UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

January 26, 2006

MEMORANDUM

SUBJECT: Revised Inorganic Chlorates. HED Chapter of the Reregistration Eligibility Decision Document (RED). Case #: 4049 DP Barcode: D303550
PC Codes: Sodium chlorate: 073301 (active) and 873301 (inert)
Calcium chlorate: 073302 (active) and 875606 (inert)
Potassium chlorate: 073303 (active) and 900583 (inert)
Magnesium chlorate: 530200 (active)
Regulatory Action: Phase 1 Reregistration Action
Risk Assessment Type: Multiple Chemicals/Aggregate

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This document provides a summary of the findings from the data evaluation and the subsequent assessment of human health risk resulting from the uses of Inorganic Chlorates. The hazard characterization was completed by Abdallah Khasawinah (HED/RRB4); the occupational and residential exposure assessment was completed by Matthew Crowley (HED/RRB4); the residue chemistry data evaluation and dietary (food) exposure estimates for the dietary risk assessment were completed by Bonnie Cropp-Kohlligian (HED/RRB4); the dietary risk assessment analysis was completed by Thurston Morton (HED/RRB4); the incident report was completed by Jerome Blondell (HED/CEB); the environmental fate characterization for chlorate residues resulting from terrestrial food/feed uses was completed by Silvia Termes (EFED); the risk assessment was compiled by Susan Hummel (HED/RRB4). The drinking water exposure characterization and exposure estimate calculations for chlorate residues as a byproduct of the disinfection of drinking water for the dietary (water) risk assessment analysis were provided by Patricia Fair of the Office of Ground Water and Drinking Water Technical Support Center.

Table of Contents

1.0 Executive Summary

A Human Health Risk Assessment is being conducted for Inorganic Chlorates (List D Reregistration Case #4049). Of the inorganic chlorates listed as active ingredients in Office of Pesticide Programs Information Network (*i.e.*, sodium chlorate (073301), calcium chlorate (073302), potassium chlorate (073303), and magnesium chlorate (530200)), only sodium chlorate (073301) is present as an active ingredient in currently registered products. Sodium chlorate (873301), calcium chlorate (875606), and potassium chlorate (900583) are present as inert ingredients in currently registered products and will also be addressed in this risk assessment.

Chlorates are strong oxidizers used in the manufacture of dyes, explosives, matches, printing fabric, paper pulp processing, agricultural desiccant/defoliant, weed killers, and as a weak antiseptic, 2-3% solutions have been used in mouth washes (OEHHA, 2002). The primary pesticidal use for sodium chlorate (073301) is as an agricultural defoliant/desiccant, primarily on cotton, however it is also applied to a wide variety of other agricultural crops. Sodium chlorate is also used as a precursor for chlorine dioxide generation, through a closed system, to bleach wood pulp/paper. Only a small percentage (less than 2 percent) is used in water systems as a precursor to chlorine dioxide generation or as a defoliant/desiccant on a number of crops to aid harvest. As inert ingredients, sodium chlorate (873301) and potassium chlorate (900583) are present in conventional (agricultural) pesticides used on food crops or in poultry premises. Also, as inert ingredients, sodium chlorate (873301) and calcium chlorate (875606) are present in antimicrobial agents used: (1) as fruit, vegetable, and egg sanitizing washes; (2) to control bacterial blotch on mushrooms; (3) as treatment to seed used for sprouting; (4) for conditioning live oysters; (5) in poultry drinking water; (6) in fish filleting; (7) pecan cracking/dyeing.

Understanding that sodium chlorate and sodium chlorite have common uses such as use in water systems as precursors in chlorine dioxide generation and the potential for interconversion of chlorate and chlorite anions in water, the environment and animals, Chemical Review Managers (CRMs) in the Special Review and Reregistration Division (SRRD) responsible for completing the Inorganic Chlorates Reregistration Eligibility Decision (List D Reregistration Case# 4049) and those in the Antimicrobial Division (AD) responsible for completing the Chlorine Dioxide and Sodium Chlorite Reregistration Eligibility Decision (List D Reregistration Case# 4023) developed a plan to coordinate the two reregistration cases. Through a series of negotiations, it was agreed that with regards to the Inorganic Chlorates Risk Assessments that: (1) the Inorganic Chlorates Risk Assessments will consider residues of chlorate only; (2) the scope of the Health Effects Division (HED) Occupational and Residential Risk Assessments will be limited to considerations of the conventional (agricultural) uses of inorganic chlorates only; and (3) AD will address the Occupational and Residential Assessment for the antimicrobial uses of the inorganic chlorates using toxicological endpoints selected by HED.

We note that AD has completed an Occupational and Residential Risk Assessment for the antimicrobial uses of the inorganic chlorates under separate cover (D312200, T. Leighton, 01/24/2005) using the appropriate toxicological endpoints selected by HED. There are no

residential exposures associated with these uses. HED will not discuss this topic further herein except to note that no risks above the Agency's level of concern were identified.

We note that tolerances and/or exemptions from the requirement of a tolerance for inorganic chlorates as active or inert ingredients in antimicrobial agents is not the purview of HED and should be addressed by AD. HED will not discuss this topic further.

We note that since Inorganic Chlorates is a List D reregistration case, the Product Chemistry Chapter for the Inorganic Chlorates Reregistration Eligibility Decision (RED) is the responsibility of the Antimicrobials Division. HED will not discuss this topic in detail.

Hazard Profile

The database for the inorganic chlorates is substantially complete in terms of endpoint studies and dose response information to characterize any potential for prenatal or postnatal risk for infants and children. No additional FQPA or database factor is required. A 28-Day Inhalation study is required to fulfill Guideline 870.3465.

Sodium chlorate is a thyroid toxicant producing thyroid gland follicular cell hypertrophy in rats and mice following chronic exposures and some evidence of follicular cell tumors in rats. The primary target of chlorate acute toxicity is rupture of red blood cell membranes with intravascular hemolysis and the irreversible oxidation of hemoglobin to methemoglobin. Potassium chlorate has produced renal tubular necrosis in animals. Metabolism studies in rats and dogs have shown that chlorates are readily absorbed by the gastrointestinal tract and are excreted in the urine primarily as chlorate (ClO_3 ; ca. 13% of the administered dose), chlorite (ClO_2 ; ca. 4% of the administered dose), and chloride (Cl ; ca. 20% of the administered dose). Using ^{36}Cl-potassium chlorate, peak blood concentration levels were reached after an hour of ingestion by rats. Elimination of the labeled chlorate from the blood was biphasic with half-lives of 6 and 36.5 hours.

In acute toxicity tests, sodium chlorate is slightly toxic by the oral (Toxicity Category IV), dermal (Toxicity Category IV), and inhalation routes (Toxicity Category IV of a 33% aerosol). Sodium chlorate crystals were mildly irritating to the rabbit eye (Toxicity Category III for the dry crystals or moistened crystals), and minimal to mild dermal irritant (Toxicity Category III for the moistened material and Toxicity Category IV for the dry crystal). Ingestion of toxic doses of sodium chlorate by humans produce gastritis, hemolysis, methemoglobinemia, hemoglobinurea, late toxic nephritis, and acute renal failure. Doses in excess of 100 mg/kg are generally fatal to humans.

There are conflicting findings regarding the subchronic/chronic toxicity of sodium chlorate. In one series of studies, rats exposed to relatively low concentrations of sodium chlorate (equivalent to1.5 or 15 mg/kg/day) for up to 11 months exhibited decreased blood glutathione, increased fragility of erythrocytes, inhibition of incorporation of tritiated thymidine into nuclei in rat testes,

decreased RBC count and hematocrit and decreased body weight. In another study, exposure of male F344 rats to 1% sodium or potassium chlorate in drinking water (654-686 mg/kg/day) for 25 weeks, the only effect reported was significant body weight reduction. Relative kidney weights were significantly increased in potassium chlorate treated rats. Rats orally administered 10-1000 mg/kg/day sodium chlorate for 90 days did not exhibit histological or clinical chemistry treatment-related effects, but had lower red blood cell counts, hematocrit and hemoglobin levels, particularly in the females. The adrenal weight was also depressed in males and females at the 1000 mg/kg/day level. In another published study in which rats were administered sodium chlorate in the drinking water at concentrations equivalent to 512 and 800 mg/kg/day for males and females, respectively for 90 days, final body weights were significantly lower in both sexes with some relative organ weight changes including the adrenal glands and reduction in RBC counts and percent hemoglobin, and prominent pituitary gland vacuolization and thyroid gland colloid depletion in both sexes. The thyroid effects were confirmed in a recent study in rats where subchronic treatment for 21 or 90 days with sodium chlorate in the drinking water at concentrations up to 2,000 mg/L (225 mg/kg/day) induced a concentration dependent increase in the incidence and severity of thyroid follicular cellular hyperplasia. Colloid depletion and hypertrophy were the most sensitive histopathological indicators of sodium chlorate exposure, with male rats more susceptible than females rats. Decreases in serum hormone levels triiodothyronine (T_3) and thyroxine (T_4) were also reported following exposure to sodium chlorate. Mice were less susceptible to the adverse effect from exposure to high levels of sodium chlorate. In a subchronic exposure study in primates where sodium chlorate was administered in drinking water for 8 weeks at 400 mg/L (58.4±27.6 mg/kg/day) to 6 male and 7 female adult African Green Monkeys (*Cercopithecus aethiops*) there was no effect on the thyroid function and the total thyroxine levels. In dogs, the only reported treatment related effect following subchronic administration of sodium chlorate up to 360 mg/kg/day was emesis.

A 2-year bioassay to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been recently reported (DRAFT NTP Report 2004). In these tests, there was some evidence of thyroid gland follicular cell carcinogenicity in male rats which may be attributed to the imbalance of thyroid hormones (reduced T_3 and T_4 and elevated TSH) seen in these studies as a result of exposure to sodium chlorate. Current EPA HED policy states that "nonmutagenic pesticides that induce elevated levels of TSH and thyroid follicular cell tumors in the rat should be classified as **not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis**" (*Assessment of Thyroid Follicular Cell Tumors*; USEPA March 1998 EPA/630/R-97/002). In female mice there was equivocal and marginal evidence of increased pancreatic islet carcinoma.

Sodium chlorate was negative in most bacterial gene mutation assays. In one assay, it showed positive effect in the TA1535 strain in the presence of metabolic activation. It also caused DNA damage in repair deficient *E. coli* strains at concentrations above 1000 ug/mL in the presence of metabolic activation but was negative in the unscheduled DNA synthesis assay. In cytogenetics tests, sodium chlorate was negative in the *in vitro* cell gene mutation assay, mammalian

erythrocyte micronucleus assay, bone marrow cytogenetics assay and sperm head abnormality assay.

Sodium chlorate did not cause developmental effects in rats tested at doses up to 1000 mg/kg/day or in rabbits tested at doses up to 500 mg/kg/day. In a two generation reproductive toxicity study in the rat, postnatal toxicity did not exceed parental toxicity. Sodium chlorate has not been evaluated for neurotoxic effects, but acute and subchronic toxicity studies did not indicate a neurotoxic potential.

There are no repeated dermal toxicity or dermal absorption data available for sodium chlorate. Based on its high water solubility and ionic nature, potential sodium chlorate (or any other inorganic chlorate) absorption by the intact skin is considered negligible.

No increase in prenatal susceptibility of rats or rabbits was seen in developmental studies with chlorate. No pre- or post-natal susceptibility was observed in a reproduction study in the rat.

Note: Lubbers *et al* (1984a, 1984b) conducted a series of studies with human volunteers which was evaluated; however, due to the limitations of these studies, the data were not deemed useful for dose-response evaluation and were not relied upon in the risk assessment.

Exposure and Aggregate Risk Assessment

Residue Chemistry

The residue chemistry database is not complete. New ruminant and poultry feeding studies are required to fulfill Guideline 860.1480. These data are considered important to the risk assessment and are needed to refine the meat/milk/poultry/egg exposure estimates in the dietary risk assessment. Also reference standards must be submitted to the Pesticide Repository to fulfill Guideline 860.1650.

No plant metabolism data have been submitted in support of the reregistration of sodium chlorate; however, no new plant metabolism data are required to support the established sodium chlorate exemptions from the requirement of a tolerance. Based on available published information (Loomis *et al.*, J. Am. Soc. Agron.; 25, 724 (1933)), sodium chlorate is highly soluble in water and is expected to readily absorb and translocate throughout plants. However, given the proposed use conditions, the means of translocation in treated plants may be substantially disrupted. Translocation of very small amounts of chlorate ion (ClO_3^-) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses may occur. Terminal residues are expected to be primarily surface residues.

Since sodium chlorate is a strong oxidizing agent, depending on environmental factors, it is expected to be easily reduced to chloride and possibly chlorite in plants. Total redox conversion

to these reduced species is not expected; hence, the terminal residues of sodium chlorate in/on plants are likely chlorate (ClO_3), chlorite (ClO_2), and chloride (Cl). By agreement within OPP, the residue of concern is the chlorate anion.

No ruminant, swine, or poultry metabolism or feeding data have been submitted in support of the reregistration of sodium chlorate; however, no new animal metabolism data are required to support the established sodium chlorate exemptions from the requirement of a tolerance. Based on published rat metabolism data (Abdel-Rahman *et al*, 1982, 1984b and 1985), terminal residues of sodium chlorate in animal tissues are expected to be chlorate (ClO_3), chlorite (ClO_2), and chloride (Cl). Chlorate is readily absorbed from the digestive tract and is excreted as chlorate, chlorite, and chloride in urine primarily and feces. Within 72 hours, about 40% of the administered dose was excreted in the urine as chlorate (ca. 13%), chlorite (ca. 4%), and chloride (ca. 20%) and about 2-4% was excreted in the feces in the same time period. Less than 1% of the administered dose was found in any of the tissues analyzed including kidney, liver, and skin. By agreement within OPP, the residue of concern is the chlorate anion.

Although some previous residue chemistry reviews for specific exemptions from the requirement of a tolerance have concluded that there is no reasonable expectation of transfer of residues to meat, milk, poultry or eggs in specific cases, re-evaluation of the available crop field trial data taken as a whole, indicate that there is the possibility of detectable residues of sodium chlorate on animal feedstuffs at harvest. Hence, secondary residues of concern in meat, milk, poultry, and eggs are possible and; therefore, new ruminant and poultry feeding data are hereby required to support the reregistration of sodium chlorate. These data are considered confirmatory.

The analytical method used to support the established exemptions from the requirement of a tolerance is a non-specific colorimetric method (Branderis, J. Sci. Food Agric., 16, 558 (1965)), deemed acceptable for data collection. The method was originally developed to estimate residual chlorate concentrations in soil and as a rapid diagnostic test for chlorate toxicity in plants. Briefly, the method involves acid extraction, clean-up by shaking with activated charcoal, and filtration. A solution of ortho-toluidine in HCl is then added to the concentrated extract and the resulting color is measured at 448 nm for low concentrations and at 490 nm for higher concentrations of dye. The method is not specific for chlorate since it measures any oxidizing agent capable of oxidizing chloride ion to free chlorine. A standard curve is prepared with sodium chlorate for comparison. The lowest limit of quantitation of the method is estimated at 1 ppm based on available fortification data from field trials. Chloride does not interfere with the method but residues of chlorite, which might be present, may also be detected with this method. This method is hereby deemed adequate for enforcement of sodium chlorate exemptions from the requirement of a tolerance. A more selective HPLC method ("Determination of Residues of Sodium Chlorate in Potatoes", Method #S57023, 4/2/91) is available for the detection of sodium chlorate residues in or on raw agricultural commodities (RACs).

Only crop field trial data have been submitted to support the reregistration of sodium chlorate. No storage stability or processing data are available. The available crop field trial data have been

re-evaluated herein. No additional plant magnitude of the residue or storage stability data are required to support the reregistration of sodium chlorate.

Exemptions from the requirement of tolerances are appropriate for sodium chlorate when used as defoliant or desiccant on beans (dry), corn, cotton, cowpeas, flax, guar, peppers (non-bell), potatoes, rice, safflower, sorghum (grain), soybeans, sunflower, and wheat since no enforcement action can be anticipated given the extremely low levels of chlorate expected in food commodities (most of the residues are on the surface), limitations of the enforcement method, and possible interconversion between chlorate and chlorite in the environment making misuse determinations difficult.

Sodium chlorate exemptions under 40 CFR 180.1020(a) from the requirement of a tolerance should be amended as follows to (1) specify defoliant and desiccant use only, (2) specify use on crops rather than raw agricultural commodities, (3) and include wheat:

40 CFR 180.1020(a) Sodium chlorate is exempt from the requirement of a tolerance for residues when used as a defoliant or desiccant in accordance with good agricultural practice on the following crops: Bean (dry), Corn, Cotton, Cowpea, Flax, Guar, Pepper (non-bell), Potato, Rice, Safflower, Sorghum (grain), Soybean, Sunflower, and Wheat.

Exemptions from the requirement of a tolerance are needed for sodium chlorate (873301) and potassium chlorate (900583) as inert ingredients in conventional pesticides under 40 CFR 180.920 and 40 CFR 180.930, respectively.

Environmental Fate

Sodium chlorate is used as a desiccant/defoliant because it is a strong oxidizer. As a strong oxidizing agent, chlorate (ClO_3^-, oxidation state V) gets reduced to chlorine species in lower oxidation states, such as the oxyanions chlorite (ClO_2^-, oxidation state III) and hypochlorite (ClO^-, oxidation state I), chlorine dioxide (oxidation state IV), and chloride (oxidation state -I). Thus, at least some and possibly substantial reduction of the applied chlorate is likely to occur in the field prior to any runoff to surface water. Under environmental (terrestrial field) redox conditions and based on chemical equilibria alone, the thermodynamically favored, end reduction product of chlorate in soil and in water is the chloride anion. Any intermediate chlorine dioxide that may form under environmental conditions will undergo photochemical reactions when exposed to sunlight. The chlorine oxyanions chlorite and hypochlorite (other possible more reduced intermediates in the ultimate reduction of chlorate to chloride) are strong oxidizers in themselves and thus, they are also reduced and/or undergo disproportionation reactions. Although reduction reactions of chlorate, chlorite, and hypochlorite are said to occur "very fast", how fast they occur is not known (*i.e.*, the actual rate constants in the environment are not known). Therefore, at any given time the distribution of reduced species (type and concentration) cannot be estimated. However, it is unlikely that a single reduced species would be present.

Dietary - Food Only

Dietary exposure (food only) to inorganic chlorates as the chlorate ion (ClO_3^-) may be expected from the following dietary exposure routes: (1) from sodium chlorate (073301) as an active ingredient in conventional (agricultural) pesticides used on food crops; (2) from sodium chlorate (873301) and potassium chlorate (900583) as inert ingredients in conventional pesticides used on food crops or in poultry premises; (3) from secondary residues in meat/milk/poultry/eggs due to residues on animal feedstuffs; (4) from sodium chlorate (873301) and calcium chlorate (875606) as inert ingredients in antimicrobial agents used as fruit, vegetable, and egg sanitizing washes, on mushrooms to control bacterial blotch, as treatments to seed used for sprouting, for conditioning live oysters, in poultry drinking water, in fish filleting, and in pecan cracking/dyeing; (5) as a potential redox of chlorine dioxide and sodium chlorite in conventional and antimicrobial pesticides; (6) from degradation of hypochlorites in antimicrobial agents used as fruit and vegetable washes; and, (7) from translocation of very small amounts of chlorate ion (ClO_3^-) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses.

A chronic Population Adjusted Dose (cPAD) of 0.03 mg chlorate/kg/day was used in the chronic (non-cancer and cancer) dietary risk assessment based on a chronic rat study (DRAFT NTP Report 2004) with sodium chlorate which found increased thyroid gland follicular cell hypertrophy and follicular cell mineralization. A NOAEL was not identified in this study. Therefore, a bench mark dose (BMD) analysis was performed. Using the BMDL as an approximation of the NOAEL (0.9 mg chlorate/kg/day) and an uncertainty factor of 30x (3x for interspecies extrapolation and 10x for intraspecies extrapolation), the cPAD was calculated at 0.03 mg chlorate/kg/day.

In the same chronic study (DRAFT NTP Report 2004) there was some evidence of thyroid gland follicular cell carcinogenicity in male rats which may be attributed to changes of thyroid hormones (reduced T_3 and T_4 and elevated TSH) as a result of exposure to high doses of sodium chlorate. Current EPA HED policy states that "nonmutagenic pesticides that induce elevated levels of TSH and thyroid follicular cell tumors in the rat should be classified as **not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis**" (*Assessment of Thyroid Follicular Cell Tumors*; USEPA March 1998 EPA/630/R-97/002). In female mice there was equivocal and marginal evidence of increased pancreatic islet carcinoma. Therefore, a cancer dietary risk assessment was conducted using an MOE approach and the BMDL as an approximation of the NOAEL (0.9 mg chlorate/kg/day). The level of concern for the Margin of Exposure was 30. (The cancer risk assessment is the same as the chronic (non-cancer) risk assessment for the U. S. General Population.)

A chronic (non-cancer and cancer) dietary risk assessment for food only were conducted using the Dietary Exposure Evaluation Model-FCID™ software with the Food Commodity Intake Database (DEEM-FCID™ Version 2.03) and food and water consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. No food monitoring data are available for this risk assessment; only limited, chemical-specific field trial data are available. Exposure estimates in

food were based on field trial data or, in the case of fruit/vegetable/other washes, was derived from a film thickness model. No chemical-specific livestock metabolism or feeding data are available; exposure estimates in meat, milk, poultry, and eggs were derived from rat metabolism data, field trial data, and livestock reference information concerning feed consumption, tissue weights, and milk production. In some cases, due to raw data limitations, food exposure estimates are calculated as sodium chlorate. Default concentration factors (no chemical-specific processing data are available), percent crop treated data, and the effects of washing after foliar treatments were also incorporated into the risk assessments.

The chronic (non-cancer and cancer) dietary risk assessment for food only is below the Agency's level of concern for the General U.S. Population and all subgroups. The highest exposed population subgroup, Children 1-2 years of age, was 28% of the chronic Population Adjusted Dose (cPAD).

Dietary - Drinking Water Only

Levels of chlorate ion (ClO_3^-) found in finished drinking water are more likely a consequence of drinking water treatment with chlorine dioxide or hypochlorite than from possible source water contamination due to inorganic chlorate pesticide uses and/or discharge from pulp mills which use inorganic chlorates in their bleaching process. Chlorate ion (ClO_3^-) is a disinfection by-product (DBP) of water treatment which can be formed during the on-site generation of chlorine dioxide (ClO_2), the decomposition of chlorine dioxide in the water treatment system, the decomposition of hypochlorite feedstock during storage, and the interaction of chlorite ion and free chlorine. Chlorate ion (ClO_3^-) may also be present in drinking water resulting from the use of sodium chlorate (073301) in water systems as a precursor to chlorine dioxide generation due to incomplete reaction of sodium chlorate in the formation of chlorine dioxide resulting in unreacted chlorate ion in the chlorine dioxide feed stream.

Data are available concerning the levels of chlorate ion (ClO_3^-) found in finished drinking water collected from water treatment facilities which use chlorine dioxide or hypochlorite to treat drinking water. No data are available concerning the levels of chlorate ion (ClO_3^-) in finished drinking water collected from the small number of water treatment facilities which use sodium chlorate as a precursor for chlorine dioxide generation, through a closed system, to treat drinking water.

While EPA Office of Ground Water and Drinking Water (OGWDW) has not established a Maximum Contamination Level (MCL) for chlorate, data concerning the occurrence of chlorate ion (ClO_3^-) in drinking water have been collected under the Information Collection Rule (ICR). Under the ICR, large water treatment systems (those serving more than 100,000 customers) that use chlorine dioxide or hypochlorite for disinfection were required to monitor levels of chlorate over an 18-month period. Data were collected from 66 water treatment systems (90 water treatment plants) which use chlorine dioxide or hypochlorite for disinfection. Data from these systems are presented separately and combined in Table 6.2.2.2.1. Concentrations of chlorate ion (ClO_3^-) in finished water from these treatment facilities ranged from <0.020 mg/L to 2.2 mg/L.

