluded based on the screening level ecological risk assessment. These findings are based solely on EPA's screening level assessment and do not constitute "may effect" findings under the Endangered Species Act.

Chronic risks to listed aquatic organisms cannot be assessed at this time; this risk will be assessed when required chronic toxicity data are submitted to and evaluated by the Agency.

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