The average concentrations of chlorate ion (ClO_3^-) in the distribution systems from these treatment facilities ranged from <0.020 mg/L to 0.69 mg/L; the 90th Percentile was 0.24 mg/L and the median was 0.11 mg/L.

The American Water Works Association Research Foundation (AwwaRF (1995)) sponsored a project to study how water systems could minimize ClO_3^- formation in the hypochlorite solutions they use for disinfection. As part of the data gathering effort, they obtained information from 185 water treatment systems concerning their use of hypochlorite solutions. Samples of source water, hypochlorite solution, and finished drinking water from 111 of the water systems were analyzed for ClO_3^-. Only one set of samples was collected for each system. Concentrations of chlorate ion (ClO_3^-) in finished water from these treatment facilities ranged from <0.010 mg/L to 9.2 mg/L (ca. 9 mg/L); the 90th Percentile was 1.160 mg/L (ca. 1.2 mg/L) and the median was 0.161 mg/L (ca. 0.2 mg/L).

Based on the available occurrence data (essentially at the tap) from the ICR AUX1 Database (USEPA, 2000d) and the AwwaRF (1995) study, the following estimated concentrations of chlorate ion (ClO_3^-) in drinking water are deemed appropriate for inclusion in the dietary risk assessments for inorganic chlorates:

- The highest annual average concentration of chlorate ion (ClO_3^-) in drinking water is estimated at 0.69 mg/L and is based on the ICR AUX1 Database (USEPA, 2000d).
- The 90th percentile average concentration of chlorate ion (ClO_3^-) in drinking water is estimated at 0.24 mg/L and is based on the ICR AUX1 Database (USEPA, 2000d).
- The treated system average concentration of chlorate ion (ClO_3^-) in drinking water is estimated at 0.11 mg/L and is based on the ICR AUX1 Database (USEPA, 2000d).

Use of the ICR AUX1 database could underestimate concentrations in drinking water since higher levels of chlorate ion (ClO_3^-) in drinking water were found at the small water treatment utilities sampled in the AwwaRF (1995) project than at the large water treatment plants included in the ICR AUX1 Database (USEPA, 2000d). However, the AwwaRF (1995) study is a less robust data set consisting of only one sample per utility and, therefore, the ICR AUX1 Database (USEPA, 2000d) was considered the more appropriate source for estimating averages from individual water treatment plants.

Chronic (non-cancer and cancer) dietary (water only) risk assessments were conducted using the Dietary Exposure Evaluation Model-FCID™ software with the Food Commodity Intake Database (DEEM-FCID™ Version 2.03) and food and water consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. Available ICR monitoring data essentially at the tap were used to estimate chlorate concentrations in drinking water. Exposures were single point estimates.

The chronic (non-cancer) dietary (water only) risk assessment for chlorate in drinking water, using the highest annual average concentration estimated at 0.69 mg/L, is below the Agency's level of concern for the General U.S. Population and all subgroups except all infants <1 year of age. The highest exposed population subgroup, all infants <1 year of age, was 159% of the chronic Population Adjusted Dose (cPAD). Using the 90th percentile annual average concentration estimated at 0.24 mg/L, the chronic (non-cancer) dietary (water only) risk for all infants <1 year of age was 55% of the cPAD and 25% of the cPAD using the median annual average concentration estimated at 0.11 mg/L.

No separate cancer dietary risk assessment for chlorate in drinking water was conducted. The estimated cancer dietary risk for the General U.S. Population is based on the chronic (non-cancer) dietary risk, and is below the Agency's level of concern (*i.e.*, % cPAD is less than the level of concern of 100%).

Residential Exposure

All residential (non-occupational) risk estimates for inorganic chlorates, as active or inert ingredients in conventional pesticide products used in residential environments, are below the Agency's level of concern (*i.e.*, Margin of Exposures are greater than the Level of Concern of 100). These uses are considered to be short-term only due to the episodic uses associated with homeowner products. Since the episodic nature of residential exposure is inconsistent with the mechanism of chlorate carcinogenicity, a residential cancer risk assessment was not conducted.

There is the potential for exposure to sodium chlorate by residential handlers in outdoor residential settings during application of conventional pesticide products containing sodium chlorate (073301) as the active ingredient. Sodium chlorate (073301) can be used as a non-selective herbicide in outdoor residential environments as a spot treatment/edging treatment to driveway cracks and crevices, around foundations, and underneath and around wood decks as required. Although there is the potential for dermal exposure, sodium chlorate is an inorganic salt, therefore, significant absorption of sodium chlorate through intact skin is not expected.

There is the potential for postapplication exposure in outdoor residential settings from entering areas previously treated by professional handlers with conventional pesticide products containing sodium chlorate (873301) as an inert ingredient. Although there is the potential for dermal exposure, sodium chlorate is an inorganic salt, therefore, significant absorption of sodium chlorate through intact skin is not expected. Also, postapplication inhalation exposure for sodium chlorate is not expected due to negligible vapor pressure.

Aggregate Risk

Evaluation of the hazard and exposure (food, water, and residential) components for inorganic chlorates indicates the need to estimate potential risks for the following scenarios: short-term inhalation, chronic (non-cancer) dietary (food + water), and cancer dietary (food + water).

The short-term aggregate risks, from residential (non-occupational) exposures (including background, chronic dietary (food + water)) are below the Agency's level of concern for the Margins of Exposure (*i.e.*, Margin of Exposures are greater that the Level of Concern of 100).

The chronic (non-cancer) dietary (food + water) risk assessment, using the highest annual average concentration estimated at 0.69 mg/L for drinking water, is below the Agency's level of concern for the General U.S. Population and all subgroups except all infants <1 year of age and Children 1-2 years. The highest exposed population subgroup, all infants <1 year of age, was 174% of the chronic Population Adjusted Dose (cPAD). Using the 90th percentile annual average concentration estimated at 0.24 mg/L, the chronic (non-cancer) dietary (food + water) risk for all infants <1 year of age was 70% of the cPAD. As previously indicated, there is some concern that the exposure estimates for water may be underestimates.

The cancer dietary (food + water) risk assessment is below the Agency's level of concern and is based on the chronic (non-cancer) dietary (food + water) risk assessment for the general population.

Occupational Exposure and Risk Assessment for Inorganic Chlorates in Conventional Pesticides

With the addition of PPE (dust/mist respirator) or engineering controls (enclosed cockpits or cabs), all occupational handler scenarios for the use of inorganic chlorates as an active or inert ingredient in conventional pesticides are below the Agency's level of concern (*i.e.*, Margin of Exposures are greater than the Level of Concern of 100). Exposure durations are short- and intermediate-term only. Since the exposure durations for occupational handlers are inconsistent with the mechanism of chlorate carcinogenicity, an occupational cancer risk assessment was not conducted.

There is potential for occupational handler exposure to inorganic chlorates from: (1) the application of sodium chlorate (073301) as the active ingredient in conventional pesticide products used on both agricultural and commercial (non-agricultural) sites (*i.e.*, mixer/loaders, applicators, flaggers, and mixer/loader/applicators); (2) the application of sodium chlorate (873301) as an inert ingredient in conventional pesticide products used on both agricultural and commercial (non-agricultural) sites (*i.e.*, mixer/loaders, applicators, flaggers, and mixer/loader/applicators); and (3) the application of potassium chlorate (900583) as an inert ingredient in conventional pesticide products used in poultry premises. Only the inhalation route of exposure needs to be included in the occupational handler risk assessment.

There are no dermal toxicity or dermal absorption data available for inorganic chlorates. Although the potential for dermal exposures exists for occupational handler, based on its high water solubility and ionic nature, significant absorption of inorganic chlorates through intact skin is not expected.

Postapplication scenarios do not need to be included in the occupational risk assessment for inorganic chlorates. Although dermal and inhalation exposures are possible, these exposures are expected to be negligible due to the physical and chemical characteristics of inorganic chlorates. Significant absorption of inorganic chlorates through intact skin is not expected. Postapplication inhalation exposure is not expected based on the negligible vapor pressure of sodium chlorate.

2.0 Ingredient Profile

Sodium chlorate is a non-selective herbicide, considered phytotoxic to all green plant parts. Sodium chlorate is absorbed rapidly by the plant through both roots and leaves causing cell death. Its oxidizing action may disrupt normal respiratory functioning leading to a buildup to toxic peroxides and greater production of ethylene which causes leaf abscission. It is 30-50 times more toxic to plants than sodium chloride. It has a soil-sterilant effect.

Sodium chlorate has a salty taste and is palatable to livestock. Animals may feed on enough freshly treated areas to become poisoned.

With respect to pesticidal uses, most sodium chlorate is used as an on-site precursor to chlorine dioxide generation for wood pulp bleaching; other uses include herbicides and water treatment. It is used as a defoliant and desiccant on a number of crops and as spot treatments on non-crop areas to control weeds. Agricultural products are all formulated as soluble concentrates/liquids; non-crop products are formulated as soluble concentrates/liquids and granules or pellets/tablets.

2.1 Summary of Registered/Proposed Conventional Uses of the Active Ingredient Sodium Chlorate (073301) Under Discussion

Table 2.1.1. Summary of Food/Feed Agricultural Uses of Sodium Chlorate as a Defoliant/Desiccant

Applic. Timing, Type, and Equip.	Formulation	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	PGI (days)
Dry Beans, Corn, Flax, Guar, Rice, Safflower, Sorghum, Southern Peas (*i.e.*, Cowpeas), Soybeans, Sunflower						
Preharvest Spray Aircraft/Ground	SC	7.5	1	7.5	14 (Corn) 7 (All others)	14
Cotton						
Preharvest Spray Aircraft/Ground	SC	7.5	2	15	7	14
Wheat (Proposed Use Rate)						
Preharvest Spray Aircraft/Ground	SC	6	1	6	3	??
Chili peppers, Potatoes						
Preharvest Spray Aircraft/Ground	SC	12.5	1	12.5	10 (Chili peppers) 7 (Potatoes)	14

Table 2.1.2. Summary of Non Food/Feed Agricultural Uses of Sodium Chlorate as a Defoliant/Desiccant						
Applic. Timing, Type, and Equip.	Formulation	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	PGI (days)
Ornamental gourds, Cucurbits (grown for seed), Fallow land						
Preharvest Spray Aircraft/Ground	SC	6	1	6		

Table 2.1.3. Summary of Industrial and Other Non-Crop Uses of Sodium Chlorate as non-selective Herbicide			
Use Site	**Formulations**	**Application Equipment**	**Application Rates [1] (lbs ai/A [2])**
Industrial/Non-Crop Sites: rights-of-way areas, building perimeters, ditch banks, bleachers, airport runways, vacant lots, fire hydrants, or as a pre-paving treatment.	Soluble concentrate/liquid	rights-of-way sprayer, handgun sprayer, groundboom, low-pressure handwand	1032
			523
			132
	Granular or pellet/tablet	belly grinder, push-type spreader, tractor-drawn spreaders	523
			240
			161

[1] Application rates are presented as ranges to reflect different product labels.
[2] Although area treated on most product labels is expressed as lbs ai/ft^2, application rates have been calculated by the reviewer (M. Crowley HED/RRB4) as lbs ai/A consistent with the standard expression for application rates used for calculation and comparison purposes.

Table 2.1.4. Summary of Residential Uses of Sodium Chlorate as non-selective Herbicide			
Use Site	**Formulations**	**Application Equipment**	**Application Rates**
Spot treatment/edging treatment: driveway cracks and crevices, around foundations, and underneath and around wood decks. Not labeled for broadcast on residential lawns or ornamentals.	Liquid	RTU sprinkler can	0.27 lb ai/gallon
	Liquid	low-pressure handwand, sprinkler can	23.7 lb ai/1000 ft^2
	Liquid	trigger-pump sprayer	0.196 lb ai/gallon
	Granular	belly grinder, push-type spreader, hand	12 lb ai/1000 ft^2

2.2 Summary of Registered Conventional Uses of the Inert Ingredients Sodium Chlorate (873301) and Potassium Chlorate (900583) Under Discussion

Sodium chlorate (873301) as an inert ingredient in herbicide formulation products can be applied professionally to agricultural (corn, guava, macadamia nuts, sorghum grain, sugarcane, wheat), commercial (non-agricultural), and residential sites. These conventional pesticide products contain < 1 % sodium chlorate and can be applied at rates no greater than 0.07 lb (as sodium chlorate) per acre.

Potassium chlorate (900583) as an inert ingredient in airborne fungicide products can be applied in poultry premises. These conventional pesticide products contain < 20% potassium chlorate and can be applied at rates not greater than 0.01 lb (as potassium chlorate) per 500 ft^3.

2.3 Summary of Uses of the Inert Ingredients Sodium Chlorate (873301) and Calcium Chlorate (875606) in Antimicrobial Agents Under Discussion Due to Dietary Concerns Only

Sodium chlorate (873301) and calcium chlorate (875606) as inert ingredients in antimicrobial products are used: (1) as fruit, vegetable, and egg sanitizing washes; (2) to control bacterial blotch on mushrooms; (3) as treatment to seed used for sprouting; (4) for conditioning live oysters; (5) in poultry drinking water; (6) in fish filleting; (7) pecan cracking/dyeing. These products contain <2% sodium chlorate or calcium chlorate and the maximum use rate is 500 ppm total available chlorine in the sanitizing wash water; exposure time is 1-2 minutes.

2.4 Chemical Formula and Nomenclature

Table 2.4. Chemical Formula and Nomenclature	
Sodium Chlorate - $NaClO_3$	
Common name	Sodium Chlorate
IUPAC name	Sodium Chlorate
CAS name	Sodium Chlorate
CAS#	7775-09-9
Current Food/Feed Site Registration	dry beans, corn, cotton, flax, guar, peppers (chili type), rice, safflower, sorghum (grain), southern peas (*i.e.*, cowpeas), soybeans, sunflowers, wheat (Section 18 Registration)
Proposed Food/Feed Site Registration	wheat
Calcium Chlorate - $CaCl_2O_6$	
Common name	Calcium Chlorate
IUPAC name	Calcium Chlorate
CAS name	Calcium Chlorate
CAS#	10137-74-3
Current Food/Feed Site Registration	None
Potassium Chlorate - $KClO_3$	
Common name	Potassium Chlorate
IUPAC name	Potassium Chlorate
CAS name	Potassium Chlorate
CAS#	3811-04-9
Current Food/Feed Site Registration	None
Magnesium Chlorate - $MgCl_2O_6$	
Common name	Magnesium Chlorate
IUPAC name	Magnesium Chlorate
CAS name	Magnesium Chlorate
CAS#	10326-21-3
Current Food/Feed Site Registration	None

2.5 Physical and Chemical Properties

Sodium chlorate is a white, odorless, crystalline solid that looks like common table salt (sodium chloride) and is highly water soluble. It is a strong oxidant, not combustible buts reacts violently with combustible and reducing materials. Vapor pressure is low (EXTOXNET lists vapor pressure as Zero).

HED is not responsible for the Product Chemistry Chapter for the Inorganic Chlorates Reregistration Eligibility Decision (RED); hence detailed physical and chemical properties of sodium chlorate, calcium chlorate, potassium chlorate, and magnesium chlorate are not provided herein.

3.0 Metabolism Assessment

By agreement within OPP, the residue of concern for inorganic chlorates is the chlorate anion. Discussions concerning residues to be included in the tolerance expression are not relevant here since residues of concern are not and will not be specified in the exemptions from the requirement of a tolerance for sodium chlorate used on crops.

3.1 Comparative Metabolic Profile

Since there are no livestock metabolism data, no comparison can be made. Based on published rat metabolism data (Abdel-Rahman *et al*, 1982, 1984b and 1985), terminal residues of sodium chlorate in animal tissues are expected to be chlorate (ClO_3^-), chlorite (ClO_2^-), and chloride (Cl^-). Chlorate is readily absorbed from the digestive tract and is excreted as chlorate, chlorite, and chloride in urine and feces. Within 72 hours, about 40% of the administered dose was excreted in the urine as chlorate (ca. 13%), chlorite (ca. 4%), and chloride (ca. 20%) and about 2-4% was excreted in the feces in the same time period. Less than 1% of the administered dose was found in any of the tissues analyzed including kidney, liver, and skin.

3.2 Nature of the Residue in Foods

3.2.1 Description of Primary Crop Metabolism

No plant metabolism data have been submitted in support of the reregistration of sodium chlorate; however, no new plant metabolism data are required to support the established sodium chlorate exemptions from the requirement of a tolerance. Based on available published information (Loomis *et al.*, J. Am. Soc. Agron.; 25, 724 (1933)), sodium chlorate is highly soluble in water and is expected to readily absorb and translocate throughout plants. However, given the proposed use conditions, the means of translocation in treated plants may be substantially disrupted. Translocation of very small amounts of chlorate ion (ClO_3^-) by plants may occur (translocation of significant amounts would be phytotoxic to plants). Terminal residues are expected to be primarily surface residues.

Since sodium chlorate is a strong oxidizing agent, depending on environmental factors, it is expected to be easily reduced to chloride and possibly chlorite in plants. Total redox conversion to these reduced species is not expected; hence, the terminal residues of sodium chlorate in/on plants are likely chlorate (ClO_3), chlorite (ClO_2), and chloride (Cl).

3.2.2 Description of Livestock Metabolism

No ruminant, swine, or poultry metabolism or feeding data have been submitted in support of the reregistration of sodium chlorate; however, no new animal metabolism data are required to support the established sodium chlorate exemptions from the requirement of a tolerance. Although some previous residue chemistry reviews for specific exemptions from the requirement of a tolerance have concluded that there is no reasonable expectation of transfer of residues to meat, milk, poultry or eggs in specific cases, re-evaluation of the available crop field trial data taken as a whole, indicate that there is the possibility of detectable residues of sodium chlorate on animal feedstuffs at harvest. Hence, secondary residues of concern in meat, milk, poultry, and eggs are possible and; therefore, new ruminant and poultry feeding data are required to support the reregistration of sodium chlorate. These data are considered confirmatory.

3.2.3 Description of Rotational Crop Metabolism

Considering the phytotoxic nature of sodium chlorate, planting crops soon after treatment of primary crops would not seem likely. Rotational crop tolerances or plant back restrictions are not necessary. Translocation of very small amounts of chlorate ion (ClO_3) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses may occur.

3.3 Environmental Degradation

Sodium chlorate is used as a desiccant/defoliant because it is a strong oxidizer. As a strong oxidizing agent, chlorate (ClO_3 , oxidation state V) gets reduced to chlorine species in lower oxidation states, such as the oxyanions chlorite (ClO_2 , oxidation state III) and hypochlorite (ClO , oxidation state I), chlorine dioxide (oxidation state IV), and chloride (oxidation state -I). Thus, at least some and possibly substantial reduction of the applied chlorate is likely to occur in the field prior to any runoff to surface water. Under environmental (terrestrial field) redox conditions and based on chemical equilibria alone, the thermodynamically favored, end reduction product of chlorate in soil and in water is the chloride anion. Any intermediate chlorine dioxide that may form under environmental conditions will undergo photochemical reactions when exposed to sunlight. The chlorine oxyanions chlorite and hypochlorite (other possible more reduced intermediates in the ultimate reduction of chlorate to chloride) are strong oxidizers in themselves and thus, they are also reduced and/or undergo disproportionation reactions. Although reduction reactions of chlorate, chlorite, and hypochlorite are said to occur “very fast”, how fast they occur is not known (*i.e.*, the actual rate constants in the environment are not known).

Therefore, at any given time the distribution of reduced species (type and concentration) cannot be estimated. However, it is unlikely that a single reduced species would be present.

4.0 Hazard Characterization/Assessment

4.1 Hazard and Dose-Response Characterization

4.1.1 Database Summary

4.1.1.1 Studies available and considered (animal, human, general literature)

Subchronic - Oral 90-day rat, 90-day mouse and 90-day dog
Repro/developmental - rat and rabbit developmental; 2- generation reproductive rat
Chronic/cancer - Two-year drinking water studies in rats and mice
Other - mutagenicity screens; metabolism in the rat; many published studies included in this hazard and dose response characterization.

4.1.1.2 Mode of action, metabolism and toxicokinetic data

Sodium chlorate is a thyroid toxicant producing thyroid gland follicular cell hypertrophy in rats and mice following chronic exposures and some evidence of follicular cell tumors in rats. The primary target of chlorate acute toxicity is rupture of red blood cell membranes with intravascular hemolysis and the irreversible oxidation of hemoglobin to methemoglobin. Potassium chlorate has produced renal tubular necrosis in animals.

Metabolism studies in rats and dogs have shown that chlorates are readily absorbed by the gastrointestinal tract and in rats are excreted in the urine as chlorate (ca. 13% of the administered dose), chlorite (ca. 4% of the dose) and chloride (ca. 20% of the dose).
Using ^{36}Cl-potassium chlorate, peak blood concentration levels were reached after an hour of ingestion by rats. Elimination of the labeled chlorate from the blood was biphasic with half-lives of 6 and 36.5 hours.

4.1.1.3 Sufficiency of studies/data

Data are sufficient for each exposure scenario and for FQPA evaluation. Data are sufficient for endpoint selection.

4.1.2 Toxicological Effects

The toxicology profile for sodium chlorate is presented in tables 4.1a and 4.1b. In acute toxicity tests, sodium chlorate is slightly toxic by the oral (Toxicity Category IV), dermal (Toxicity Category IV), and inhalation routes (Toxicity Category IV of a 33% aerosol). Sodium chlorate crystals were mildly irritating to the rabbit eye (Toxicity Category III for the dry crystals or moistened crystals), and minimal to mild dermal irritant (Toxicity Category III for the moistened material and Toxicity Category IV for the dry crystal). Ingestion of toxic doses of sodium chlorate by humans produce gastritis, hemolysis, methemoglobinemia, hemoglobinurea, late toxic

nephritis, and acute renal failure. An acute or cumulative dose of 7.5-35 grams is lethal in adults. Ingestion of 1 g amounts of potassium chlorate was reported to be fatal in infants.

There are conflicting findings regarding the subchronic/chronic toxicity of sodium chlorate. In one series of studies, rats exposed to relatively low concentrations of sodium chlorate (equivalent to1.5 and 15 mg/kg/day) for up to 11 months exhibited decreased blood glutathione, increased fragility of erythrocytes, inhibition of incorporation of tritiated thymidine into nuclei in rat testes, decreased RBC count and hematocrit and decreased body weight. In another study, male F344 rats were exposed to 1% sodium or potassium chlorate in drinking water (654-686 mg/kg/day) for 25 weeks and the only effect reported was significant body weight reduction. Relative kidney weights were significantly increased in potassium chlorate treated rats. Rats orally administered 10-1000 mg/kg/day sodium chlorate for 90 days did not exhibit histological or clinical chemistry treatment-related effects, but had decreased red blood cell counts, hematocrit and hemoglobin levels, particularly in the females. Adrenal weights were also depressed in males and females at the 1000 mg/kg/day level. In another published study in which rats were administered sodium chlorate in the drinking water at concentrations equivalent to 512 and 800 mg/kg/day for males and females, respectively for 90 days, final body weights were significantly lower in both sexes with some relative organ weight changes including the adrenal glands and reduction in RBC counts and percent hemoglobin, and prominent pituitary gland vacuolization and thyroid gland colloid depletion in both sexes. The thyroid effects were confirmed in a recent study in rats where subchronic treatment for 21 or 90 days with sodium chlorate in the drinking water at concentrations up to 2,000 mg/L (225 mg/kg/day) induced a concentration dependent increase in the incidence and severity of thyroid follicular cellular hyperplasia. Colloid depletion and hypertrophy were the most sensitive histopathological indicators of sodium chlorate exposure, with male rats more susceptible than females rats. Decreases in serum hormone levels of triiodothyronine (T_3) and thyroxine (T_4) were also reported following exposure to sodium chlorate. Mice were less susceptible to the adverse effect from exposure to high levels of sodium chlorate. In dogs, the only reported treatment related effect following subchronic administration of sodium chlorate up to 360 mg/kg/day was emesis.

A 2-year study to determine the potential of sodium chlorate to cause tumors in laboratory animals (rats and mice) has been recently reported (NTP 2004). A final report of this study is expected during 2005. In these tests, there was some evidence of thyroid gland follicular cell carcinogenicity in male rats which may be attributed to the imbalance of thyroid hormones (reduced T_3 and T_4 levels and elevated TSH) seen in these studies as a result of exposure to sodium chlorate. Current EPA HED policy states that "nonmutagenic pesticides that induce elevated levels of TSH and thyroid follicular cell tumors in the rat should be classified as **not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis**" (*Assessment of Thyroid Follicular Cell Tumors*; USEPA March 1998 EPA/630/R-97/002). In female mice there was equivocal and marginal evidence of increased pancreatic islet carcinoma.

Sodium chlorate was negative in most bacterial gene mutation assays. In one assay (Ames test), it showed positive effect in the TA1535 strain in the presence of metabolic activation. It also caused DNA damage in repair deficient *E. coli* strains at concentrations above 1000 ug/mL in the presence of metabolic activation but was negative in the unscheduled DNA synthesis assay. In cytogenetics tests, sodium chlorate was negative in the *in vitro* cell gene mutation assay, mammalian erythrocyte micronucleus assay, bone marrow cytogenetics assay and sperm head abnormality assay.

Sodium chlorate did not cause developmental effects in rats tested at doses up to 1000 mg/kg/day or in rabbits tested at doses up to 500 mg/kg/day. In a two generation reproductive toxicity study in the rat, postnatal toxicity did not exceed parental toxicity. Sodium chlorate has not been evaluated for neurotoxic effects, but acute and subchronic toxicity studies did not indicate a neurotoxic potential.

There are no repeated dermal toxicity or dermal absorption data available for sodium chlorate. Based on its high water solubility and ionic nature, potential sodium chlorate (or any other inorganic chlorate) absorption by the intact skin is considered negligible.

4.1.3 Dose-response

Subchronic, developmental and reproductive studies were considered. An endpoint of concern attributable to a single dose was not identified, and therefore an acute RfD is not established. The oral endpoints for other durations were based on subchronic and chronic studies in rats. The toxic effects seen in the subchronic study were on the pituitary (vacuolization) and thyroid gland (colloid depletion), body weight decrease and organ weight changes and reduction in erythrocyte counts and hemoglobin content. In the chronic drinking water study in rats, an endpoint of toxicity was derived on the basis of thyroid follicular cell hypertrophy. There were no dermal toxicity studies available. Sodium chlorate is an inorganic salt and its dermal absorption is unlikely. Therefore, a toxicity endpoint for dermal exposure is not selected. There were no inhalation studies available suitable for assessment of inhalation risks. For the risk assessment of inhalation exposure from sodium chlorate, the endpoint of oral toxicity for short and intermediate exposures is used with a 100% absorption factor.

Table 4.1a. Acute Toxicity Profile - Sodium Chlorate				
Guideline No./ Study Type	Study Type	MRID No.	**Results**	**Toxicity Category**
870.1100	Acute oral -Rats	41819901	$\geq$ 5000 mg/kg (rat)	IV
870.1200	Acute dermal - Rabbits	41819902 42497601	LD_{50} = > 2000 mg/kg (dry crystal) LD_{50} = > 2000 mg/kg (moistened)	IV IV
870.1300	Acute inhalation - Rats	41819903	LC_{50} = 5.59 mg/L	IV
870.2400	Acute eye irritation - Rabbit	00085090 00102998 41819904	mildly irritating mildly irritating	III III
870.2500	Acute dermal irritation - Rabbit	41819905 42497602	non-irritating (dry crystal) minimally irritating (moistened)	IV III
870.2600	Skin sensitization - guinea pigs	41819906	not a dermal sensitizer	NA

Table 4.1b Subchronic, Chronic and Other Toxicity Profile: Sodium Chlorate		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3100 90-Day oral toxicity (Sprague-Dawley Rats)	40444801(1987) Acceptable/guideline 0, 10, 40, 100 or 1000 mg/kg/day, oral gavage	**NOAEL** = 100 mg/kg/day **LOAEL** = 1000 mg/kg/day based on hematological effects (hemoglobin concentration, hematocrit, RBC counts were statistically significantly decreased, and reticulocyte count was statistically significantly increased in females. In males, only the hematocrit was statistically significantly decreased. The adrenal weight was depressed in both males and females.
Non-Guideline 25-week tumor promotion toxicity study (Male F344 Rats)	Kurokawa *et al*, 1985 1% $NaClO_3$ or $KClO_3$ in drinking water(654-686 mg/kg/day) for 25 weeks following 2-week initiation with 0.05% N-ethyl-N-hydroxyethylnitrosamine	**LOAEL** = 654-686 mg/kg/day (only dose tested). Significant decrease in mean body weights compared to the controls. This dose was the maximum tolerated dose based on a 6-week screening study at 0.25, 0.5, 1 and 2% doses in drinking water. Relative kidney weights of the chlorate treated rats were significantly increased over the control group. $NaClO_3$ or $KClO_3$ showed no promoting effect in rat renal carcinogenesis
Non-Guideline 90-Day oral toxicity (Sprague-Dawley Rats)	McCauley *et al*, 1995 SD rats (10/sex/group) $NaClO_3$ in the drinking water 3.0, 12.0, or 48 mM for 90 days M: 30, 100 and 512 mg/kg/day (chlorate) F: 42, 158, and 800 mg/kg/day (chlorate)	**NOAEL** = 30 and 42 mg chlorate/kg/ day in males and females. **LOAEL** = 100 mg chlorate/kg/day in males and 150 mg/kg/day in females, based on the pituitary effects (vacuolization) and thyroid gland effects (colloid depletion), the body weight decrease and organ weight changes and reduction in erythrocyte counts and hemoglobin content.
Non-Guideline 90-Day oral toxicity (F344 rats and B6C3F1 mice)	Hooth *et al*, 2001 $NaClO_3$ in drinking water at 0, 0.125, 0.25, 0.5, 1.0 or 2 g/L for 21 days or 90 days in rats (14, 28, 56, 112, 225 mg/kg/day in males; 20, 40, 80, 160 or 320 mg/kg/day in females). Additional groups of male rats at 0, 0.001, 0.01, 0.1, 1.0, 2.0 and females at 0, 0.5, 1.0, 2.0, 4.0, 6.0 g/L for 90-105 days. Groups of mice were also treated.	**NOAEL** = 0.25 g/L (28 mg/kg/day for males) **LOAEL** = 1.0 g/L based on colloid depletion and follicular cell hyperplasia, (112 mg/kg/day for males). Females were less susceptible to the chlorate toxicity. Total serum triiodothyronine (T_3) and thyroxine (T_4) concentrations were decreased significantly and TSH levels increased significantly in male and female rats after 4 days of treatment with 1.0 or 2.0 g/L and after 21 days of treatment with 2.0 g/L. TSH levels also increased significantly in male rats after 21 days of treatment with 1.0 g/L. Serum T_3 and T_4 levels were comparable to controls in male and female rats after 90 days of treatment, but TSH levels were increased in both sexes. Follicular cell hyperplasia was not present in male or female mice.

Table 4.1b Subchronic, Chronic and Other Toxicity Profile: Sodium Chlorate		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Non-Guideline 11-month oral toxicity -Rats	Abdel-Rahman *et al.* 1984 chlorine dioxide (0, 1, 10, 100, 1000 mg/L) and its conversion products chlorite and chlorate (10, 100 mg/L) in drinking water (1.5, 15 mg/kg/day)	**LOAEL** =1.5 mg/kg/day (lowest dose tested). At 9 months the osmotic fragility of RBCs was decreased in all treatment groups, while a decreased blood glutathione was only observed in the chlorite/chlorate groups. At 2, 4 and 6 months, no significant hematologic changes were noted in treated rats compared to control. After 9 month RBC counts, hematocrit and Hb were decreased in all treatment groups. The incorporation of ^{3}H-thymidine into nuclei of testes was inhibited in all treated groups, also in the liver of the chlorite groups and in the kidney of 100 mg/L chlorine dioxide treatment. The incorporation in small intestinal nuclei was increased in 10 and 100 mg/L chlorine dioxide and in 10 mg/L chlorite groups. Rat body weight was decreased in all groups after 10 and 11 months
870.3150 90-Day oral toxicity (Beagle Dogs)	MRID 40460402 (1987) Acceptable/Guideline oral gavage 0, 30, 60 or 360 mg/kg/day for 90 d	**NOAEL** = 360 mg/kg/day (HDT) **LOAEL** = greater than 360 mg/kg/day based on lack of detectable adverse effects. Higher dose levels were not possible due to occurrence of emesis at higher doses.
Non-Guideline subacute study in dogs	Heywood *et al*, 1972 doses of 200 to 326 mg/kg/day of sodium chlorate administered daily by intubation as 50 ml of 6% solution to 8 dogs for 5 days	**LOAEL** = 200 mg/kg/day (LDT). Sodium chlorate caused reduction of packed cell volume, hemoglobin and red blood cells. A consistent increase in plasma urea concentration was also observed. Two animals that received 308 or 326 mg/kg/day suffered appetite loss, body weight decline and appearance of blood in their urine or feces. One of the animals died after 4 days of exposure. Postmortem examination of both animals revealed typical signs of chlorate poisoning, including cyanotic kidney surface and evidence of necrosis and hemolysis in the kidney. Five of the 8 animals displayed tissue pathology indicative of hemolysis such as Kupffer cells containing brown pigment.
Non-Guideline 21 day oral toxicity study (B6C3F1 mice)	NTP Study (2004) 10/sex/dose: 0, 125, 250, 500, 1000 or 2000 mg/L M: 20, 45, 90, 175 or 350 mg/kg/day F: 0, 20, 45, 95, 190 or 365 mg/kg/day	**NOAEL** = 350/360 mg/kg/day (HDT). Sodium chlorate had no effect on survival, body weights, clinical signs, water consumption, hematology parameters, methemoglobin concentration, or organ weights of either sex. There were no gross or microscopic lesions that were considered to be due to sodium chlorate treatment.

Table 4.1b Subchronic, Chronic and Other Toxicity Profile: Sodium Chlorate		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Non-Guideline 21 day oral toxicity study (Fisher 344 rats)	NTP Study (2004) 10/sex/dose: 0, 125, 250, 500, 1000 or 2000 mg/L M: 0, 20, 35, 75, 170, 300 mg/kg/day F: 0, 20, 40, 75, 150 or 340 mg/kg/day	**NOAEL/LOAEL** unclear from study summary. Sodium chlorate had no effect on survival, body weights, clinical signs or water consumption. A moderate to severe neutropenia was observed in both sexes on day 4 and 22. Very mild decreases in erythrocyte counts, hemoglobin, and hematocrit were considered not to be biologically significant. The only gross or microscopic lesion that was considered to be treatment related was a minimal to mild follicular cell hyperplasia of the thyroid gland seen in males at 500 mg/L or greater and in females at 250 mg/L or greater.
870.3200 21/28-Day dermal toxicity	Not required. Sodium chlorate has very low acute dermal toxicity. Dermal absorption is also unlikely due to its ionic nature and high water solubility.	
870.3250 90-Day dermal toxicity	Not required. Sodium chlorate has very low acute dermal toxicity. Dermal absorption is also unlikely due to its ionic nature and high water solubility.	
870.3465 90-Day inhalation toxicity	NA	
870.3700a Prenatal developmental (rats)	MRID 40460401(1987) Acceptable/Guideline oral gavage 0, 10, 100 or 1000 mg/kg/d on GD 6-15	**Maternal NOAEL** = 1000 mg/kg/day (HDT) **LOAEL** = >1000 mg/kg/day. **Developmental NOAEL** = 1000 mg/kg/day (HDT) **LOAEL** = >1000 mg/kg/day based on lack of effects
870.3700b Prenatal developmental (Rabbits)	NTP (2002) Acceptable/Guideline 0, 100, 250, or 475 mg/kg/d on GD 6-29. Range finding study: 0, 100, 250, 500, 750 or 1000 mg/kg/d	**Maternal NOAEL** = 475 mg/kg/day (HDT) **LOAEL** = 500 mg/kg/day based on mortality in range finding study. **Developmental NOAEL** = 475 mg/kg/day (HDT) **LOAEL** = >475 mg/kg/day

Table 4.1b Subchronic, Chronic and Other Toxicity Profile: Sodium Chlorate		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3800 Reproduction and fertility effects (Rats)	MRID 46524001(2004) Acceptable/Guideline 0, 10, 70 or 500 mg/kg/day (gavage)	**Parental/Systemic NOAEL** = 10/70 (M/F) mg/kg/day **LOAEL** = 70/500 (M/F) mg/kg/day based on lower BW gain and food consumption (F1 M), decreased RBC counts and hemoglobin (P males and females), increased absolute and relative thyroid weight (F1 males), increased incidence of slight to moderate hyperactivity of the thyroid glands (P and F1 males and females) (only in P and F1 males at 70 mg/kg/day). **Reproductive NOAEL** = 500 mg/kg/day (HDT) **Offspring NOAEL** = 70 mg/kg/day **LOAEL** = 500 mg/kg/day based on increased relative thyroid weight (F1 and F2 males).
870.4100a Chronic toxicity rodents	A 2-year NTP bioassay (2004) to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been reported in a draft form. F344 rats (50/sex/group) were exposed to drinking water at 0, 125, 1,000, or 2,000 mg/L sodium chlorate for 2 years (5, 35, and 75 mg/kg /day in males and 5, 45, and 95 mg/kg/day in females). T_4 and T_3 were significantly reduced in 1,000 and 2,000 mg/L on day 4 and in 2,000 mg/L males and females at week 3. TSH was significantly increased in 1,000 and 2,000 mg/L males on day 4 and at week 3, in 1,000 and 2,000 mg/L females on day 4, in 2,000 mg/L females at week 3, and in 2,000 mg/L males and females at week 13. There were positive trends in the incidences of thyroid gland follicular cell carcinoma in male rats (0/47, 0/44, 0/43, 4/47) and of thyroid gland follicular cell adenoma or carcinoma (combined) in males (1/47, 0/44, 0/43, 6/47) and females (1/47, 0/47, 1/43, 4/46). The incidences of thyroid gland follicular cell hypertrophy were significantly increased in all exposed groups of males (4/47, 13/44, 33/43, 40/47) and in 1,000 and 2,000 mg/L females (3/47, 7/47, 27/43, 42/46). Thyroid gland focal follicle mineralization occurred in most 1,000 and 2,000 mg/L female rats. The incidences of hematopoietic cell proliferation in the spleen of 2,000 mg/L males (2/48, 6/49, 4/49, 11/50) and bone marrow hyperplasia in 1,000 and 2,000 mg/L males (28/48, 35/48, 41/50, 40/49) were significantly greater than those in the controls. The **LOAEL** for non neoplastic effects derived from this study is 125 mg/L (5 mg/kg/day) based on increased thyroid gland follicular cell hypertrophy and follicular cell mineralization. The **NOAEL** is less than 5 mg/kg/day. B6C3F_1 mice 950/sex/group) were exposed to drinking water at 0, 500, 1,000, or 2,000 mg/L sodium chlorate for 2 years (40, 80, and 160 mg/kg/day to male mice and 30, 60, and 120 mg/kg/day to female mice). There was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) in female mice (0/46, 2/47, 2/49, 4/49). Thyroid gland follicular cell hypertrophy was significantly increased in 2,000 mg/L females (3/48, 2/50, 5/49, 14/50). The incidences of bone marrow hyperplasia were significantly increased in all exposed groups of females (14/50, 28/50, 29/50, 31/50).	

Table 4.1b Subchronic, Chronic and Other Toxicity Profile: Sodium Chlorate		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.4100b Chronic toxicity dogs	Not available	
870.4200 Carcinogenicity rats	A 2-year NTP bioassay to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been reported in a draft form (2004). In these tests, there was some evidence of thyroid gland follicular cell carcinogenicity in male rats which may be attributed to the imbalance of thyroid hormones (reduced T_3 and T_4 and elevated TSH) seen in these studies as a result of exposure to sodium chlorate. Current EPA HED policy considers nonmutagenic pesticides that induce elevated levels of TSH and thyroid follicular cell tumors in the rat should as not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis.	
870.4300 Carcinogenicity mice	NTP 2004 Study. A 2-year NTP bioassay to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been reported in a draft form (2004). In female mice there was equivocal and marginal evidence of increased pancreatic islet carcinoma.	
Gene Mutation 870. 5100	MRID 41256201 (1989) Acceptable/Guideline	Sodium chlorate was negative for inducing reverse gene mutation in Ames (bacterial) strains of *Salmonella typhimurium* exposed with or without activation up to 5000 ug/plate (limit dose).
	Moriya *et al*, 1983	Sodium chlorate was negative for inducing reverse gene mutation in Ames (bacterial) strains of *Salmonella typhimurium* exposed with or without activation up to 5000 ug/plate (limit dose).
	Eckhardt *et al*, 1982	Sodium chlorate showed mutagenic activity in the TA1535 strain +S9
	Olivier and Marzin 1987	Potassium chlorate was not mutagenic in the SOS chromotest using *E. coli* strain PQ37 without metabolic activation tested at 1-6000 nM/ml.
	NTP, 2004	Sodium chlorate tested up to 10,000 ug/plate was negative in strains TA97, TA98, TA100, TA102, TA1535 with or without S9
870.5500 Bacterial DNA damage/Repair	MRID 41256204 (1989) Acceptable/Guideline	Sodium chlorate caused DNA damage in repair deficient *E. coli* strains at concentrations above 1000 ug/mL in the presence or absence of S9 fractions. It was tested up to 10000 ug/mL.

Table 4.1b Subchronic, Chronic and Other Toxicity Profile: Sodium Chlorate		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Cytogenetics 870.5300, *in vitro* mammalian cell gene mutation assay	MRID 41256202 (1989) Acceptable/Guideline	Sodium chlorate was negative for inducing forward gene mutation at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus in the Chinese hamster lung (V79) cells (HGPRT $^{+}$, $^{-}$) Exposed in activated (+s9) or non-activated (-S9) culture tested up to the limit dose of 5000 ug/mL.
870.5395 Mammalian erythrocyte micronucleus test	MRID 41256203 (1989) Acceptable/Guideline	Sodium chlorate was negative (not clastogenic) for inducing micronuclei in polychromatic erythrocytes of male mice with single oral doses of 200, 1000 or 5000 (limit dose) mg/kg.
870.5395 Mammalian erythrocyte micronucleus test	NTP, 2004	Sodium chlorate did not increase the number of micronucleated erythrocytes in B6C3F1 mice treated in the drinking water with 20, 45, 95, 190, or 365 mg/kg/day for 3 weeks.
micronucleus test	Eckhardt *et al*, 1982	Sodium chlorate did not induce chromosomal damage.
micronucleus test	Meier *et al*, 1985	Sodium chlorate did not increase the number of micronucleated polychromatic erythrocytes in CD-1 mice treated by gavage with 8, 20 or 40 mg/kg/day for 5 days.
870.5385 Bone marrow cytogenetics assay	Meier *et al*, 1985	Sodium chlorate did not cause structural or numerical chromosomal aberrations in mice treated by gavage with 8, 20 or 40 mg/kg/day for 5 days.
Sperm head abnormality assay	Meier *et al*, 1985	Sodium chlorate did not induce sperm head abnormalities in B6C3FA male mice treated by gavage with 8, 20 or 40 mg/kg/day for 5 days.
Other Effects 870.5550, Unscheduled DNA Synthesis	MRID412546205 Acceptable/Guideline	Sodium chlorate was negative for unscheduled DNA synthesis (UDS) in human cells (HeLa-S3) exposed up to 10,000 ug/mL, with or without metabolic activation. The incorporation of thymidine was decreased in a dose-dependent manner between doses of 100 and 10,000 ug/mL indicating cytotoxicity.
870.5275 recessive lethal: Drosophila	Eckhardt *et al*, 1982	Sodium chlorate was mutagenic in this system.
870.6200a Acute neurotoxicity screening battery	Not required for this chemical	

Table 4.1b Subchronic, Chronic and Other Toxicity Profile: Sodium Chlorate		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.6200b Subchronic neurotoxicity screening battery Not required for this chemical		
870.6300 Developmental neurotoxicity NA		
870.7485 Metabolism and pharmacokinetics	Abdel-Rahman *et al*, 1982, 984b, 1985-rats Non-Guideline National Research Council, 1980 - dogs (OEHHA, 2002) Non-Guideline	There are no guideline studies available. However, published studies provide reasonable information on the pharmacokinetics and metabolism of the chlorate ion in the rat and the dog. Chlorate is readily absorbed from the digestive tract and is excreted in urine mainly and feces. In dogs the excretion is entirely as chlorate and is complete after 72 hours. In rats, about 40% of the administered dose was excreted after 72 hours and it is excreted as chloride, chlorite and chlorate. In Cl^{36} labeled potassium-chlorate studies in rats, Cl^{36} radioactivity was detected at the end or 72 hours after the initial oral treatment in several tissues. Although the chlorites and the chlorates are structurally related, their pharmacokinetics is different.
870.7600 Dermal penetration	Not required	It is not required for sodium chlorate. Acute dermal toxicity is low and sodium chlorate is very polar being an inorganic salt would not be readily absorbed through the skin.
Special studies	Beinfeld (1994) Mintz *et al* (1994)	Sodium chlorate is *in vitro* inhibitor of ATP-sulfurylase and protein sulfation
Special Studies	Roy *et al* (1988)	Sodium chlorate did not affect bile production from isolated perfused guinea pig livers suggesting that it is not a general liver poison

4.2 FQPA Hazard Considerations

The database with respect to the standard guideline studies is adequate to characterize potential for prenatal or postnatal risk for infants and children. No increase in prenatal susceptibility of rats or rabbits was seen in developmental studies with chlorate, and no increase in pre- or postnatal susceptibility was evident in a 2-generation reproduction study in rats. Based on this, there are no residual uncertainties from guideline studies and the special FQPA safety factor is reduced to 1X. There is, however, need for additional data on potential neuroendocrine effects on the developing young based on chlorate-induced thyroid effects.

4.2.1 Adequacy of the Toxicity Data Base

The toxicity data base is complete with respect to the normal complement of guideline studies except for a 21/28 day inhalation study. Because the inorganic chlorates affect the thyroid gland

in rats and dogs, there is concern for potential neuroendocrine pre- and postnatal effects to developing young and a comparative thyroid study in which T4, T3 and TSH are analyzed in adults and in neonates is required to address this concern.

4.2.2 Evidence of Neurotoxicity

Sodium chlorate did not show neurotoxic effects in acute, subchronic testing.

4.2.3 Developmental Toxicity Studies

DEVELOPMENTAL - RAT

In a developmental toxicity study (MRID 40460401), 24 pregnant Sprague-Dawley CD rats per group were administered technical grade sodium chlorate (100% a.i., white granular solid) by oral gavage at 0 (distilled water) 10, 100, or 1000 mg/kg/day on gestation days (GD) 6-15, inclusive. On GD 20, all dams were sacrificed and all fetuses were examined for external, visceral, and skeletal malformations/variations. All animals survived until scheduled sacrifice except for one control that died prior to terminal sacrifice. No adverse clinical signs were reported. There were no dose or treatment related effects detected in the dams or embryos/fetuses. Maternal body weights, food consumption were comparable to controls. Necropsy of treated animals did not reveal any treatment related effect. There was no treatment related effect on pregnancy rate, corpora lutea, implantation sites, viable fetuses, dead fetuses, resorptions or fetal weights. Fetal examinations did not reveal any anomalies attributed to treatment. The **LOAEL** derived from this study for maternal and developmental toxicity in the rat is >1000 mg/kg/day and the **NOAEL** is at least 1000 mg/kg/day. This study is considered Acceptable/guideline.

DEVELOPMENTAL - RABBIT

There are no registrant guideline studies available. There is an NTP study reported in 2002, where 24 timed naturally mated female New Zealand rabbits/ dose were dosed by gavage with sodium chlorate at 0 (deionized distilled water), 100, 250, or 475 mg/kg/day on gestation days 6 through 29. The study was conducted in a two replicate design where 12 rabbits/dose were dosed in each replicate. The doses were selected on the basis of a range finding study conducted at 0, 100, 250, 500, 750, or 1000 mg/kg/day. In this range finding study, excessive maternal toxicity (morbidity and mortality) resulted in termination of the groups treated with 750 and 1000 mg/kg/day by gestation day 24. One maternal death occurred in the 500 mg/kg/day group and one doe was lethargic with respiratory distress. Clinical signs were minimal in the 100 and 250 mg/kg/day groups. These included animals with discolored urine (red, orange, orange/white or brown). Body weights were decreased during treatment only at doses higher than 500 mg/kg/day. Developmental toxicity was not evident at doses up to 500 mg/kg/day. In the final study, transient changes in maternal food intake, urinary color (orange or brown) and /or urine output were noted at 100 mg/kg/day and greater, but clear evidence of toxicity occurred only at doses greater than 475 mg/kg/day as observed in the range finding study. According to the study authors, comparison of the results from the range finding study and the developmental toxicity study suggests that the dose-effect curve for maternal effects is very steep as demonstrated by mortality at 500 mg/kg/day on the range finding study, but not at the 475 mg/kg/day in the final

study. No significant treatment related developmental toxicity attributable to sodium chlorate occurred under the conditions of this study. It was concluded that the maternal and developmental toxicity **NOAEL**s were equal to or greater than 475 mg/kg/day (the HDT). The **LOAEL** for maternal toxicity is 500 mg/kg/day based on mortality observed in the range finding study. This study satisfies guideline requirements and is acceptable/guideline.

4.2.4 Reproductive Toxicity Study

In an Acceptable/Guideline 2-generation reproduction study (MRID 46524001), sodium chlorate (99.68% a.i.; batch/lot 1E012IUM) was administered to 25 Sprague-Dawley rats of each sex per dose by gavage at dose levels of 0, 10, 70, or 500 mg/kg/day. P males were exposed to the test material for 10 weeks prior to mating and after mating until the pups were weaned; P females were exposed for 10 weeks prior to mating and then throughout gestation and lactation. Selection of parents (4 males and 4 females per litter) for the F_1 generation was made when the pups were 4 days of age. F_1 parents were exposed in the same manner as P parents.

Oral administration of sodium chlorate resulted in parental toxicity at 70 and 500 mg/kg/day. Treatment-related effects at 500 mg/kg/day consisted of slightly lower body weight gain and food consumption (F_1 males); decreased red blood cell counts (P males and females); decreased hemoglobin concentration (P males and females); increased absolute and relative thyroid weight (F_1 males); increased incidence of slight to moderate follicular hyperplasia (P and F_1 males and females); and increased incidence of slight to moderate hyperactivity of the thyroid glands (P and F_1 males and females). The thyroid gland appeared to be the target organ.

At 70 mg/kg/day, treatment-related effects consisted of a marginal increased incidence of hyperactivity of the thyroid glands (P and F_1 males). **Based on these results, a NOAEL of 10 mg/kg/day for males (LOAEL 70 mg/kg/day)** was established. In females a **NOAEL of 70 mg/kg/day and a LOAEL of 500 mg/kg/day** was established.

For offspring, exposure to sodium chlorate resulted in toxicity at 500 mg/kg/day. Treatment-related effects at 500 mg/kg/day consisted of increased relative thyroid weight in F_1 and F_2 males. **The offspring LOAEL is 500 mg/kg/day, based on increased relative thyroid weight. The offspring NOAEL is 70 mg/kg/day.**

There were no treatment-related reproductive effects observed at any dose level for either generation. **Consequently, the reproductive NOAEL is 500 mg/kg/day.**

4.2.5 Additional Information from Literature Sources

In a case control study evaluating chlorination by-products in drinking water and adverse pregnancy outcomes in Italy (Aggazzotti *et al*, 2004), no association was found between preterm births and exposure to chlorination by products (trihalomethanes, chlorites and chlorates), but there was a weak association between small weight gestational term (weighing less than the lowest 10^{th} percentile) and high levels of trihalomethanes ($\geq$ 30 ug/L drinking water) and chlorites and chlorates ($\geq$ 200 ug/L drinking water).

In a subchronic exposure study in primates where sodium chlorate was administered in drinking water for 8 weeks at 400 mg/L (58.4±27.6 mg/kg/day) to 6 male and 7 female adult African Green Monkeys (*Cercopithecus aethiops*) there was no effect on the thyroid function and the total thyroxine levels (Bercz *et al*, 1982). Based on this study the **NOAEL** for sodium chlorate thyroid effects in the monkey would be at least 58 mg/kg/day.

4.2.6 Pre-and/or Postnatal Toxicity

Prenatal toxicity of sodium chlorate has been evaluated in developmental toxicity studies in the rat and the rabbit. In both species, prenatal toxicity was not observed at the highest doses tested (1000 mg/kg/day in the rat, and 475 mg/kg/day in the rabbit). In a 2-generation reproduction test in the rat, there were thyroid effects to the offspring at the highest dose tested - 500 mg/kg. No other offspring effects were noted in the study,

4.2.6.1 Determination of Susceptibility

Based on the developmental studies in rats and rabbits and the reproductive toxicity study in rats, fetal or neonatal toxicity from administration of sodium chlorate did not occur at doses lower than doses causing effects in parental animals.

4.2.6.2 Degree of Concern Analysis and Residual Uncertainties for Pre and/or Post-natal Susceptibility

No increase in prenatal susceptibility of rats or rabbits was seen in developmental studies, and no pre- or postnatal susceptibility was observed in a reproduction study in the rat. Based on this, there are no residual uncertainties that indicate the need for a special safety factor. The hazard factor is thus 1X.

4.2.7 Recommendation for a Developmental Neurotoxicity Study

4.2.7.1 Evidence that supports requiring a Developmental Neurotoxicity study

There is no evidence for requiring such a study. Sodium chlorate did not show neurotoxic effects in acute, subchronic testing.

4.2.7.2 Evidence that supports not requiring for a Developmental Neurotoxicity study

No neurotoxic effects were seen in acute, subchronic studies with sodium chlorate.

4.3 Safety Factor for Infants and Children.

There was no pre- or postnatal sensitivity or susceptibility observed in the submitted developmental studies in rats and rabbits and the 2-generation reproduction study in rats. However, there is a concern for developing offspring because of the effects of inorganic chlorate on thyroid function in rats and dogs. The thyroid hormone system plays a critical role in development, and it is therefore important to understand whether the thyroid hormone system in the developing young differs in response to thyroid toxicants compared to adults. There exists therefore a database uncertainty for information on comparative thyroid response in young vs adult rats; however, a database factor reflecting the uncertainty in comparative response is not necessary and the default 10X FQPA factor can be removed.

The rationale for removal of the factor lies in the comparative thyroid physiology of rats vs. humans (see further discussion of the differences in physiology under the chronic RfD). As a consequence of these dynamic differences, rats are much more sensitive to thyroid toxicants such as chlorate than humans and non-human primates. As discussed in section **4.4.3** below, the chronic RfD for inorganic chlorates is 0.03 mg/kg/day based on thyroid hypertrophy in adult rats. There is a study of the effects of chlorate on adult monkeys (Bercz et al, 1982), in which the NOAEL for effects on blood thyroxine levels was 58 mg/kg/day. If the NOAEL from the monkey study were used to derive a chronic RfD with uncertainty factors of 10X for interspecies extrapolation and 10X for intraspecies variability and an FQPA factor of 10x reflecting uncertainties in effects to the young, the chronic RfD would be 0.06 mg/kg/day. The chronic RfD selected by the risk assessment team of 0.03 mg/kg/day derived from the chronic rat NTP study is therefore protective of thyroid effects in primates (including a 10X factor for uncertainty with respect to developing young) without the necessity of an additional uncertainty factor applied to the rat data.

4.4 Hazard Identification and Toxicity Endpoint Selection

4.4.1 Acute Reference Dose (aRfD) - Females age 13-49

An acute RfD for females age 13-49 was not identified from the available developmental toxicity studies in rats and rabbits.

4.4.2 Acute Reference Dose (aRfD) - General Population

An endpoint of concern attributable to a single dose was not identified although several studies were considered. The developmental NTP study in rabbits discussed above provided a NOAEL for maternal toxicity of 475 mg/kg/day based on maternal morbidity and mortality at 500 mg/kg/day in a range finding study. In a subacute toxicity study, 200 to 326 mg of sodium chlorate/kg administered daily for 5 days to a total of 8 dogs, all dogs experienced toxicity including death at the higher dose. However, in a guideline study (MRID 40460402) sodium chlorate administered to dogs by oral gavage daily for 90 days did not exert any toxicity at the highest dose tested of 360 mg/kg/day. None of these studies provided an endpoint of toxicity attributable to a single exposure. An acute RfD for the general population is not established.

The published literature provides numerous references to sodium chlorate poisoning in humans. Doses in excess of 100 mg/kg (7 grams for a 70 kg adult and 0.5 grams for a 5 kg child) are generally fatal (Warrington 2002, Cosmetic Ingredient Review Panel 1995). Pesticide incident data are not used for establishing dietary endpoints, but the chlorate incident data indicate that there is a concern for direct ingestion of chlorate formulations.

4.4.3 Chronic Reference Dose (cRfD)

A chronic study with sodium chlorate in rats has been completed in 2004 and reported in a draft form (NTP 2004). In this NTP study, groups of 50 male and 50 female F344 rats were exposed to drinking water containing 0, 125, 1,000, or 2,000 mg/L sodium chlorate for 2 years (equivalent to average daily doses of approximately 5, 35, and 75 mg/kg per day in male rats and 5, 45, and 95 mg/kg per day in female rats). Survival of exposed rats was similar to that of the control groups. Mean body weights of all exposed groups were similar to those of the control groups throughout the study. Water consumption by exposed rats was generally similar to that by controls throughout the study (14-17 g of water/male rat/day and 10.6-13.2 g of water/female rat/day). Serum concentrations of thyroxine (T_4) and triiodothyronine (T_3) were significantly reduced in 1,000 and 2,000 mg/L males and females on day 4 and in 2,000 mg/L males and females at week 3. Serum concentrations of thyroid stimulating hormone (TSH) were significantly increased in 1,000 and 2,000 mg/L males on day 4 and at week 3, in 1,000 and 2,000 mg/L females on day 4, in 2,000 mg/L females at week 3, and in 2,000 mg/L males and females at week 13. All special study rats in the 1,000 and 2,000 mg/L groups had thyroid gland follicular cell hypertrophy at 3 and 13 weeks. There were positive trends in the incidences of thyroid gland follicular cell carcinoma in male rats (0/47, 0/44, 0/43, 4/47) and of thyroid gland follicular cell adenoma or carcinoma (combined) in males (1/47, 0/44, 0/43, 6/47) and females (1/47, 0/47, 1/43, 4/46). The incidences of thyroid gland follicular cell hypertrophy were significantly increased in all exposed groups of males (4/47, 13/44, 33/43, 40/47) and in 1,000 and 2,000 mg/L females (3/47, 7/47, 27/43, 42/46). Thyroid gland focal follicle mineralization occurred in most 1,000 and 2,000 mg/L female rats (25/47, 26/47, 40/43, 44/46). The incidences of hematopoietic cell proliferation in the spleen of 2,000 mg/L males (2/48, 6/49, 4/49, 11/50) and bone marrow hyperplasia in 1,000 and 2,000 mg/L males (28/48, 35/48, 41/50, 40/49) were significantly greater than those in the controls. The **LOAEL** for non neoplastic effects derived from this study is 125 mg/L (5 mg/kg/day) based on increased thyroid gland follicular cell

hypertrophy and follicular cell mineralization. A **NOAEL** for non neoplastic effects cannot be derived from this study. Therefore a bench mark dose (BMD) analysis was performed and a BMDL of 28 mg/L as sodium chlorate (22 mg/L as chlorate) was obtained (See Memorandum from Becky Daiss to Abdallah Khasawinah, Jan. 26, 2005). This corresponds to 0.9 mg chlorate/kg/day oral dose. Using the BMDL as an approximation of the NOAEL, the oral RfD using a composite 30 X uncertainty factor (3X for interspecies and 10X for intraspecies) is:

$$\textbf{Chronic RfD} = \frac{0.9 \text{ mg/kg/day (BMDL)}}{30 \text{ (UF)}} = \textbf{0.03 mg/kg/day}$$

The usual interspecies uncertainty factor is 10X, but there are several important quantitative dynamic differences between rats and humans with respect to thyroid function that permit an interspecies factor of less than 10X for a thyroid toxicant like chlorate. The half-life of T4 in rats is approximately 12 hours, whereas in humans, the half-life is 5-9 days (Dohler et al., 1979). The shorter half-life in rats is likely related to a high-affinity binding globulin for thyroxin that is present in humans, but absent in rodents. Specifically, binding of the hormone to thyroxin binding globulin accounts for slower metabolic degradation and clearance in humans. Increased turnover and hepatic clearance of T3 and T4 renders the basal activity of the thyroid gland markedly more active in rats compared to humans. In the absence of a functional thyroid gland, a rat requires approximately 10-times more T4 than an adult human for full reconstitution (Dohler, et al., 1979). Constitutive TSH levels are nearly 25-times higher in rats than in humans, reflecting the increased activity of the thyroid-pituitary axis in rats (Dohler et al., 1979; McClain, 1992). Therefore, the 10X interspecies factor (which is subdivided into 3X for differences in toxicokinetics and 3X for differences in toxicodynamics) can be reduced to 3X based on dynamic considerations.

The BMDL of 0.9 mg/kg/day for chlorate based on thyroid effects in the rat, the most sensitive species for such an effect, will be protective of any other toxicity produced by chlorate.

4.4.4 Incidental Oral Exposure (short and intermediate durations: 1 day - 6 months)

There are three 90-day toxicity studies in rats available for selecting the endpoint to assess this exposure. In MRID 40444801, the NOAEL was 100 mg/kg/day based on hematological effects (hemoglobin concentration, hematocrit, RBC counts were statistically significantly decreased, and reticulocyte count was statistically significantly increased in females at 1000 mg/kg/day. In males, only the hematocrit was statistically significantly decreased. The adrenal weight was depressed in both males and females. In the McCauley *et al*, 1995 study, the NOAEL was 30 and 42 mg/kg/day (as chlorate) for males and females, respectively, based on the pituitary effects (vacuolization) and thyroid gland effects (colloid depletion), the body weight decrease and organ weight changes and reduction in erythrocyte counts and hemoglobin content at the LOAEL of 100 and 150 mg/kg/day in males and females, respectively. In the third study (Hooth *et al*, 2002), the NOAEL was 28 and 40 mg/kg/day in males and females, respectively, based on thyroid colloid

depletion and follicular cell hyperplasia, at 112 & 160 mg/kg/day for males and females, respectively. Based on these subchronic studies with sodium chlorate, an appropriate endpoint would be 30 mg/kg/day as chlorate (McCauley study). For the incidental oral exposure, the 30 mg/kg/day dose is appropriate for this risk assessment and is selected for the toxic endpoint with an MOE of 100.

4.4.5 Dermal Absorption

There are no dermal absorption studies available for sodium chlorate. Based on its high water solubility and ionic nature, sodium chlorate absorption by the intact skin is considered negligible.

4.4.6 Dermal Exposure (Short, Intermediate and Long Term)

There are no subchronic dermal toxicity studies available. Because sodium chlorate is unlikely to be absorbed by the skin, a risk assessment for dermal exposure is not needed.

4.4.7 Inhalation Exposure (Short and Intermediate Term)

There are no subacute or subchronic inhalation studies available for sodium chlorate. The toxic endpoint from the subchronic oral rat study discussed above with a NOAEL of 30 mg/kg/day is used for assessing the risks from the inhalation exposure to sodium chlorate and the 100% default absorption factor for using an oral dose is applied.

4.4.8 Margins of Exposure

The Margin of Exposure is 100 for all occupational and residential exposure scenarios.

4.4.9 Recommendation for Aggregate Exposure Risk Assessments

As per FQPA of 1996, when there are potential residential exposures to the pesticide, aggregate risk assessment must consider exposures from residues in food commodities and drinking water, as well as exposures arising from non-dietary sources (incidental oral, dermal and inhalation exposures) from the residential scenarios.

4.4.10 Classification of Carcinogenic Potential

A 2-year NTP bioassay to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been recently reported in a draft form (NTP, 2004). A final report of this study is expected during 2005. In these tests, there was some evidence of thyroid gland follicular cell carcinogenicity in male rats which may be attributed to changes of thyroid hormones (reduced T_3 and T_4 and elevated TSH) seen in these studies as a result of exposure to high doses of sodium chlorate. Current EPA HED policy states that "nonmutagenic pesticides that induce elevated levels of TSH and thyroid follicular cell tumors in the rat should be classified as **not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis**" (*Assessment of Thyroid Follicular Cell Tumors*; USEPA March 1998 EPA/630/R-97/002). In female mice there was equivocal and marginal evidence of increased pancreatic islet carcinoma.

Table 4.4. Summary of Toxicological Doses and Endpoints for Chlorate *per se* for Use in Human Risk Assessments for Inorganic Chlorates			
Exposure Scenario	**Dose (as chlorate) *per se* Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Chronic Dietary (all populations)	BMDL** =0.9 mg/kg/day UF = 30	1X	Chronic Study in rats (NTP, 2004). The **LOAEL**= 5 mg/kg/day based on increased thyroid gland follicular cell hypertrophy and follicular cell mineralization.
Incidental Oral Short-Term (1 - 30 days)	NOAEL =30 mg/kg/day MOE = 100	1X	Subchronic study in rats McCauley *et al*, 1995. Pituitary effects (vacuolization) and thyroid gland effects (colloid depletion), the body weight decrease and organ weight changes and reduction in erythrocyte counts and hemoglobin content at the LOAEL of 100 and 150 mg/kg/day in males and females, respectively
Incidental Oral Intermediate-Term (1 - 6 months)	NOAEL =30 mg/kg/day MOE = 100	1X	McCauley *et al*, 1995
Dermal all durations	Not required: dermal absorption is unlikely due to the ionic nature and water solubility of sodium chlorate		
Inhalation Short-Term (1 - 30 days)	NOAEL =30 mg/kg/day UF = 100	1X	McCauley *et al*, 1995
Inhalation Intermediate-Term (1 - 6 months)	NOAEL =30*** mg/kg/day UF = 100	1X	McCauley *et al*, 1995

Table 4.4. Summary of Toxicological Doses and Endpoints for Chlorate *per se* for Use in Human Risk Assessments for Inorganic Chlorates			
Exposure Scenario	**Dose (as chlorate) *per se* Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Cancer (oral, dermal, inhalation)	**Classification:** A 2-year NTP bioassay to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been recently reported in a draft form (NTP, 2004). A final report of this study is expected during 2005. There was some evidence of thyroid gland follicular cell carcinogenicity in male rats which may be attributed to the imbalance of thyroid hormones (reduced T_3 and T_4 and elevated TSH) seen in these studies as a result of exposure to high doses of sodium chlorate. Current EPA HED policy states that "nonmutagenic pesticides that induce elevated levels of TSH and thyroid follicular cell tumors in the rat should be classified as **not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis**" (*Assessment of Thyroid Follicular Cell Tumors*; USEPA March 1998 EPA/630/R-97/002). In female mice there was equivocal and marginal evidence of increased pancreatic islet carcinoma.		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = Margin of Exposure, LOC = level of concern, NA = Not Applicable

* Refer to Section 4.5

** A **NOAEL** was not identified in this study. Therefore a bench mark dose (BMD) analysis was performed and a BMDL of 28 mg sodium chlorate/L (22 mg chlorate/L) was calculated. This corresponds to 0.9 mg chlorate/kg/day oral dose.

*** A 100% absorption factor is used for using an oral endpoint of toxicity.

4.5 Endocrine disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor 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 recommendation 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 the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

The available toxicity studies on sodium chlorate, demonstrate the thyroid gland to be its target of toxicity.

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

5.0 Public Health Data

Sodium chlorate has been documented to cause irritation to skin, eyes, and mucous membranes of the upper respiratory tract. Death can occur from ingestion of substantial quantities, almost always due to suicide. **Doses in excess of 100 mg/kg are generally fatal to humans.**

5.1 Incident Reports

Available sources of incident data in humans were reviewed for the active ingredients Sodium Chlorate (073301) and Calcium Chlorate (073302). Data were available from the following sources: OPP Incident Data System (IDS) consisting of reports submitted to EPA by registrants, other federal and state health and environmental agencies and the public since 1992, Poison Control Centers (1993-2001), California Department of Pesticide Regulation for pesticide poisoning since 1982, National Pesticide Telecommunications Network (NPTN) for ranking of the top 200 active ingredients for which phone calls were received during calender years 1984-1991, and National Institute of Occupational Safety and Health's Sentinel Event Notification System for Occupational Risks (NIOSH SENSOR) from 1998-2002.

A total of 21 cases were located in Poison Control Center records from 1993 through 2001. Seven reported minor symptoms and two reported moderate medical outcomes, primarily due to dermal effects such as swelling and rash. It is difficult to draw any conclusions on such a small number of cases.

Detailed descriptions of 36 cases submitted to the California Pesticide Illness Surveillance Program (1982-2002) were reviewed. However, in just four of these cases was sodium chlorate determined to be the primary cause of illness and all four occurred in an agricultural setting (three in cotton fields, one unknown). Two of these cases were classified as systemic and one each involved skin or eye effects. The two systemic cases involved applicators; one with nausea and the other with nausea, headache, and itching skin after spraying for one week. Both of these cases were classified as possibly due to sodium chlorate. The skin case involved a worker exposed to drift from an adjacent field and the eye case occurred when a worker bumped into a spray nozzle while getting off the tractor and was splashed in the face. The skin case was classified as probably, and the eye case as definitely due to sodium chlorate.

5.2 Other

A number of suicidal ingestions of sodium chlorate have been reported in the literature. Many of these have led to death and were summarized by Clarkson (2001). The following is taken from Clarkson's review:

> ***Accidental and Intentional Poisoning*** *The majority of deaths caused by sodium chlorate have been the result of suicide (Mengele et al., 1969; Motin et al., 1970; Oliver et al., 1972; Timperman and Maes, 1966). The chance of ingesting a fatal dose accidentally is small unless the compound is mistaken for a drug and taken purposely, as*

occurred when the potassium salt mistakenly was substituted for potassium chloride (Cochran and Smith, 1940). However, completely typical, near-fatal poisoning occurred when a 13-year-old boy "tasted" crystals of this weed killer which he found in his father's shed. In spite of intensive treatment, recovery did not begin until about the 15th day and required a little over 40 days (Starvou et al., 1978).

Dermal absorption associated with agricultural use of sodium chlorate is not sufficient to cause systemic poisoning. Even by mouth, a large dose is required to produce illness. A 6.35% solution of potassium chlorate was long used as a gargle, or a 300-mg tablet was allowed to dissolve slowly in the mouth to treat pharyngitis before modern antibiotics became available. The toxicities of the sodium and potassium salts are similar. It was considered that a dose of 10,000 mg was fatal (Cochrane ad Smith, 1940; Sollman, 1957). The smallest recorded fatal dose was 7500 mg (Bernstein, 1930). However, vigorous treatment saved one person who had ingested about 40,000 mg (Knight et al., 1967).

6.0 Exposure Characterization/Assessment

6.1 Dietary Exposure/Risk Pathway

Dietary exposure (food only) to inorganic chlorates as the chlorate ion (ClO_3^-) may be expected from the following dietary exposure routes: (1) from sodium chlorate (073301) as an active ingredient in conventional (agricultural) pesticides used on food crops; (2) from sodium chlorate (873301) and potassium chlorate (900583) as inert ingredients in conventional pesticides used on food crops or in poultry premises; (3) from secondary residues in meat/milk/poultry/eggs due to residues in animal feedstuffs; (4) from sodium chlorate (873301) and calcium chlorate (875606) as inert ingredients in antimicrobial agents used as fruit, vegetable, and egg sanitizing washes, on mushrooms to control bacterial blotch, as treatments to seed used for sprouting, for conditioning live oysters, in poultry drinking water, in fish filleting, and in pecan cracking/dyeing; (5) as a potential redox of chlorine dioxide and sodium chlorite in conventional and antimicrobial pesticides; (6) from degradation of hypochlorites in antimicrobial agents used as fruit and vegetable washes; and, (7) from translocation of very small amounts of chlorate ion (ClO_3^-) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses.

No food monitoring data are available for this risk assessment; only limited, chemical-specific field trial data are available. Exposure estimates in food were based on field trial data or, in the case of fruit/vegetable/other washes, was derived from a film thickness model. No chemical-specific livestock metabolism or feeding data are available; exposure estimates in meat, milk, poultry, and eggs were derived from rat metabolism data, field trial data, and livestock reference information concerning feed consumption, tissue weights, and milk production. In some cases, due to raw data limitations, food exposure estimates are calculated as sodium chlorate. Default concentration factors (no chemical-specific processing data are available), percent crop treated data (chronic (non-cancer) and cancer assessments only), and the effects of washing after foliar treatments were also incorporated into the risk assessments.

6.1.1 Residue Profile

Sodium chlorate is currently registered for preharvest and foliar applications as a defoliant or desiccant to the following food/feed crops: dry beans, corn, cotton, flax, guar, chili peppers, potatoes, rice, safflower, sorghum (grain), southern peas (*i.e.*, cowpeas), soybeans, and sunflowers. For food/feed uses, sodium chlorate is formulated as a soluble concentrate (SC) with the active ingredient ranging from 18% to 47.2%. Sodium chlorate may be applied using aircraft or ground spray equipment, including high and low volume equipment.

Uses of sodium chlorate as a defoliant or desiccant on cauliflower, cucurbit vegetables, and okra grown for seed only are considered non-food uses. Uses of sodium chlorate on ornamental gourds and fallow lands are also considered non-food uses. These non-food uses will not be discussed further with regards to residue chemistry or dietary exposure/risk considerations.

Under 40 CFR 180.1020 (a) Sodium chlorate is exempt from the requirement of a tolerance for residues in or on the following raw agricultural commodities when used as a defoliant, desiccant, or fungicide in accordance with good agricultural practice: beans (dry, edible), corn (fodder), corn (forage), corn (grain), cottonseed, flaxseed, flax (straw), guar beans, peas (southern), peppers (chili), potatoes, rice, rice (straw), safflower (grain), sorghum (grain), sorghum (fodder), sorghum (forage), soybeans and sunflower seed.

Under 40 CFR 180.1020 (b) A time-limited exemption from the requirement of a tolerance is established for residues of the defoliant/desiccant in connection with use of the pesticide under section 18 emergency exemptions granted by EPA. This exemption has been granted for wheat and will expire on 12/31/04. As requested by the Registration Division (*Sodium Chlorate Use Closure Memo Amendment*; J. Guerry; dated 11/15/2004) the use of sodium chlorate on wheat is also addressed herein with the intention to convert the time-limited exemption status to a permanent exemption from the requirement of a tolerance under 40 CFR.1020 (a). The proposed use rate is for a single application of sodium chlorate to wheat at 6 lbs ai/A with a 3-day PHI.

No plant metabolism data have been submitted in support of the reregistration of sodium chlorate; however, no new plant metabolism data are required to support the established sodium chlorate tolerance exempts. Based on available published information (Loomis *et al.*, J. Am. Soc. Agron.; 25, 724 (1933)), sodium chlorate is highly soluble in water and is expected to readily absorb and translocate throughout plants. However, given the proposed use conditions, the means of translocation in treated plants may be substantially disrupted. Translocation of very small amounts of chlorate ion (ClO_3) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses may occur. Terminal residues are expected to be primarily surface residues.

Since sodium chlorate is a strong oxidizing agent, depending on environmental factors, it is expected to be easily reduced to chloride and possibly chlorite in plants. Total redox conversion to these reduced species is not expected; hence, the terminal residues of sodium chlorate in/on plants are likely chlorate (ClO_3), chlorite (ClO_2), and chloride (Cl).

No ruminant, swine, or poultry metabolism or feeding data have been submitted in support of the reregistration of sodium chlorate; however, no new animal metabolism data are required to support the established sodium chlorate exemptions from the requirement of a tolerance. Based on published rat metabolism data (Abdel-Rahman *et al*, 1982, 1984b and 1985), terminal residues of sodium chlorate in animal tissues are expected to be chlorate (ClO_3), chlorite (ClO_2), and chloride (Cl). Chlorate is readily absorbed from the digestive tract and is excreted as chlorate, chlorite, and chloride in urine primarily and feces. Within 72 hours, about 40% of the administered dose was excreted in the urine as chlorate (ca. 13%), chlorite (ca. 4%), and chloride (ca. 20%) and about 2-4% was excreted in the feces in the same time period. Less than 1% of the administered dose was found in any of the tissues analyzed including kidney, liver, and skin.

Although some previous residue chemistry reviews for specific exemptions from the requirement of a tolerance have concluded that there is no reasonable expectation of transfer of residues to meat, milk, poultry or eggs in specific cases, re-evaluation of the available crop field trial data taken as a whole, indicate that there is the possibility of detectable residues of sodium chlorate on animal feedstuffs at harvest. Hence, secondary residues of concern in meat, milk, poultry, and eggs are possible and; therefore, new ruminant and poultry feeding data are hereby required to support the reregistration of sodium chlorate. These data are considered confirmatory.

The analytical method used to support the established exemptions from the requirement of a tolerance is a non-specific colorimetric method (Branderis, J. Sci. Food Agric., 16, 558 (1965)), deemed acceptable for data collection. The method was originally developed to estimate residual chlorate concentrations in soil and as a rapid diagnostic test for chlorate toxicity in plants. Briefly, the method involves acid extraction, clean-up by shaking with activated charcoal, and filtration. A solution of ortho-toluidine in HCl is then added to the concentrated extract and the resulting color is measured at 448 nm for low concentrations and at 490 nm for higher concentrations of dye. The method is not specific for chlorate since it measures any oxidizing agent capable of oxidizing chloride ion to free chlorine. A standard curve is prepared with sodium chlorate for comparison. The lowest sensitivity of the method is estimated at 1 ppm based on available fortification data from field trials. Chloride does not interfere with the method but residues of chlorite, which might be present, may also be detected with this method. This method is hereby deemed adequate for enforcement of sodium chlorate exemptions from the requirement of a tolerance. [Note: If needed, a more selective HPLC method ("Determination of Residues of Sodium Chlorate in Potatoes", Method #S57023, 4/2/91) is available for the detection of sodium chlorate residues in or on raw agricultural commodities (RACs).]

New reference standards must be supplied to the EPA National Pesticide Standards Repository.

Only crop field trial data have been submitted to support the reregistration of sodium chlorate. No storage stability or processing data are available. The available crop field trial data have been re-evaluated herein. No additional plant magnitude of the residue or storage stability data are required to support the reregistration of sodium chlorate. Available crop field trial data deemed the primary sources of information to support the reregistration of sodium chlorate are briefly discussed below and summarized in Table C.5. All other available crop field trial data are considered supplemental and will not be discussed further.

The subject data, except the potato tuber data, were all collected using the colorimetric method (Branderis, J. Sci. Food Agric., 16, 558 (1965)), deemed acceptable for data collection and enforcement of the established sodium chlorate exemptions from the requirement of a tolerance. The potato tuber data were collected with a more selective HPLC method ("Determination of Residues of Sodium Chlorate in Potatoes", Method #S57023, 4/2/91) deemed adequate for data collection. The lowest limits of quantitation (LOQs) of these methods is estimated at 1 ppm.

Based on the available flax, guar, southern pea, soybean, and sunflower field trial data no detectable residues of sodium chlorate (<1 ppm) are expected in/on dry beans, guar beans, southern peas, soybeans, flaxseed, safflower seed, and sunflower seed at the point of harvest from the maximum use rate of sodium chlorate on dry beans, guar, southern peas, soybeans, flax, safflower, and sunflower (1 application; 7.5 lbs ai/A; 7-day PHI). Furthermore, no detectable residues of sodium chlorate (<1 ppm) are expected in/on cottonseed at the point of harvest from the maximum use rate of sodium chlorate on cotton (2 applications, 7.5 lbs ai/A/application; 7-day PHI). Any residues which might be detected at the point of harvest are expected to be primarily surface residues which would be substantially removed prior to the point of consumption.

Based on the available chili pepper field trial data, it is possible that detectable residues of sodium chlorate (ca. 13 ppm) might be found on the surface of unwashed chili peppers treated with sodium chlorate at the maximum use rate of sodium chlorate on chili peppers (1 application; 12.5 lbs ai/A/application; 10-day PHI). However, these residues are primarily surface residues present at the point of harvest which would be substantially removed by washing (<1 ppm) prior to the point of consumption.

Based on the available potato field trial data, no detectable residue of sodium chlorate (<1 ppm) are expected in/on potato tubers at the point of harvest from the maximum use rate of sodium chlorate on potatoes (1 application; 12.5 lbs ai/A; 7-day PHI). As demonstrated by the chili pepper field trial data, any residues present at harvest are expected to be primarily surface residues which would be substantially removed by washing prior to the point of consumption.

Based on the available oat, rice, sorghum, and wheat field trial data, it is possible that detectable residues of sodium chlorate (ca. 70 ppm (maximum) as demonstrated by sorghum grain) might be found on the surface of cereal grains retaining their outer hulls at harvest (such as oats and sorghum) from the maximum use rate of sodium chlorate on rice and sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) and wheat (1 application; 6 lbs ai/A; 3-day PHI). However, once the outer hulls are removed (either at harvest or during processing), no detectable residues of sodium chlorate (<1 ppm) are expected in/on cereal grains such as rice and wheat (as demonstrated by rice w/out hulls and wheat grain data).

Based on the available sorghum field trial data alone, **maximum** residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate for sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 70 ppm. On **average**, residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate on sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 40 ppm.

Translating the available sorghum field trial data to corn, residues of sodium chlorate are not expected to exceed 20 ppm (ca. 10 ppm on average) in/on corn grain at the point of harvest from the maximum use rate of sodium chlorate on corn (1 application, 7.5 lbs ai/A; 14-day PHI). As demonstrated by the chili pepper field trial data, any residues present at harvest are expected to be primarily surface residues which would be substantially removed by washing prior to the point of

consumption. Hence, residues of sodium chlorate in/on sweet corn after washing and prior to consumption would not be expected to exceed 1 ppm.

Based on the available straw (flax, oat, wheat, rice) and forage (guar plants, sorghum stalks, soybean forage) data, **maximum** residues of sodium chlorate in/on straw and forage livestock feedstuffs harvested 3-7 days after treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application) are not expected to exceed 300 ppm at the point of harvest. On **average**, residues in/on straw and forage livestock feedstuffs should not exceed 100 ppm when harvested 7-14 days after foliar treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application).

The highest average residues of chlorate (excluding percent crop treated data) in meat, poultry, and eggs are expected to be <4 ppm and in milk are expected to be <0.5 ppm based on the following information and assumptions:

- The highest average theoretical dietary burden for livestock is 175 ppm for cattle feed on a dry wt. basis
- Cattle eat a maximum of 9.1 kg of feed per day on a dry wt. basis (Update of Livestock Feed Consumption, 1993); hence, the highest average theoretical dietary exposure for sodium chlorate to livestock is 1600 mg per day
- Based on the available rat metabolism data, <1% of the initial dose of chlorate is expected to be incurred in animal tissues 72 hours after exposure (Abdel-Rahman *et al*, 1982, 1984b and 1985); hence <16 mg is expected to be incurred in any livestock tissue of interest
- Assuming that kidneys have the lowest weight of the organs/tissues of interest (other than milk) in livestock (*i.e.*, compared to meat, liver, fat, and eggs)
- Assuming that the average weight of cattle kidneys is about 4 kg (Update of Livestock Feed Consumption, 1993; cattle kidneys weigh 3.6-4.5 kg)
- Assuming that the average milk production per day is about 30 kg (Frank, 2002; milk production is 50-90 lb milk/cow/day)

Calculations:

$$\frac{\text{Highest Average Theoretical Dietary Exposure (1600 mg)} \times \text{Percent of Dietary Exposure Expected in Organs (< 1\%)}}{\text{Average Weight of the Organ/Tissue of Interest (Kidney at 4 Kg or Milk at 30 Kg)}}$$

Highest Average Residue Estimate in Meat, Poultry, and Eggs = <4 ppm
Highest Average Residue Estimate in Milk = <0.5 ppm

The maximum residues of chlorate (excluding percent crop treated data) in meat, poultry, and eggs are expected to be <12 ppm and in milk are expected to be <2 ppm based on the following information and assumptions:

- The maximum theoretical dietary burden for livestock is 500 ppm for cattle feed on a dry wt. basis
- Cattle eat a maximum of 9.1 kg of feed per day on a dry wt. basis (Update of Livestock Feed Consumption, 1993); hence, the highest average theoretical dietary exposure for sodium chlorate to livestock is 4600 mg per day
- Based on the available rat metabolism data, <1% of the initial dose of chlorate is expected to be incurred in animal tissues 72 hours after exposure (Abdel-Rahman *et al*, 1982, 1984b and 1985); hence <46 mg is expected to be incurred in any livestock tissue of interest
- Assuming that kidneys have the lowest weight of the organs/tissues of interest (other than milk) in livestock (*i.e.*, compared to meat, liver, fat, and eggs)
- Assuming that the average weight of cattle kidneys is about 4 kg (Update of Livestock Feed Consumption, 1993; cattle kidneys weigh 3.6-4.5 kg)
- Assuming that the average milk production per day is about 30 kg (Frank, 2002; milk production is 50-90 lb milk/cow/day)

Calculations:

$$\frac{\text{(Maximum Theoretical Dietary Exposure (4600 mg) x Percent of Dietary Exposure Expected in Organs (< 1\%)}}{\text{Average Weight of the Organ/Tissue of Interest (Kidney at 4 Kg or Milk at 30 Kg)}}$$

Maximum Residue Estimate in Meat, Poultry, and Eggs = <12 ppm
Maximum Residue Estimate in Milk = <2 ppm

6.1.2 Chronic (non-cancer) Dietary (food only) Exposure and Risk

A chronic (non-cancer) dietary risk assessment was conducted for all potential chlorate dietary exposure routes, using the Dietary Exposure Evaluation Model-FCID™ software with the Food Commodity Intake Database (DEEM-FCID™ Version 2.03) and food consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. In this analysis the chronic dietary exposure and risk estimates resulting from food intake were determined for the general U.S. population and various population subgroups.

No food monitoring data are available for this risk assessment; only limited, chemical-specific field trial data are available. Exposure estimates in food were based on field trial data or, in the case of fruit/vegetable/other washes, was derived from a film thickness model. No chemical-specific livestock metabolism or feeding data are available; exposure estimates in meat, milk, poultry, and eggs were derived from rat metabolism data, field trial data, and livestock reference information concerning feed consumption, tissue weights, and milk production. In some cases, due to raw data limitations, food exposure estimates are calculated as sodium chlorate. Default concentration factors (no chemical-specific processing data are available) and the effects of washing after foliar treatments were also incorporated into the risk assessment. Percent crop treated data were used in this analysis. Exposures were single point estimates.

The chronic (non-cancer) dietary (food only) risk assessment is below the Agency's level of concern for the General U.S. Population and all subgroups. The highest exposed population subgroup, Children 1-2 years of age, was 28% of the chronic Population Adjusted Dose (cPAD). See Table 6.1.2 below for details.

Table 6.1.2. Summary of Chronic (non-cancer) Dietary (food only) Exposure and Risk for Inorganic Chlorates

Population Subgroup	cPAD [a] mg/kg/day	% cPAD
General U.S. Population	0.03	9
All Infants (< 1 yr)		15
Children 1-2 yrs		28
Children 3-5 yrs		23
Children 6-12 yrs		14
Youth 13-19 yrs		8
Adults 20-49 yrs		7
Adults 50+ yrs		6
Females 13-49 yrs		7

[a] The BMDL is 0.9 mg chlorate/kg/day. The level of concern for the Margin of Exposure (MOE) is 30.

6.1.3 Cancer Dietary (food only) Exposure and Risk

A cancer dietary risk assessment was conducted for all potential chlorate dietary exposure routes, using the same dietary (food only) exposure estimates used in the chronic (non-cancer) dietary risk assessment for the U. S. Population, with a 9% cPAD.

Note: Sodium chlorate is a thyroid toxicant producing thyroid gland follicular cell hypertrophy in rats and mice following chronic exposures and some evidence of follicular cell tumors in rats. The lack of mutagenicity indicates that the thyroid tumors are induced by a non-mutagenic mechanism. Therefore, for the purposes of this risk assessment, the Margin of Exposure (MOE) approach is used to estimate inorganic chlorate cancer risk. Children are not expected to be more susceptible to chlorate-induced thyroid effects than adults and the endpoint selected for the thyroid effects is protective for all populations, including children.

6.2 Water Exposure/Risk Pathway

6.2.1 Environmental Fate

Sodium chlorate is used as a desiccant/defoliant because it is a strong oxidizer. As a strong oxidizing agent, chlorate (ClO_3^-, oxidation state V) gets reduced to chlorine species in lower oxidation states, such as the oxyanions chlorite (ClO_2^-, oxidation state III) and hypochlorite (ClO^-, oxidation state I), chlorine dioxide (oxidation state IV), and chloride (oxidation state -I). Thus, at least some and possibly substantial reduction of the applied chlorate is likely to occur in the field prior to any runoff to surface water. Under environmental (terrestrial field) redox conditions and based on chemical equilibria alone, the thermodynamically favored, end reduction product of chlorate in soil and in water is the chloride anion. Any intermediate chlorine dioxide that may form under environmental conditions will undergo photochemical reactions when exposed to sunlight. The chlorine oxyanions chlorite and hypochlorite (other possible more reduced intermediates in the ultimate reduction of chlorate to chloride) are strong oxidizers in themselves and thus, they are also reduced and/or undergo disproportionation reactions. Although reduction reactions of chlorate, chlorite, and hypochlorite are said to occur "very fast", how fast they occur is not known (*i.e.*, the actual rate constants in the environment are not known). Therefore, at any given time the distribution of reduced species (type and concentration) cannot be estimated. However, it is unlikely that a single reduced species would be present.

6.2.2 Drinking Water

6.2.2.1 Sources and Control of Chlorate Ion

Chlorate ion (ClO_3^-) is primarily present in drinking water as a result of the use of chlorine dioxide or hypochlorite solutions for oxidation/disinfection in the treatment process. It may also be present in the untreated source water, but the ClO_3^- concentrations contributed to drinking water by ambient water are generally much lower than those resulting from the treatment process.

The American Water Works Association (AWWA) Disinfection Systems Committee tracks disinfection practices in US community water systems. Their most recent comprehensive survey (completed in 1998) estimated that approximately 20% of the systems serving populations greater than 10,000 use sodium hypochlorite (2% generated it on-site), 8% use chlorine dioxide, and <1% use calcium hypochlorite. (AWWA, 2000a) For systems serving populations less than 10,000, the survey estimated that approximately 34% use sodium hypochlorite, none use chlorine dioxide, and at least 4.5% use calcium hypochlorite. (AWWA, 2000b)

Chlorine Dioxide: The use of chlorine dioxide can introduce ClO_3^- into the finished water by several routes. Drinking water plants generally use sodium chlorite as a starting material in the production of chlorine dioxide. Chlorate ion may be present as a contaminant in the feedstock material (usually less than four percent of the active chlorite is chlorate). A typical range of ClO_3^- carryover to the finished water from chlorite feedstock contamination is about 50 µg/L for a 1-mg/L dose of chlorine dioxide. (Gates, 1998) Technology to generate chlorine dioxide using sodium chlorate is now available to the drinking water industry, which introduces the possibility of ClO_3^- carryover to the finished water from the chlorate feedstock.

Chlorate ion may also be produced due to inefficient generation of chlorine dioxide. Excess chlorine will favor the production of ClO_3^- over chlorine dioxide, as will keeping the generator mixtures at highly alkaline (pH > 11) or acidic (pH < 3) conditions. If the concentrations of feedstock reactants are too low or too much dilution water is added during the reaction, ClO_3^- formation is also favored.

Chlorite ion (ClO_2^-) is a major degradation product resulting from the reaction of chlorine dioxide with inorganic and organic constituents in the water. When free chlorine is used after the application of chlorine dioxide in the treatment process, ClO_2^- is oxidized to ClO_3^-. This conversion will continue over time as the water travels through the distribution system. Chlorate ion is also formed by photodecomposition of chlorine dioxide when treated water is exposed to bright sunlight in open basins.

The primary ways in which water systems can control the levels of ClO_3^- in the finished water is through high efficiency operation of their chlorine dioxide generators and by reducing ClO_2^- concentrations prior to the addition of free chlorine. Careful control of the generation process minimizes ClO_3^- formation. Ferrous ion, which is a coagulant aid, can be used to convert ClO_2^- to chloride ion and thus prevent it from reacting with free chlorine to form ClO_3^-.

Hypochlorite: Some water systems use sodium hypochlorite or calcium hypochlorite as their source of free chlorine. Chlorate ion can be formed in these products during the manufacturing process, but the decomposition of hypochlorite solutions during storage is the more significant source of ClO_3^- in systems using hypochlorite. Sodium hypochlorite is usually purchased as a solution, and ClO_3^- concentrations increase between the time of manufacture and delivery to the water plant. Calcium hypochlorite is a solid, and thus ClO_3^- concentrations don't increase until calcium hypochlorite solutions are prepared for use at the water treatment plant.

The rate at which hypochlorite ion (OCl^-) disproportionates to ClO_3^- is influenced by concentration of OCl^-, pH, and temperature. The rate of decomposition increases as the concentration of OCl^- increases, so water systems can use dilution as one control strategy. The pH should be in the 12 to 13 range to minimize decomposition; a pH below 11 greatly increases the rate of decomposition. Hypochlorite solutions should be protected from high temperatures and sunlight. Storage time should be minimized; both from the time of manufacture to delivery and from the time of delivery to use.

6.2.2.2 Chlorate Ion Occurrence Data

Data on the occurrence of ClO_3^- in drinking water are available from two primary sources: the Information Collection Rule (ICR) Auxiliary 1 Database, Version 5.0 (USEPA, 2000) and the AwwaRF research study on the control of ClO_3^- in hypochlorite solutions (Gordon et al, 1995).

Information Collection Rule: The most extensive data on the occurrence of ClO_3^- in drinking water is from the ICR (USEPA, 1996). Source water and drinking water were monitored for ClO_3^- between July 1997 and December 1998. Water systems serving a population of at least 100,000 were required to monitor for ClO_3^- at treatment plants using chlorine dioxide or hypochlorite solutions in the treatment process. Plants using chlorine dioxide collected monthly samples of the source water entering the plant, the finished water leaving the plant, and at three sample points in the distribution system (near the first customer, an average residence time and a maximum residence time). Plants using hypochlorite solutions were only required to collect quarterly samples of the water entering and leaving the plant. If chlorine dioxide or hypochlorite solutions were used intermittently at a plant, ClO_3^- samples were only required in sample periods in which they were in use.

Chlorine dioxide was used by 22 water systems (29 treatment plants) during at least one of the 18 monthly ICR sampling periods. Data from 413 samples collected at the entry point to the distribution system showed ClO_3^- concentrations ranging from < 20 µg/L to 1,600 µg/L. The ClO_3^- concentrations ranged from < 20 µg/L to 2,200 µg/L in the 1084 samples collected in the distribution system. The distribution of average ClO_3^- concentrations calculated for each treatment plant and sample point are summarized in Table 6.2.2.2.1. The distribution system average concentrations determined for each water plant by averaging the data from the three distribution system sample points are summarized in the last column of Table 6.2.2.2.1. The median distribution system average concentration is 129 µg/L with a range from < 20 µg/L to 691 µg/L.

Sodium hypochlorite solutions were in use in 44 water systems (61 treatment plants) during the six quarterly ICR sampling periods. (None of the systems reported using calcium hypochlorite as the source of their chlorine solutions.) Data from 312 samples were reported with concentrations ranging from < 20 µg/L to a maximum of 1,400 µg/L. The average ClO_3 concentration in the finished drinking water for each treatment plant ranged from < 20 µg/L to 502 µg/L with a median concentration of 99 µg/L. The table below summarizes the distribution of average ClO_3 concentrations calculated for each plant.

Table 6.2.2.2.1. Chlorate Concentrations[1] (µg/L) - ICR Data

	Hypochlorite Plants	Chlorine Dioxide Plants	Combined Hypochlorite and Chlorine Dioxide Plants
10th Percentile	23	56	24
20th Percentile	37	77	53
50th Percentile	99	119	108
80th Percentile	155	195	179
90th Percentile	239	226	242
Maximum	502	687	691
# WTPs	61	29	90
# PWSs	44	22	66

[1]The average chlorate concentration was calculated for each sample point at each water treatment plant (WTP) over the entire ICR monitoring program. The distribution of these averages is presented in this table.
[2]The distribution system average chlorate concentration was calculated for each WTP using the three distribution system sample points. The distribution of these averages is presented in this column.

AwwaRF Hypochlorite Project: The American Water Works Association Research Foundation sponsored a project to study how water systems could minimize ClO_3 formation in the hypochlorite solutions they use for disinfection. As part of the data gathering effort, they obtained information from 185 water systems concerning their use of hypochlorite solutions. Samples of source water, hypochlorite solution, and finished drinking water from 111 of the water systems were analyzed for ClO_3 . Only one set of samples was collected for each system.

Background information on the subset of 111 water systems that provided samples was not reported separately from the 185 systems who answered the questionnaire. Therefore, the ClO_3

concentrations cannot be directly related to the size of the water system or type of hypochlorite solution in use. However, 73.5 % of the systems who responded to the questionnaire served populations less than 100,000 with a subset of 66% serving populations less than 10,000. There is a possibility that a few systems using calcium hypochlorite were sampled in the AwwaRF project, since 13% of the 185 systems reported using calcium hypochlorite and 85% reported using sodium hypochlorite.

The ClO_3^- concentrations reported in the finished water are summarized in Table 2. The median concentration in the finished water is 161 µg/L. The distribution of ClO_3^- is shown below in Table 6.2.2.2.2. The ClO_3^- concentrations in the hypochlorite solutions used to treat the water ranged from 0.03 to 113 g/L.

Table 6.2.2.2.2. Chlorate Concentrations - AwwaRF Project (PWSs using Hypochlorite Solutions)[1]

	Finished Water Chlorate Concentration (µg/L)
Minimum	<10
10th Percentile	15
20th Percentile	41
50th Percentile	161
80th Percentile	611
90th Percentile	1,160
Max	9,180
# PWSs	111
# States	13

[1] A single sample was collected from each of the public water systems (PWSs) in the survey.

6.2.2.3 Chronic Exposure to Chlorate Ion

The ICR data were collected from systems suspected of having ClO_3^- contamination due to the treatment process in use. It is reasonable to assume that there were not significant ClO_3^- levels in the systems in the same size category that were not sampled. This is based on earlier drinking water studies that found ClO_3^- concentrations in source water were too low to impact the levels in drinking water on the same scale as treating the water with either chlorine dioxide or hypochlorite (Bolyard et al, 1993).

The ICR data confirm the presence of ClO_3^- in source water (75 of 744 samples of water entering the treatment plants contained measurable ClO_3^-), but also demonstrate that the concentrations are generally very low, can vary considerably over time at the same sample site, and are minor compared to those observed from chlorine dioxide or hypochlorite use. Data were reported from 105 treatment plant influent sample points in the ICR and samples from 33 of those sites contained ClO_3^- concentrations of 20 µg/L or greater. Chlorate concentrations were reported in influent samples from both surface and ground water sources. Samples from fifteen of the 33 sites contained measurable ClO_3^- in more than one sampling period, but with one exception, the concentrations were all ≤120 µg/L; 70% were between 20 and 50 µg/L. One influent water had a ClO_3^- concentration of 944 µg/L in one sample period, but the concentrations were ≤ 100 µg/L in the other sample periods. Three influent waters contained a high ClO_3^- concentration (1,300 to 1,600 µg/L) in one sample period and none in the other sample periods. The ICR data indicate that the influence of source water ClO_3^- (as reflected by the influent samples) on the concentrations in finished drinking water is minimal compared to the contribution from using chlorine dioxide or hypochlorite solutions in the treatment process.

The ICR data set provides the best available estimate of long term exposure to ClO_3^- from drinking water, because multiple samples were collected over an 18 month period. Only systems serving populations of at least 100,000 were sampled during the ICR. Even though this size category includes roughly one percent of the total number of drinking water systems in the United States, it serves almost 60 percent of the population. During the ICR, there were 296 water systems in this size category; 7% used chlorine dioxide and 15% used hypochlorite solutions.

When chlorine dioxide is the source of ClO_3^- in drinking water, it is appropriate to use the average concentration in the distribution system to estimate exposure. This is because the concentration is expected to change within the system due to the conversion of ClO_2 to ClO_3^- in the presence of chlorine. Fifty percent of the chlorine dioxide plants had average distribution system ClO_3^- concentrations of ≤129 µg/L. Ninety percent had concentrations ≤264 µg/L.

The average ClO_3^- concentration at the entry point to the distribution system can be used to estimate exposure when hypochlorite solutions are the source of the ClO_3^- contamination. No additional ClO_3^- is expected to be formed in the distribution system. Fifty percent of the plants using hypochlorite solutions had finished water ClO_3^- concentrations of ≤99 µg/L. Ninety percent had concentrations ≤239 µg/L.

The AwwaRF data set is much smaller than the ICR data set, because the 111 systems from 13 states were only sampled once. Low levels of ClO_3^- were measured in almost 20% of the source waters with 90 percent of the samples having concentrations less than 35 µg/L. (Over 30% of the source waters sampled during the ICR contained measurable concentrations of ClO_3^- with 90 percent having concentrations less than 23 µg/L.) The finished water ClO_3^- concentrations measured in the AwwaRF study are generally higher than those observed in the ICR. This difference could be the result of a number of factors such as: 1) The AwwaRF data represents a single point in time while the ICR data reflects an average over 18 months; 2) Most of the

AwwaRF samples were collected from utilities that served population of less than 100,000, while all of the ICR samples were from utilities serving at least 100,000; and 3) Hypochlorite treatment practices may have changed between when the AwwaRF samples were collected (1993) and the ICR samples were collected (1997-98).

Section 6.2.2.1 explains the mode of conversion of hypochlorite ion (OCl^-) to ClO_3^- for systems using hypochlorite as their source of free chlorine. The conversion is influenced by the solution concentration, pH, and ambient temperature. For systems using chlorine dioxide, ClO_3^- level in the finished water depends on concentration of chlorate ion in the feedstock, the efficiency of chlorine dioxide generation, and subsequent disinfection techniques. Awareness of these factors is critical in controlling chlorate concentrations in finished water. Smaller systems using chlorine dioxide or hypochlorite, those serving fewer than 100,000, may be more likely to have finished water with higher levels of chlorate due to smaller budgets and, consequently, fewer resources to devote to running their systems or training their staff. An untrained staff may not know, for example, that when free chlorine is used after the application of chlorine dioxide, that ClO_2^- is oxidized to ClO_3^-.

Both the AwwaRF study and the ICR data reveal high concentrations of chlorate ion to be a local problem affecting a relatively small number of systems. Section 6.2.2.1 outlines simple measures that systems of any size can use to maintain low levels of chlorate ion in finished drinking water.

6.2.2.4. Estimated Concentrations of Chlorate Ion Deemed Appropriate for Inclusion in the Dietary Risk Assessment(s)

Based on the available occurrence data (essentially at the tap) from the ICR AUX1 Database (USEPA, 2000d) and the AwwaRF (1995) survey study, which are discussed above, the following estimated concentrations of chlorate ion (ClO_3^-) in drinking water are deemed appropriate for inclusion in the dietary risk assessment for inorganic chlorates:

- The highest annual average concentration of chlorate ion (ClO_3^-) in drinking water is estimated at 0.69 mg/L and is based on the ICR AUX1 Database (USEPA, 2000d).
- The 90th percentile average concentration of chlorate ion (ClO_3^-) in drinking water is estimated at 0.24 mg/L and is based on the ICR AUX1 Database (USEPA, 2000d).
- The treatment system median average concentration of chlorate ion (ClO_3^-) in drinking water in tested large treatment systems is estimated at 0.11 mg/L and is based on the ICR AUX1 Database (USEPA, 2000d).

Use of the ICR AUX1 database could underestimate concentrations in drinking water since higher levels of chlorate ion (ClO_3^-) in drinking water were found at the small water treatment utilities sampled in the AwwaRF (1995) project than at the large water treatment plants included in the ICR AUX1 Database (USEPA, 2000d). However, the AwwaRF (1995) survey study is a less robust data set consisting of only one sample per utility and, therefore, the ICR AUX1 Database

(USEPA, 2000d) was considered the more appropriate source for estimating averages from individual water treatment plants.

Chronic (non-cancer) dietary and cancer dietary risk assessments for water only were conducted using the Dietary Exposure Evaluation Model-FCID™ software with the Food Commodity Intake Database (DEEM-FCID™ Version 2.03) and food and water consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. Available ICR and AwwaRF monitoring data were used to estimate chlorate concentrations in drinking water. Exposures were single point estimates.

The chronic (non-cancer) dietary risk assessment for chlorate in drinking water (highest annual average concentration estimated at 0.69 mg/L) is below the Agency's level of concern for the General U.S. Population and all subgroups, except all infants (< 1 year of age). The highest exposed population subgroup, all infants <1 year of age, was 159% of the chronic Population Adjusted Dose (cPAD). See Table 6.2.2.4 below for details.

Table 6.2.2.4. Summary of Estimated Chronic (non-cancer and cancer) Dietary (water only) Exposure and Risk for Inorganic Chlorates by Average Annual Concentration in Large Drinking Water Systems[a]

Population Subgroup[b]	cPAD mg/kg/day[c]	% cPAD		
		Water Estimated at the Highest Annual Average (0.69 mg/L)	Water Estimated at the 90th Percentile Annual Average (0.24 mg/L)	Water Estimated at the Median Annual Average (0.11 mg/L)
General U.S. Population	0.03	49	17	8
All Infants (< 1 yr)		**159**	**55**	**25**
Children 1-2 yrs		72	25	12
Children 3-5 yrs		67	23	11
Children 6-12 yrs		47	16	7
Youth 13-19 yrs		35	12	6
Adults 20-49 yrs		45	16	7
Adults 50+ yrs		48	17	8
Females 13-49 yrs		45	16	7

[a] The estimated exposures and risks are based on the ICR data (multiple data points per water system). Higher concentrations of chlorate ion (ClO_3^-) in drinking water were reported in the AwwaRF data set (only a single data point per water system), which sampled smaller water systems.
[b] The values for the population with the highest risk for each type of risk assessment are bolded.
[C] The BMDL is 0.9 mg chlorate/kg/day. The level of concern for the Margin of Exposure (MOE) is 30.

The Office of Water characterizes the population included in the ICR data as follows:

- "EPA collected data required by the Information Collection Rule (ICR) to support future regulation of microbial contaminants, disinfectants, and disinfection byproducts. The systems represented in the ICR database serve 60% of the US population.
- "Included in the ICR are levels of chlorate ion concentrations in the finished water of these systems. The agency's level of concern for chlorate ion is 370 ppb. During the ICR, four water treatment plants had average chlorate ion levels above the agency's level of concern and represented 0.5% of the ICR population (621,000 persons).
- "One treatment plant serving 218,000 persons had average chlorate ion concentrations of 0.69 mg/L. This corresponds to 0.17% of the ICR population; 98 percent of this ICR population received finished water with average chlorate ion concentrations at or below 0.2 mg/L; 93 percent received finished water with average chlorate ion concentration at or below 0.1 mg/L; and over 99 percent receives finished water below the Agency's level of concern of 0.37 mg/L.
- "1 percent of the ICR population (1,260,000 persons) is exposed to chlorate concentrations at or greater than the 90th percentile concentration of 0.24 mg/L, while, 6.5 percent (8,490,000 persons) is exposed to chlorate concentrations at or greater than the median concentration of 0.11 mg/L.
- "The best way for these systems to lower the level of chlorate ion in their finished water is to implement the simple measures explained above."

No separate cancer dietary risk assessment for chlorate in drinking water (lifetime average concentration estimated at 0.1 mg/L) was conducted. The cancer dietary risk assessment is based on the chronic (non-cancer) dietary risk assessment for the General U.S. Population The cancer dietary risk assessment for chlorate in drinking water is below the Agency's level of concern (*i.e.*, % cPAD less than 100).

6.3 Residential (Non-Occupational) Exposure/Risk Pathway - Conventional Pesticides

All residential (non-occupational) risk estimates for inorganic chlorates, as active or inert ingredients in conventional pesticide products used in residential environments, are below the Agency's level of concern (*i.e.*, Margin of Exposures (MOEs) are greater than the Level of Concern (LOC) of 100). These uses are considered to be short-term only due to the episodic uses associated with homeowner products. Since the episodic nature of residential exposure is inconsistent with the mechanism of chlorate carcinogenicity, a residential cancer risk assessment was not conducted.

6.3.1 Home Uses

6.3.1.1 Sodium Chlorate (073301) as an active ingredient in conventional pesticide products - Short-Term Residential Handler Exposure *via* Inhalation Route only

There is the potential for exposure to sodium chlorate by residential handlers in outdoor residential settings during the application of conventional pesticide products containing sodium chlorate (073301) as the active ingredient. Sodium chlorate (073301) can be used as a non-selective herbicide in outdoor residential environments as a spot treatment or edging treatment around patios, along fence lines, lawn edges, around foundations, underneath or around wood decks, and in cracks and crevices of driveways. Residential handler exposure scenarios are considered to be short-term only due to the episodic uses associated with homeowner products. Although there is the potential for dermal exposure by residential handlers, sodium chlorate is an inorganic salt, therefore, significant absorption of sodium chlorate through intact skin is not expected. Hence, a short-term risk assessment for residential handlers *via* the inhalation exposure route was conducted for sodium chlorate as the active ingredient in conventional pesticide products.

Although there is the potential for exposure to sodium chlorate in outdoor residential settings from entering areas previously treated with sodium chlorate (073301), as the active ingredient in conventional pesticide products, a residential postapplication exposure risk assessment for sodium chlorate was not conducted because:

- Although there is the potential for postapplication dermal exposure in residential settings, sodium chlorate is an inorganic salt, therefore, significant dermal absorption of sodium chlorate through intact skin is not expected.
- Postapplication inhalation exposure for sodium chlorate is not expected due to negligible vapor pressure.
- Postapplication exposure assessments for residential settings are not typically performed for spot treatments.

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessment. Each assumption and factor is detailed below. In addition to these factors,

unit exposures were used to calculate risk estimates. Unit exposures were taken from PHED, ORETF studies, and one proprietary study. [Note: Several of the assumptions and factors used for the assessment are similar to those used in the occupational assessment presented under Section 9.1. As such, only factors that are unique to the residential scenarios are presented here.] The assumptions and factors used in the risk calculations include:

- Due to the lack of chemical specific data, exposures from a scenario deemed similar might be used. As an example, mixer/loader/applicator data for hose-end sprayers were used to assess sprinkler can applications. These application methods are believed to be similar enough to bridge the data.

- HED always considers the maximum application rates allowed by labels in its risk assessments. If additional information such as average or typical rates are available, these values also may be used to allow risk managers to make a more informed risk management decision.

- Residential risk assessments are based on estimates of what homeowners would typically treat, such as the size of a lawn, or the size of a garden. The factors used for the sodium chlorate assessment were from the Health Effects Division Science Advisory Council for Exposure *Policy 12: Recommended Revisions To The Standard Operating Procedures For Residential Exposure Assessment* which was completed on February 22, 2001 and on professional judgement. The daily volumes handled and area treated, used in each residential scenario, include:

    - 1000 square feet when mixing/loading/applying liquids as a spot treatment with a low-pressure handwand and sprinkler cans;
    - 1 gallon when applying with a RTU sprinkler can and trigger pump sprayer; and,
    - 1000 square feet for granular formulation spot treatments.

Short-term risks for residential handlers *via* the inhalation exposure route are presented below in Table 6.3.1.1. All risks are below the Agency's level of concern (*i.e*, Margin of Exposures (MOEs) are greater than the Level of Concern (LOC) of 100). The scenarios assessed represent worse-case exposures and risks. It should also be noted that there were many other scenarios where medium to low PHED quality data were used to complete the assessment. Data quality should be considered in the interpretation of the uncertainties associated with each risk value presented.

Table 6.3.1.1. Sodium Chlorate (073301) - Short Term Residential Inhalation Exposure[1]				
Exposure Scenario (Scenario #)	**Daily Area Treated[2]**	**Crop/Target[3]**	**Application Rate[4]**	**Inhalation MOE[5]**
Mixer/Loader/Applicators, Loader/Applicators, & Applicators				
M/L/A liquids with a Low Pressure Handwand Sprayer (1)	1000	Spot/edging treatment	23.7	3000
L/A RTU liquid with a Trigger Pump Sprayer (2)	1	Spot/edging treatment	0.196	87000
M/L/A liquids with a Sprinkler Can (3)	1000	Spot/edging treatment	23.7	5200
Applying liquid with a RTU Sprinkler Can (4)	1	Spot/edging treatment	0.27	710000
Applying granules by Hand (5)	1000	Spot/edging treatment	12	370
L/A granules with a Belly Grinder (6)	1000	Spot/edging treatment	12	2800
L/A granules with a Push-type Spreader (7)	1000	Spot/edging treatment	12	200000

[1] Residential exposures assessments do not include PPE.
[2] Amount treated is presented in ft^2/day, except for Scenario #s 2 and 4 which are presented in gallons/day. (Standard EPA/OPP/HED values).
[3] Crops and use patterns are from label extractions (Appendix 1), BEAD's LUIS reports, and the Sodium Chlorate Use Closure Memo (J. Guerry, 8/5/04; 10/13/04; 11/15/04).
[4] Ranges of application rates are based on values from label extractions (Appendix 1), BEAD's LUIS reports, and the Sodium Chlorate Use Closure Memo (J. Guerry, 8/5/04; 10/13/04; 11/15/04). Application rates upon which the analysis is based are presented as lb ai/1000 ft^2, except for Scenario #s 2 and 4 which are presented in lb ai/gallon.
[5] Inhalation MOE = Oral NOAEL (30 mg/kg/day) / Daily Inhalation Dose. HED LOC for MOE is 100.

6.3.1.2 Sodium Chlorate (873301) as an inert ingredient in conventional pesticide products - Short-Term Residential Postapplication Exposure *via* Incidental Oral Route only

There is the potential for postapplication exposure in outdoor residential settings from entering areas previously treated with conventional pesticide products containing sodium chlorate (873301) as an inert ingredient. Hence, a residential postapplication risk assessment was conducted. However, since these products are professionally applied, residential handler exposure is not of concern.

Sodium chlorate (873301) as an inert ingredient in herbicide formulation products can be applied professionally to residential sites. These conventional pesticide products contain < 1 % sodium chlorate and can be applied at rates no greater than 0.07 lb (as sodium chlorate) per acre.

As an inert ingredient in herbicide formulations broadcast on residential sites, there is potential for children to have incidental oral exposures (hand-to-mouth (HTM), object-to-mouth(OTM), and soil ingestion (SI)); however, residential postapplication exposures *via* dermal and inhalation routes are not of concern because:

- Although there is the potential for postapplication dermal exposure in residential settings, sodium chlorate is an inorganic salt, therefore, significant dermal absorption of sodium chlorate through intact skin is not expected.

- Postapplication inhalation exposure for sodium chlorate is not expected due to negligible vapor pressure.

A series of assumptions and exposure factors served as the basis for completing the residential postapplication risk assessments. Each assumption and factor is detailed below.

- Residential exposure and risk estimates are conducted assuming no personal protective equipment (*i.e.*, short-sleeved shirt, shorts, shoes/socks, and no respirator).
- Residential postapplication exposures are assessed on the day of pesticide application.
- 15 kg represents the body weight of a toddler (3 year old).
- 5% of the application rate has been used to calculate the day-zero residue levels used for assessing risks from HTM behaviors.
- 20% of the application rate has been used to calculate the day-zero residue levels used for assessing risks from OTM behaviors.
- 100% of the application rate has been used to calculate the day-zero soil residue levels used for assessing risks from SI.
- Hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm^2 representing the palmar surfaces of three fingers;
- 50% saliva extraction factor for HTM exposures.
- OTM exposures are based on a 25 cm^2 surface area.
- Exposure durations are expected to be 2 hours.

- Soil residues are contained in the top 1 centimeter and soil density is 0.67 cm^3/gram.

Table 6.3.1.2 below shows the risk estimates for incidental oral exposures to sodium chlorate (877301) for children playing in treated areas following its application.

Table 6.3.1.2. Short-term Residential Postapplication Risk Estimates for Sodium Chlorate (873301)

Population Subgroup	Scenario	Route	MOE	Combined MOE
Child	Hand-to-Mouth	Oral	29000	23000
	Object-to-Mouth	Oral	110000	
	Soil Ingestion	Oral	8600000	

6.3.2 Recreational Uses

Recreational exposures are expected to be similar to, or in many cases, less than, those evaluated in Section 6.3.1 Home Uses; therefore, a separate recreational exposure assessment was not conducted.

6.3.3 Other (Spray Drift, etc.)

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for sodium chlorate. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. On a chemical by chemical basis, the Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift with specific products with significant risks associated with drift.

7.0 Aggregate Risk Assessments and Risk Characterization

Evaluation of the hazard and exposure (food, water, and residential) components for inorganic chlorates indicates the need to estimate potential risks for the following scenarios: Short-term inhalation, screening level acute dietary (food + water), chronic (non-cancer) dietary (food + water), and cancer dietary (food + water).

7.1 Short-Term Aggregate Risk - Residential Handler Inhalation plus background (chronic dietary (food + water))

Table 7.1. Short-Term Aggregate Risk Calculations

Population	Target Aggregate MOE [1]	MOE food+water [2]	MOE inhalation [3]	Aggregate MOE (food+water and residential) [4]
Adult	100	1715	400	324

[1] Inhalation MOE = Oral NOAEL (30 mg/kg/day) / Daily Inhalation Dose. HED LOC for MOE is 100.
[2] MOE food+water = [(Short-Term oral NOAEL = 30 mg/kg/day)/(chronic dietary exposure food + water)
Chronic dietary exposure food + water = 0.002730mg/kg/day(food) + 0.01476mg/kg/day(water) = 0.01749mg/kg/day
[3] MOE inhalation = [(Short-Term inhalation NOAEL = 30 mg/kg/day)/(high-end inhalation residential exposure)]
[4] Aggregate MOE (food+water and residential) = 1÷[[(1÷MOE food+water) + (1÷MOE inhalation)]]

7.2 Chronic (non-cancer) Dietary Risk - Food + Water

Table 7.2. Summary of Chronic (non-cancer) Dietary (food + water) Exposure and Risk for Inorganic Chlorates

Population Subgroup [a]	cPAD mg/kg/day	% cPAD		
		Food + Water Estimated at the Highest Annual Average (0.69 mg/L)	Food + Water Estimated at the 90th Percentile Annual Average (0.24 mg/L)	Food+Water Estimated at the Median Annual Average (0.11 mg/L)
General U.S. Population	0.03	58	26	17
All Infants (< 1 yr)		**174**	70	40
Children 1-2 yrs		100	53	39
Children 3-5 yrs		90	47	34
Children 6-12 yrs		60	30	21
Youth 13-19 yrs		43	20	14
Adults 20-49 yrs		52	23	14
Adults 50+ yrs		54	23	14
Females 13-49 yrs		52	23	14

[a] The values for the population with the highest risk for each type of risk assessment are bolded.

[b] The BMDL is 0.9 mg chlorate/kg/day. The level of concern for the Margin of Exposure (MOE) is 30.

7.3 Cancer Dietary Risk - Food + Water

No separate cancer dietary (food + water) risk assessment was conducted. The chronic (food + water) dietary risk assessment is protective for cancer for the General U. S. Population. (See Table 7.2.) The estimated risk does not exceed our level of concern (less than 100% cPAD).

Note: Sodium chlorate is a thyroid toxicant producing thyroid gland follicular cell hypertrophy in rats and mice following chronic exposures and some evidence of follicular cell tumors in rats. The lack of mutagenicity indicates that the thyroid tumors are induced by a non-mutagenic mechanism. Therefore, for the purposes of this risk assessment, the Margin of Exposure (MOE) approach is used to estimate inorganic chlorate cancer risk. Children are not expected to be more susceptible to chlorate-induced thyroid effects than adults and the endpoint selected for the thyroid effects is protective for all populations, including children.

8.0 Cumulative Risk Characterization/Assessment

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to inorganic chlorates and any other substances. However, available data indicate that there may be some interconversion between chlorate and chlorite in water, in the environment, and in the gut.

For the purposes of this tolerance action, EPA has not assumed that inorganic chlorates have 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/.

9.0 Occupational Exposure/Risk Pathway - Conventional Pesticide Products Only

9.1 Short/Intermediate/Long-Term Handler Risk

There is potential for occupational handler exposure to inorganic chlorates from: (1) the application of sodium chlorate (073301) as the active ingredient in conventional pesticide products used on both agricultural and commercial (non-agricultural) sites (*i.e.*, mixer/loaders, applicators, flaggers, and mixer/loader/applicators); (2) the application of sodium chlorate (873301) as an inert ingredient in conventional pesticide products used on both agricultural and commercial (non-agricultural) sites (*i.e.*, mixer/loaders, applicators, flaggers, and mixer/loader/applicators); and (3) the application of potassium chlorate (900583) as an inert ingredient in conventional pesticide products used in poultry premises.

With the addition of PPE (dust/mist respirator) or engineering controls (enclosed cockpits or cabs), all occupational handler scenarios for the use of inorganic chlorates as an active or inert ingredient in conventional pesticides are below the Agency's level of concern (*i.e.*, Margin of Exposures (MOEs) are greater than the Level of Concern (LOC) of 100). Exposure durations are short- and intermediate-term only. Since the exposure durations for occupational handlers are inconsistent with the mechanism of chlorate carcinogenicity, an occupational cancer risk assessment was not conducted.

9.1.1 Sodium chlorate (073301) as the active ingredient in conventional pesticide products - Short-/Intermediate-Term Occupational Handler Exposure *via* Inhalation Route only

There is potential for occupational handler exposure to sodium chlorate from the application of sodium chlorate (073301) as the active ingredient in conventional pesticide products used on both agricultural and commercial (non-agricultural) sites (*i.e.*, mixer/loaders, applicators, flaggers, and mixer/loader/applicators). Occupational handler scenarios were identified for which exposure to sodium chlorate is expected (see Table 9.1.1).

Sodium chlorate is an agricultural defoliant/desiccant and a commercial herbicide. Use patterns vary from short- to intermediate-term exposure durations. Occupational handlers may be exposed dermal and inhalation routes; however, sodium chlorate is an inorganic salt, therefore, significant absorption of sodium chlorate through intact skin is not expected. Hence, only short- and intermediate-term sodium chlorate risk assessment for occupational handlers *via* the inhalation exposure route was conducted.

Risk for most occupational handler baseline (without a respirator) inhalation exposure scenarios do not exceed the Agency's level of concern (*i.e.*, Margin of Exposures (MOEs) are greater than the Level of Concern (LOC) of 100). However, occupational handler risks for some of the high end application rates (1032 and 523 lb ai/A) did exceed the Agency's level of concern at baseline. Risk mitigation for these scenarios was accomplished with the addition of a dust/mist respirator (with an

80% reduction factor), or, for certain scenarios, with engineering controls (enclosed cabs or cockpits).

No chemical-specific handler exposure data are available and, therefore, the following data and assumptions were used to assess the subject handler exposures and risks:

- Occupational handler exposure estimates were based on surrogate data from: (1) the Pesticide Handlers Exposure Database (PHED), and (2) Outdoor Residential Exposure Task Force (ORETF).

- Average body weight of an adult handler is 70 kg because the toxicity endpoint values used for the assessments are appropriate for average adult body weight representing the general population. This is the case because none of the effects identified in the selected toxicity studies were sex specific.

- Exposure factors used to calculate daily exposures to handlers are based on applicable data if available. For lack of appropriate data, values from a scenario deemed similar enough by the assessor might be used. As an example, for sodium chlorate handler exposures, ORETF data for hose-end sprayer equipment were used to assess sprinkling can applications. The nature of these application methods are believed to be similar enough to bridge the data.

- HED always considers the maximum application rates allowed by labels in its risk assessments. If additional information such as a different range of rates are available, these values also may be used to allow risk managers to make a more informed risk management decision.

- The typical occupational workday is assumed to be 8 hours.

- The daily area treated was defined for each handler scenario (in appropriate units) by determining the amount that can be reasonably treated in a single day (e.g. acres, square feet, or gallons per day). When possible, the assumptions for daily areas treated is taken from ExpoSAC SOP #9: Standard Values for Daily Acres Treated in Agriculture which was completed on July 5, 2000. Assumptions for these scenarios, including further refinements based on HED estimates, are listed below.

  Agricultural Scenarios
  - Aerial applications: 350 acres (typical field crop assumption) for guar beans, southern peas, chili peppers (for processing only), potatoes, ornamental gourds, and cucurbits (grown for seed); 1200 acres (high acreage crop assumption) for cotton, corn, rice, dry beans, sorghum, flax, safflower, sunflower, soybeans, wheat, and fallow land.
  - Groundboom: 80 acres (typical field crop assumption) for guar beans, southern peas, chili peppers (for processing only), potatoes, ornamental gourds, and cucurbits (grown for seeds); 200 acres (high acreage crop assumption) for cotton, corn, rice, dry beans, sorghum, flax, safflower, sunflower, soybeans, wheat and fallow land.

- Flaggers: 350 acres.

Refinements into “typical field” and “high acreage” crops was performed with help from HED crop expert Bernard Schneider (email from B. Schneider, 5/24/04).

Industrial/Non-Crop Sites

- Rights-of-Way Sprayer and Handgun Sprayer: 5 acres per day;
- Low Pressure Handwand Sprayer: 2 acres per day;

  Note: Although assessments for applications involving rights-of-way sprayers and low pressure handwands typically use a volume-based approach for amount handled/treated per day (1000 gallons and 40 gallons, respectively, from ExpoSAC Policy #9), label-specific application rates and their respective dilution factors for larger application settings are better represented by a daily unit *area* treated than a volume based approach. For example, the label-specific application of 8 pints per 100 square feet [EPA Reg. No. 7701-34] yields the application rate of 1032 lb ai in 2196 gallons of solution per acre. At this rate, the volume-based approach of 1000 gallons per day would have a worker treating approximately ½ acres per day. Because a rights-of-way sprayer would likely treat more than ½ acre per day, a daily unit area of 5 acres was used as more appropriate estimate.

- Belly grinder: 1 acre per day.
- Push-type spreader: 5 acres per day
- Groundboom and Tractor-drawn Spreader: 40 acres per day.

Table 9.1.1. Sodium Chlorate (073301): Short- and Intermediate-Term Occupational Inhalation Exposure					
Exposure Scenario (Scenario #)	**Daily Area Treated[1]**	**Crop/Target[2]**	**Application Rate[3]**	**Inhalation MOE[4]**	**Mitigation Level[5]**
Mixer/Loader					
Mixing/Loading liquids for Aerial application (1a)	1200	Cotton, Corn, Rice, Dry Beans, Grain Sorghum, Flax, Safflower, Sunflower, Soybeans	7.5	190	Baseline
		Fallow Land, Wheat	6	240	Baseline
	350	Chili Peppers (for processing only), Potatoes	12.5	400	Baseline
		Ornamental Gourds, Cucurbits (grown for seed)	6	830	Baseline
		Guar Beans, Southern Peas	7.5	670	Baseline
Mixing/Loading liquids for Groundboom application (1b)	200	Cotton, Corn, Rice, Dry Beans, Grain Sorghum, Flax, Safflower, Sunflower, Soybeans	7.5	1200	Baseline
		Fallow Land, Wheat	6	1500	Baseline
	80	Chili Peppers (for processing only), Potatoes	12.5	1800	Baseline
		Ornamental Gourds, Cucurbits (grown for seed)	6	3600	Baseline
		Guar Beans, Southern Peas	7.5	2900	Baseline
	40	Industrial/Non-Crop Sites	1032	210	PPE - 80% R
			523	420	PPE - 80% R
			132	330	Baseline
Mixing/Loading liquids for Rights-of-Way Sprayer application (1c)	5	Rights-of-Way & Industrial/Non-Crop Sites	1032	340	Baseline
			523	670	Baseline
			132	2700	Baseline
Loading granules for Tractor-drawn Spreader application (2)	40	Industrial/Non-Crop Sites	523	300	PPE - 80% R
			240	130	Baseline
			161	190	Baseline
Applicator					

Table 9.1.1. Sodium Chlorate (073301): Short- and Intermediate-Term Occupational Inhalation Exposure					
Exposure Scenario (Scenario #)	**Daily Area Treated[1]**	**Crop/Target[2]**	**Application Rate[3]**	**Inhalation MOE[4]**	**Mitigation Level[5]**
Aerial spray applications (3a)	1200	Cotton, Corn, Rice, Dry Beans, Grain Sorghum, Flax, Safflower, Sunflower, Soybeans	7.50	3400	Engineering Control
		Fallow Land, Wheat	6	4300	Engineering Control
	350	Guar Beans, Southern Peas	7.5	12000	Engineering Control
		Chili Peppers (for processing only), Potatoes	12.5	7100	Engineering Control
		Ornamental Gourds, Cucurbits (grown for seed)	6	15000	Engineering Control
Groundboom spray applications (3b)	1200	Cotton, Corn, Rice, Dry Beans, Grain Sorghum, Flax, Safflower, Sunflower, Soybeans	7.5	1900	Baseline
		Fallow Land, Wheat	6	2400	Baseline
	350	Guar Beans, Southern Peas	7.5	4700	Baseline
		Chili Peppers (for processing only), Potatoes	12.5	2800	Baseline
		Ornamental Gourds, Cucurbits (grown for seed)	6	5900	Baseline
	40	Industrial/Non-Crop Sites	1032	350	PPE - 80% R
				1200	Engineering Control
			523	140	Baseline
				2300	Engineering Control
			132	540	Baseline
				9200	Engineering Control
Rights-of-Way Sprayer Applications (3c)	5	Rights-of-Way & Industrial/Non-Crop Sites	1032	110	Baseline
			523	210	Baseline
			132	820	Baseline
Tractor-drawn Spreader Applications (4)	40	Industrial/Non-Crop Sites	523	420	PPE - 80% R
				460	Engineering Control
			240	180	Baseline

Table 9.1.1. Sodium Chlorate (073301): Short- and Intermediate-Term Occupational Inhalation Exposure					
Exposure Scenario (Scenario #)	**Daily Area Treated[1]**	**Crop/Target[2]**	**Application Rate[3]**	**Inhalation MOE[4]**	**Mitigation Level[5]**
				990	Engineering Control
			161	270	Baseline
				1500	Engineering Control

Table 9.1.1. Sodium Chlorate (073301): Short- and Intermediate-Term Occupational Inhalation Exposure					
Exposure Scenario (Scenario #)	**Daily Area Treated[1]**	**Crop/Target[2]**	**Application Rate[3]**	**Inhalation MOE[4]**	**Mitigation Level[5]**
Flagger					
Flagging for Aerial Spray applications (5)	350	Various Agricultural Crops	12.5	1400	Baseline
Mixer/Loader/Applicators & Loader/Applicators					
M/L/A liquids with a Low Pressure Handwand Sprayer (6)	2	Industrial/Non-Crop Sites	1032	170	PPE - 80% R
			523	330	PPE - 80% R
			132	270	Baseline
M/L/A liquids with a Handgun Sprayer (7)	5	Industrial/Non-Crop Sites	1032	230	Baseline
			523	450	Baseline
			132	1800	Baseline
L/A granules with a Belly Grinder (8)	1	Industrial/Non-Crop Sites	523	320	PPE - 80% R
			240	140	Baseline
			161	210	Baseline
L/A granules with a Push-type Spreader (9)	5	Industrial/Non-Crop Sites	523	110	Baseline
			240	240	Baseline
			161	360	Baseline

[1] Amount treated is presented in acres/day. (Standard EPA/OPP/HED values).
[2] Crops and use patterns are from label extractions (Appendix 1), BEAD's LUIS reports, and the Sodium Chlorate Use Closure Memo (J. Guerry, 8/5/04; 10/13/04; 11/15/04).
[3] Ranges of application rates are based on values from label extractions (Appendix 1), BEAD's LUIS reports, and the Sodium Chlorate Use Closure Memo (J. Guerry, 8/5/04; 10/13/04; 11/15/04). Application rates upon which the analysis is based are presented as lb ai/acre.
[4] Inhalation MOE = Oral NOAEL (30 mg/kg/day) / Daily Inhalation Dose. HED LOC for MOE is 100.

[5] Mitigation Levels

Baseline: No respirator
PPE - 80% R: Dust/mist respirator with an 80% reduction factor
Engineering Control: Closed cockpit or cab

9.1.2 Sodium chlorate (873301) as an inert ingredient in conventional pesticide products - Short-/Intermediate-Term Occupational Handler Exposure *via* Inhalation Route only

There is potential for occupational handler exposure to chlorate from the application of sodium chlorate (873301) as an inert ingredient in conventional pesticide products used on both agricultural and commercial (non-agricultural) sites (*i.e.*, mixer/loaders, applicators, flaggers, and mixer/loader/applicators). Occupational handler scenarios were identified for which exposure to sodium chlorate is expected (see Table 9.1.2).

Herbicide formulations containing < 1% sodium chlorate (873301) as an inert ingredient may be professionally applied to agricultural and commercial (non-agricultural) sites at the maximum use rate of 0.07 lb (as sodium chlorate) per acre. Use patterns vary from short- to intermediate-term exposure durations. Occupational handlers may be exposed dermal and inhalation routes; however, sodium chlorate is an inorganic salt, therefore, significant absorption of sodium chlorate through intact skin is not expected. Hence, only short- and intermediate-term sodium chlorate risk assessment for occupational handlers *via* the inhalation exposure route was conducted.

No chemical-specific handler exposure data are available and, therefore, the following data and assumptions were used to assess the subject handler exposures and risks:

- Assumptions for daily area treated are taken from ExpoSAC SOP #9: Standard Values for Daily Acres Treated in Agriculture (July 5, 2000) or from professional judgement.
- Unit exposures are from the PHED Surrogate Exposure Guide (August, 1998) or data from the Outdoor Residential Exposure Task Force (ORETF).
- Baseline personal protective equipment (PPE) represents (in terms of inhalation exposure and risk) a worker without a respirator.
- Average body weight of an adult handler is 70 kg because the toxicity endpoint values used for the assessments are appropriate for average adult body weight representing the general population. This is the case because none of the effects identified in the selected toxicity studies were sex specific.

Table 9.1.2. Short-/Intermediate-Term Occupational Inhalation Exposure Risk Estimates for Sodium Chlorate (873301) as an Inert Ingredient in Herbicide Formulations						
Exposure Scenario	**Unit Exposure**	**Daily Area Treated**	**Crop/Target**	**Application Rate**	**Non-Cancer MOE**	**Mitigation Level**
Mixer/Loader						
Mixing/Loading liquids for Aerial application	0.0012	1200	Agricultural crops	0.07	21000	Baseline
Mixing/Loading liquids for Groundboom application	0.0012	350	Agricultural crops	0.07	71000	Baseline
Mixing/Loading liquids for Rights-of-Way Sprayer application	0.0012	5	Non-agricultural sites	0.07	5000000	Baseline
Mixing/Loading liquids for Handgun Sprayer application	0.0012	100	Residential sites	0.07	250000	Baseline
Applicator						
Aerial spray applications	0.000068	1200	Agricultural crops	0.07	370000	Engineering Control
Groundboom spray applications (open cab)	0.00074	350	Agricultural crops	0.07	120000	Baseline
Rights-of-Way Sprayer Applications	0.0039	5	Non-agricultural sites	0.07	1500000	Baseline
Flagger						
Flagging for Aerial Spray applications	0.00035	350	Agricultural Crops	0.07	240000	Baseline
Mixer/Loader/Applicators						
M/L/A liquids with a Low Pressure Handwand Sprayer	0.03	1	Residential sites	0.07	1000000	Baseline
M/L/A liquids with a Handgun Sprayer	0.0018	5	Residential sites	0.07	3300000	Baseline
M/L/A liquids with a Backpack Sprayer	0.03	1	Residential sites	0.07	1000000	Baseline

9.1.3 Potassium chlorate (900583) as an inert ingredient in conventional pesticide products - Short-/Intermediate-Term Occupational Handler Exposure *via* Inhalation Route only

There is potential for occupational handler exposure to potassium chlorate from the application of potassium chlorate (900583) as an inert ingredient in conventional pesticide products used in poultry premises. Occupational handler scenarios were identified for which exposure to potassium chlorate is expected (see Table 9.1.3).

Potassium chlorate (900583) as an inert ingredient in airborne fungicide products can be applied in poultry premises. These conventional pesticide products contain < 20% potassium chlorate and can be applied at rates not greater than 0.01 lb (as potassium chlorate) per 500 ft^3.

Use patterns vary from short- to intermediate-term exposure durations. Occupational handlers may be exposed dermal and inhalation routes; however, potassium chlorate is an inorganic salt, therefore, significant absorption of potassium chlorate through intact skin is not expected. Hence, only short- and intermediate-term potassium chlorate risk assessment for occupational handlers *via* the inhalation exposure route was conducted.

No chemical-specific handler exposure data are available and, therefore, the following data and assumptions were used to assess the subject handler exposures and risks:

- This risk calculation is assumed to be a very conservative estimate. It assumes that *all* the potassium chlorate (no greater than 0.01 lb) is present in the air, and available for inhalation, following application of the airborne fungicide.
- Baseline PPE represents (in terms of inhalation exposure and risk) a worker without a respirator.
- Exposure duration is estimated to be 1 minute per day.
- Adult inhalation rate for light activity is 16.6 l/min.
- Average body weight of an adult handler is 70 kg because the toxicity endpoint values used for the assessments are appropriate for average adult body weight representing the general population. This is the case because none of the effects identified in the selected toxicity studies were sex specific.

Table 9.1.3. Short-/Intermediate-Term Occupational Inhalation Exposure Risk Estimates for Potassium Chlorate (900583) as an Inert Ingredient Used in Airbourne Fungicides

Exposure Scenario	Application Rate	Maximum Potential Airborne Concentration (mg $KClO_3$/l)	Non-Cancer MOE	Mitigation Level
Airborne Application of Fungicide	0.01 lb/500 ft^3	0.32	400	Baseline

9.2 Short/Intermediate/Long-Term Postapplication Risk

Postapplication exposures do not need to be included in the occupational risk assessment for inorganic chlorates. Although dermal and inhalation exposures are possible, these exposures are expected to be negligible due to the physical and chemical characteristics of inorganic chlorates.

10.0 Data Needs and Label Requirements

10.1 Toxicology

870.3465 28-Day Inhalation Study

These data are needed to refine the need for additional PPE (dust/mist respirator) or engineering controls (enclosed cockpit or cabs) to protect occupational handlers from potential inhalation exposure resulting from conventional agricultural use of sodium chlorate.

10.2 Residue Chemistry

860.1480 Magnitude of the Residue - Meat, Milk, Poultry, Eggs

New ruminant and poultry feeding studies are required.

860.1650 Submittal of Analytical Reference Standards

Submission of a reasonable amount of the analytical reference standards for sodium chlorate to the Pesticide Repository is required and replenishment of standards as requested by the repository.

10.3 Occupational and Residential Exposure

Sodium chlorate (073301) end-use product labels should be amended, as necessary, to include application rates in terms of lbs/acre treated for clarification.

Unpublished References:

Benchmark Dose Analysis of Sodium Chlorate FCH Response in Rats: No DP Barcode, B. Daiss, 01/26/2005.

Chlorate Ion in Drinking Water, memo from Patricia Fair (Office of Ground Water and Drinking Water Technical Support Center) to Jacqueline Guerry (OPPTS/OPP/SRRD/RB3), dated 08/10/2005.

Drinking Water Assessment of Sodium Chlorate as a Desiccant/Defoliant on Food/Feed Terrestrial Uses: D303556, S. Termes, 01/05/2005.

Incident Report: D310573, J. Blondell, 03/31/2005.

Inorganic Chlorates Dietary Exposure Assessment for the Reregistration Eligibility Decision: D303555. T. Morton, 01/26/2006.

Occupational and Residential Exposure Assessment for Sodium Chlorate (073301) as an Active Ingredient in Conventional Pesticides: D307365, M. Crowley, 06/13/2005.

Occupational and Residential Exposure Assessment for Inorganic Chlorates in Antimicrobial Pesticides: D312200, T. Leighton, 01/24/2005.

Occupational and Residential Exposure Assessment for Inorganic Chlorates as Inert Ingredients in Conventional Pesticides: D318045, M. Crowley, 06/13/2005.

Response to Sodium Chlorate Preliminary Risk Assessment, memo of OW to Jacqueline Guerry, SRRD, 10/20/2005.

Note: Residue Chemistry Considerations are addressed under Appendix C.

Published References:

AWWA Water Quality Division Disinfection Systems Committee, Committee Report: Disinfection at Large and Medium-Size Systems, May 2000a, p 32-43.

AWWA Water Quality Division Disinfection Systems Committee, Committee Report: Disinfection at Small Systems, May 2000b, p 24-31.

Bolyard, M., Fair, P.S., and Hautman, D.P. "Sources of Chlorate Ion in US Drinking Water," Journal AWWA Vol 85(9) 81-88, 1993.

Dohler, K. D., Wong, C. C., Von Zur Muhlen, A. (1979) The rat as a model for the study of drug effects on thyroid function: Consideration of methodological problems. Pharmacol. Ther. 5, 305-318

Gates, D.J. *The Chlorine Dioxide Handbook*. American Water Works Association, Denver, CO, 1998.

Gordon, G.G., Adam, L., and Bubnis, B. *Minimizing Chlorate Ion Formation in Drinking Water When Hypochlorite Ion is the Chlorinating Agent*. American Water Works Association Research Foundation, Denver, CO, 1995.

McClain, R. M. (1992). Thyroid gland neoplasia: non-genotoxic mechanisms. Toxicol. Lett. 64/65, 397-408.

USEPA, 1996. National Primary Drinking Water Regulation: Monitoring Requirements for Public Drinking Water Supplies: *Cryptosporidium*, Giardia, Viruses, Disinfection Byproducts, Water Treatment Plant Data and Other Information Requirements. Final Rule. FR 61:94:24354-24388 (May 14, 1996).

USEPA, 2000. *ICR Auxiliary 1 Database*. EPA 815-C-00-002. Office of Water, Cincinnati, OH, April 2000.

APPENDIX A TOXICOLOGY DATA REQUIREMENTS

Test	Technical	
	Required	**Satisfied**
870.1100 Acute Oral Toxicity	yes	yes
870.1200 Acute Dermal Toxicity	yes	yes
870.1300 Acute Inhalation Toxicity	yes	yes
870.2400 Primary Eye Irritation	yes	yes
870.2500 Primary Dermal Irritation	yes	yes
870.2600 Dermal Sensitization	yes	yes
870.3100 Oral Subchronic (Rodent)	yes	yes
870.3150 Oral Subchronic (Non-Rodent)	yes	yes
870.3200 21-Day Dermal	no	-
870.3250 90-Day Dermal	no	-
870.3465 28-Day Inhalation	**yes**	**no**
870.3700a Developmental Toxicity (Rodent)	yes	yes
870.3700b Developmental Toxicity(Non-rodent)	yes	yes*
870.3800 Reproduction	yes	yes**
870.4100a Chronic Toxicity (Rodent)	yes	yes*
870.4100b Chronic Toxicity (Non-rodent)	yes	yes***
870.4200a Oncogenicity (Rat)	yes	yes*
870.4200b Oncogenicity (Mouse)	yes	yes*
870.4300 Chronic/Oncogenicity	yes	yes*
870.5100 Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300 Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5395 Mutagenicity— Erythrocyte Micronucleus	yes	yes*
870.5385 Mutagenicity— Bone Marrow Cytogenetics	yes	yes*
870.5550 Mutagenicity—Unscheduled DNA Synthesis	yes	yes
870.5275 Mutagenicity— Recessive lethal in Drosophila	yes	yes*
870.6100a Acute Delayed Neurotox. (Hen)	no	-
870.6100b 90-Day Neurotoxicity Hen)	no	-
870.6200a Acute Neurotoxicity. Screening Battery (Rat)	no	-
870.6200b 90 Day Neurotoxicity Screening Battery (Rat)	no	-
870.6300 Develop. Neurotoxicity	no	-
870.7485 General Metabolism	yes	yes*
870.7600 Dermal Penetration	no	-
Special Studies for Ocular Effects	no	-
Acute Oral (Rat)	no	-
Subchronic Oral (Rat)	no	-
Six-month Oral (Dog)		

- Not Applicable

* Chlorate published study

** Chlorite published study

*** The 2-year NTP (DRAFT NTP Report 2004) study in the rat satisfies this requirement. No toxicity was seen in the subchronic study in dogs administered sodium chlorate by oral gavage except for emesis at the highest dose of 360 mg/kg/day.

APPENDIX B TOXICOLOGY STUDIES

The executive summaries of tox studies presented in the sodium chlorate toxicology profile are provided below.

Acute Toxicity

The acute oral LD50 of potassium chlorate has been reported to be 1870 mg/kg in rats and the lowest oral lethal dose in rats was 7000 mg/kg, in rabbits 2000 mg/kg and in dogs 1200 mg/kg (Cosmetic Ingredient Review Panel, 1995)

The published literature provides numerous references to sodium chlorate poisoning. In one report (Helliwell & Nunn, 1979), 14 cases of deliberate and accidental sodium chlorate poisonings in individuals (males and females) ranging in age from 3- 55 years old are described. In one case a 48 year old female died after 20 hours of accidentally ingesting 15 g of sodium chlorate. Death is described occurring from massive intra vascular hemolysis and acute renal failure. Recovery from sodium chlorate poisoning was low even with medical intervention. The clinical features of sodium chlorate poisonings in these cases were nausea and vomiting, cyanosis, abdominal pain, diarrhea, dyspnea. In the patients who died, a "constant necropsy finding was a chocolate discoloration of the blood and viscera due to staining by bilirubin and methemoglobin".

The acute toxic effects of potassium chlorate are summarized in the 1995 Cosmetic Ingredient Review Panel, 1995. The toxic dose of potassium chlorate is often reported to be 5 g with the lethal adult dose being 15-35 g. Mortality of a child has been reported after ingestion of 1 g of potassium chlorate. Human chlorate ingestion can produce gastritis, a late toxic nephritis, hemolysis, methemoglobinemia, hemoglobinuria and acute renal failure. The toxic effects of potassium chlorate appear cumulative because of the slow excretion of the chlorate ion; repeated 1 g ingestions have been fatal. Dermal irritation and burns have been reported in industrial uses. Use of potassium chlorate in toothpastes may have caused inflammation and bleeding of the gums.

In a case of severe chlorate poisoning of a 26 year old female who ingested 150-200 grams of sodium chlorate, methemoglobinaemia was described as the early symptom of intoxication (Steffen and Seitz, 1981). Methemoglobin was converted to hematin. The patient was deeply cyanotic when admitted to hospital approximately 5 hours after ingesting the material. After extensive gastric lavage and administration of methylene blue and ascorbic acid intravenously, 7.4 grams of sodium chlorate were excreted in the urine. The patient voided clear urine initially, turning dark brown becoming muddy before it completely subsided, the result of renal failure. After the renal failure, the patient required several weeks of hemodialysis. Renal function was absent for 10 days and recovered slowly and the patient was discharged after 3 months. Liver function was only moderately disturbed. Serum tranasaminases were elevated during the first 10 days. Bilirubin was only slightly elevated for 3 weeks.

Subchronic Toxicity

870.3100 90-Day Oral Toxicity - Rat

In a subchronic oral toxicity study (MRID 40444801), Sprague-Dawley CD rats (15/sex/group) were dosed with technical grade sodium chlorate (100% a.i., white granular solid) gavage at 0

(distilled water), 10, 40, 100, or 1000 mg/kg/day for 90 consecutive days. Body weight gain was lower in females of all dosed groups compared to controls which had abnormal body weight gain. The body weights of males were minimally lower (not statistically significant) in the two highest dose groups. The most notable effects of sodium chlorate dosing were on the hematological parameters. At the 1000 mg/kg/dose, hemoglobin concentration, hematocrit, red blood cell counts were statistically significantly decreased, and reticulocyte count was statistically significantly increased in females. In males, only the hematocrit was statistically significantly decreased at the highest dose tested (HDT). The adrenal weight was depressed in both males and females at the HDT. Histological lesions were detected in all groups but with no apparent dose relationship. The **LOAEL** derived from this study was 1000 mg/kg/day based on the hematological effects and the **NOAEL** was 100 mg/kg/day. This study is considered Acceptable/guideline.

In a published study (Kurokawa *et al*, 1985) it was reported that administration of 1% sodium or potassium chlorate in the drinking water (654-686 mg/kg/day) to male F344 rats for 25 weeks produced significant decrease in mean body weights compared to the controls. This dose was the maximum tolerated dose based on a 6-week screening study at 0.25, 0.5, 1 and 2% doses in drinking water. Relative kidney weights of the potassium chlorate treated rats were significantly increased over the control group, suggesting renal toxicity.

Studies were conducted to determine the toxicity of chlorine dioxide (0, 1, 10, 100, 1000 mg/L) and its conversion products chlorite and chlorate (10, 100 mg/L) in drinking water in rats. After 9 month treatment the osmotic fragility of the red blood cells (RBC) was decreased in all treatment groups, while a decreased blood glutathione was only observed in the chlorite/chlorate groups. At 2, 4 and 6 months, no significant hematologic changes were noted in treated rats compared to control. After 9 month RBC counts, hematocrit and Hb were decreased in all treatment groups. Chlorine dioxide, chlorite and chlorate administered chronically in drinking water for 3 months inhibited the incorporation of ^{3}H-thymidine into nuclei of rat testes. This inhibition was observed in the liver of the chlorite groups and in the kidney of 100 mg/L chlorine dioxide treatment. The incorporation in small intestinal nuclei was increased in 10 and 100 mg/L chlorine dioxide and in 10 mg/L chlorite groups. Rat body weight was decreased in all groups after 10 and 11 months (Abdel-Rahman *et al.* 1984)

EPA/PATHOLOGY ASSOCIATES Study

In a published study conducted by USEPA Risk Reduction Engineering Laboratory/Environmental Monitoring Systems Laboratory in Cincinnati, Ohio and by Pathology Associates in Ohio (McCauley *et al*, 1995), Sprague Dawley rats (10/sex/group) were exposed to sodium chlorate in the drinking water at concentrations of 0 (distilled water control), 48 mM saline (sodium chloride) control, 3.0 mM sodium chlorate, 12 mM sodium chlorate or 48 mM sodium chlorate for 90 days. The final sodium concentration was 48.0 mM for each group except for the distilled water control. At the end of 90 day exposure animals were sacrificed and organs were collected for gross pathological and histopathological examination. Blood was collected for clinical and hematological evaluation.

During the course of chlorate exposure, no behavioral or clinical abnormalities were noted and there were no compound related deaths. The water consumption was 100 g/kg/day for the distilled water control group males and the mid-dose group males. The other male groups consumed 20 to 30% more. The water consumption for the females was 133, 167, 172, 163, and 200 g/kg/day for the distilled water control, saline control, low-, mid- and high-dose groups, respectively. Based on the water consumption, the mean delivered doses were calculated to be 0.36 mM (30 mg), 1.2 mM (100 mg), and 6.14 mM (510 mg) chlorate/kg/day for the low-, mid- and high- dose males and 0.5 (42 mg), 1.9 (158 mg), and 9.6 mM (797 mg) chlorate/kg/day for the low-, mid- and high- dose females, respectively. Treatment-related effects were conspicuous in the high dose group. These included significant body weight reduction throughout the exposure group in both sexes, significant decreases in male relative organ weights of the heart, kidneys and liver with relative brain and testes weights increased, significant declines in female relative weights of adrenals, thymus and spleen with significant brain weight increased, significant decreases in clinical chemistry parameters: ALT, AST, calcium, creatine, and phosphorus and an increase in the serum cholesterol. Calcium and creatinine also declined in the mid-dose group, serum BUN levels were decreased in the low dose females. The biological relevance of the clinical chemistry changes in all chlorate groups was considered doubtful, since most of the values were within the normal reference ranges. There was a significant decrease in hematocrit concentration and red and white blood cell counts in the high dose animals while females of this group exhibited a trend towards decreased erythrocyte and hematocrit values. Histopathologically, thyroid colloid depletion was noted in both control and treated animals in a dose related manner and was characterized by an increased number of smaller follicles which were lined by a prominent cuboidal epithelium but devoid of colloid. The control group had an incidence of 30% with a minimal to mild severity while those in the mid and high dose groups exhibited a 100% incidence level with a moderate to marked severity. The authors cite a published study (Harrington and Shertzer, 1985) which demonstrates the effects of chlorine dioxide on the bioavailability of iodide in drinking water and diet. In that paper, it was concluded that chlorine dioxide in drinking water oxidizes iodide to a reactive form which binds to tissues of the digestive tract while with dietary chow it converts iodide to a less easily absorbed by organification to dietary constituents. According to current study authors “these findings suggest a possible mechanism by which chlorate, a by-product of chloride dioxide degradation, may

accentuate colloid depletion due to this anti-thyroid effect of reducing iodide availability". The study authors concluded that based on the biologically significant changes noted in the mid and high dose groups of both sexes (thyroid colloid depletion) and hematological effects at the high dose, the **LOAEL** is 1.20 mM (100 mg chlorate)/kg bw/day in males and 1.9 mM (158 mg chlorate)/kg bw/day for females and the **NOAEL** is 0.36 mM (30 mg chlorate/kg bw/day in males) and 0.50 mM (42 mg chlorate/kg bw/day for females).

EPA/NTP Studies

In a 21 day oral toxicity study (NTP 1999a and 1999b), B6C3F1 mice and Fisher 344 rats (10/sex/dose) were exposed to sodium chlorate in the drinking water at 0, 125, 500, 1000 or 2000 mg/L . Measured consumption was 0, 22, 43, 173 or 348 mg/kg/day for male mice, 0, 20, 44, 94, 192 or 363 mg/kg/day for female mice; 0, 20, 36, 77 or 170 mg/kg/day for male rats and 0, 21, 38, 73, 152 or 338 mg/kg/day for female rats. In mice, sodium chlorate had no effect on survival, body weights, clinical signs, water consumption, hematology parameters, methemoglobin concentration, or organ weights of either sex. There were no gross or microscopic lesions that were considered to be due to sodium chlorate treatment. In rats, sodium chlorate had no effect on survival, body weights, clinical signs or water consumption. A moderate to severe neutropenia was observed in both sexes on day 4 and 22. Very mild decreases in erythrocyte counts, hemoglobin, and hematocrit were considered not to be biologically significant. The only gross or microscopic lesion that was considered to be treatment related was a minimal to mild follicular cell hyperplasia of the thyroid gland seen in males at 500 mg/L or greater and in females at 250 mg/L or greater. The thyroid gland was considered to be a target organ for sodium chlorate toxicity in the rat.

In a published study conducted by USEPA National Health and Environmental Effects Research Laboratory and the NTP National Institute of Environmental Health Sciences in North Carolina (Hooth *et al*, 2001), to evaluate development of thyroid lesions in rodents exposed to sodium chlorate in the drinking water, male and female F344 rats and B6C3F_1 mice (10/group) were exposed to sodium chlorate in drinking water at 0, 0.125, 0.25, 1 or 2 g/L for 21 days (NTP study) . In another test, male and female rats (10/group) were exposed at 0, 0.125, 1 or 2 g/L for 4, 21 or 90 days (NTP study). Additional male rats (10/group) were exposed to 0, 0.001, 0.01, 0.1, 1 or 2 g/L for 90 days (EPA study). Mean compound consumption at these water concentrations was estimated by the reviewer to be 0.112, 1.12, 11.2, 112, and 225 mg/kg/day for the males and 0.16, 1.6, 16.0, 160, 320 mg/kg/day for the females based on water consumption values reported in the McCauley *et al*, 1995 article. Additional female rats and female mice (6/group) were exposed to 0, 0.500, 1, 2, 4, or 6 g/L for 105 days (EPA study) (82, 165, 330, 660, 990 estimated mg/kg/day). Animals were observed daily and moribund animals were necropsied. Prior to necropsy, a blood sample was collected from animals treated for 4, 21 or 90 days and the serum was separated and frozen (NTP study). Complete necropsies were performed on all animals and tissues of interest were removed, examined macroscopically, and fixed in 10% neutral buffered formalin. Fixed thyroid tissues were processed by routine methods to 5 um paraffin sections and stained with hematoxylin and eosin for histological examination by light

microscopy. The thyroids were examined for the presence of colloid depletion, follicular cell hypertrophy, and follicular cell hyperplasia.

Total serum triiodothyronine (T_3) and thyroxine (T_4) concentrations were determined as well as the thyroid stimulating hormone (TSH) concentrations. Serum T_3 and T_4 levels were decreased significantly and TSH levels increased significantly in male and female rats after 4 days of treatment with 1.0 or 2.0 g/L sodium chlorate and after 21 days of treatment with 2.0 g/L. TSH levels also increased significantly in male rats after 21 days of treatment with 1.0 g/L. Serum T_3 and T_4 levels were comparable to controls in male and female rats after 90 days of treatment, but TSH levels were increased in both sexes.

Thyroid alterations were initially diagnosed using standard published methods. According to this method, follicular cell hyperplasia and severe colloid depletion were present in all male and female F344 rats following 21 days of treatment with 1.0 g/L treatment of sodium chlorate or greater. The severity of the lesions was the same in all animals. The present study utilized a "novel" method of diagnosis detailed in the article. According to this diagnosis colloid depletion and hypertrophy were present in male and female rats treated with 0.125 g/L or greater, but were statistically significant ($p<0.05$) at 0.5 g/L treatments. In males, the incidence and severity of thyroid alterations was greater at 1.0 g/L Sodium chlorate than 2.0 g/L, but in females, it was the opposite. After 90 days of treatment, significant colloid depletion was diagnosed in most treated male F344 rats but the incidences were similar in all groups. Colloid depletion was more significant in female rats treated with 1.0 or 2.0 g/L sodium chlorate for 21 days than for 105 days. Significant colloid depletion was diagnosed in female F344 rats treated for 105 days at sodium chlorate concentrations of 2.0 g/L or greater.

Follicular cell hypertrophy was present in most male and female rats after 21 or 90 days of sodium chlorate treatment, but the incidence did not increase in a concentration dependent manner. The incidence of follicular cell hypertrophy was higher in female rats treated with 1.0 or 2.0 g/L sodium chlorate for 21 days than for 105 days. At 105 days, 6.0 g/L of sodium chlorate caused a significant increase in the incidence of follicular cell hypertrophy. Complex papillary infolding or branching was more frequent in thyroid tissue from male rats at the 1.0 and 2.0 g/L concentrations. The area of the thyroid tissue affected in male rats increased in a concentration dependent manner following 90 days of treatment. **Thyroid alterations were not present in male or female mice.**

It was concluded by the study authors that sodium chlorate treatment induced a concentration dependent increase in the incidence and severity of thyroid follicular cell hyperplasia. Colloid depletion and hypertrophy were the most sensitive histopathological indicators of sodium chlorate exposure in male F344 rats at 21 and 90 days, although the hypertrophy response was variable when concentration dependency was evaluated. Male rats were more sensitive to the effects of sodium chlorate treatment than female rats. Decreases in serum hormone levels observed in the present study may suggest that sodium chlorate has the potential to induce acute detrimental neurodevelopmental effects. Hormone and histological alterations may reflect a transient

physiologic response of the thyroid to sodium chlorate exposure. It is not known whether the histological effects of sodium chlorate are reversible following cessation of chemical exposure. Alternatively, the concentration dependent increase in incidence and severity of thyroid follicular cell hyperplasia may indicate an increased likelihood of the lesions progressing to cancer. The study authors did not provide a **NOAEL** for the effects of sodium chlorate treatment in rats, but based on the article, a **NOAEL** may be derived at 0.5 g/L (28 mg/kg/day in males and 40 mg/kg/day in females) based on colloid depletion and follicular cell hyperplasia at a **LOAEL** of 1.0 g/L (112 mg/kg day for males and 160 mg/kg/day for females) sodium chlorate after 90 days of exposure. Chlorate is related in structure to bromate and perchlorate, both are thyroid toxicants and chemical oxidants.

870.3150 90-Day Oral Toxicity - Dog

In a subchronic oral toxicity study (MRID 40460402), beagle dogs (4/sex/group) were dosed with technical grade sodium chlorate (100% a.i., white granular solid) by oral gavage at dose levels of 0 (distilled water), 30, 60, or 360 mg/kg/day for 90 consecutive days. All dogs survived the treatment. Clinical signs were sporadic, one female in the high dose group exhibited emesis during the first three weeks of dosing and two other females developed yellow/brown watery stool. There were no effects on hematological parameters, clinical chemistry (including methemoglobin), opthalmology or histopathology. Urinalysis was not conducted. The adrenal, and spleen weights, and organ/body weight ratios in males were increased at the HDT. Only the spleen weights in females were increased at the HDT. Hypercellularality of the bone marrow of males appeared to increase in severity and number of animals responding as the dose was increased. The effect was less pronounced in females. None of these effects are sufficiently adverse to establish an effect level. The dose levels used in this study were too low to detect unequivocal toxicity. At higher dose levels in a range-finding study, emesis occurred, and it was stated that emesis would have precluded a study at higher dose levels. The **LOAEL** derived from this study is >360 mg/kg/day and the **NOAEL** is 360 mg/kg/day (the HDT). This study is considered Acceptable/guideline (The study was originally classified supplementary because of missing data regarding incomplete histopathological examination of mammary tissues, and number of animals examined opthalmologicaly was not stated. These do not impact the acceptability of the study).

In a sub-acute exposure study in dogs, doses of 200 to 326 mg/kg/day of sodium chlorate administered daily by intubation as 50 ml of 6% solution to 8 dogs for 5 days caused reduction of packed cell volume, hemoglobin and red blood cells (Heywood *et al*, 1972 cited in the Final Draft Drinking Water Criteria, Clement International Corp., 1994). A consistent increase in plasma urea concentration was also observed, suggesting some compromise of renal function. Two animals that received 308 or 326 mg/kg/day suffered appetite loss, body weight decline and appearance of blood in their urine or feces. One of the animals (not specified) died after 4 days of exposure. Postmortem examination of both animals revealed typical signs of chlorate poisoning, including cyanotic kidney surface and evidence of necrosis and hemolysis in the kidney. Five of the 8 animals displayed tissue pathology indicative of hemolysis such as Kupffer cells containing

brown pigment. Hematological values of red blood cells were reduced in all animals. The highest methemoglobin concentrations was seen in the animal that died. Methemoglobinemia was not correlated with changes in the other hematological parameters.

870.4100a Chronic Toxicity - Mouse

In the NTP (DRAFT NTP Report 2004) study presented in a draft form, Groups of 50 male and 50 female B6C3F_1 mice were exposed to drinking water containing 0, 500, 1,000, or 2,000 mg/L sodium chlorate for 2 years (equivalent to average daily doses of approximately 40, 80, and 160 mg/kg per day to male mice and 30, 60, and 120 mg/kg per day to female mice). Survival of exposed mice was similar to that of the control groups. Mean body weights of exposed females were generally less (88-90% of controls in all treated females at week 104) than those of the control groups after week 84 of the study. Water consumption by exposed mice was generally similar to that by controls throughout the study (3.4-4.2 g/male/day; 2.5-3.6 g/female/day). There was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) in female mice (0/46, 2/47, 2/49, 4/49). Thyroid gland follicular cell hypertrophy was significantly increased in 2,000 mg/L females (3/48, 2/50, 5/49, 14/50). The incidences of bone marrow hyperplasia were significantly increased in all exposed groups of females (14/50, 28/50, 29/50, 31/50).

Carcinogenicity

870.4200a Carcinogenicity Study - rat

A 2-year bioassay to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been recently reported in a draft form. A final report of this study is expected during 2005. In the NTP (2004) study summarized in Section 4.4.3 of the main body of this memo, there was some evidence of thyroid gland follicular cell carcinogenicity in male rats which may be attributed to the imbalance of thyroid hormones (reduced T_3 and T_4 and elevated TSH) seen in these studies as a result of exposure to high doses of sodium chlorate. Current EPA HED policy considers nonmutagenic pesticides that induce elevated levels of TSH and thyroid follicular cell tumors in the rat as not likely to be cargencogenic to humans at doses that do not alter rat thyroid hormone homeostasis.

In a published study, sodium chlorate and potassium chlorate were tested for potential promoting effect in a two stage rat renal carcinogenesis assay (Kurokawa *et al*, 1985). In this assay three groups of 15 male F344 rats were given N-ethyl-N-hydroxyethylnitrosamine (EHEN) at 0.05% concentration in the drinking water for the first 2 weeks during the initiation phase. Subsequently, one group of the initiated rats was treated with 1% sodium chlorate, second group with 1% potassium chlorate and the third group with distilled water for 25 weeks. Three other groups (controls) were treated similarly, except that distilled water was given in the initiation phase.

These doses were selected on the basis of 6 week study where male F344 rats were administered the test compounds in the drinking water at 0, 0.25%, 1% or 2% concentrations and found that 1% concentration was the maximum tolerated concentration for both test compounds. All animals survived the treatment in the main study. The mean final body weight in the sodium chlorate and potassium chlorate groups with or without initiation were significantly lower ($p < 0.05$-0.01) than the controls. The mean intake of drinking water (water consumption) in rats treated with sodium chlorate or potassium chlorate was slightly lower than the controls and it ranged from 19.2 - 22.1 ml/day/rat. The mean consumption of sodium chlorate was 654-686 mg/kg/day for sodium chlorate and 667 to 675 mg/kg/day for the potassium chlorate. At the end of promotion phase, rats were sacrificed and kidneys examined histopathologically for renal neoplastic lesions which were classified as dysplastic foci and renal cell tumors. The mean absolute kidney weights were comparable in all groups, but the mean relative kidney weights given the sodium chlorate or potassium chlorate with or without initiation were significantly ($p<0.01$-0.05) lower than the control group. There were no statistically significant differences in the incidences in the mean number of the types of the kidney lesions between the test compounds and the distilled water treated rats initiated with EHEN, it was concluded that sodium chlorate and potassium chlorate did not have a promoting effect in rat renal carcinogenesis assay (Kurokawa *et al*, 1985).

870.4200b Carcinogenicity (feeding) - Mouse

A 2-year bioassay to determine the potential of sodium chlorate to induce thyroid tumors in laboratory animals (rats and mice) has been recently reported in a draft form (DRAFT NTP Report 2004). A final report of this study is expected during 2005. As summarized above, there was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) in female mice (0/46, 2/47, 2/49, 4/49). This finding was considered to be equivocal evidence.

870.7485 Metabolism - Rat

The pharmacokinetics of chlorite ion and chlorate ion was studied in rats (Abdel-Rahman *et al*, 1982, 1984b and 1985). Two groups of male Sprague-Dawley rats (4/group) were administered orally ^{36}Cl- labeled potassium chlorate or potassium chlorite at concentrations of 10 mg/L. In one group, blood samples were collected at selected times between 5 minutes and 48 hours after dosing and assayed for ^{36}Cl- activity and at 72 hours, the rats were killed and the tissue distribution of ^{36}Cl- activity was determined. In the other group, expired air, urine, and fecal samples were obtained for up to 72 hours and assayed for ^{36}Cl- activity. Maximum blood ^{36}Cl- concentrations occurred 2 hours after dosing with potassium chlorite and 1 hour after treatment with potassium chlorate. Potassium chlorate elimination from the blood was biphasic, with half lives of 6 hours for the first phase and 36.7 hours for the second phase. Potassium chlorite elimination was monophasic with a half life of 35 hours. After 72 hours, ^{36}Cl- activity was highest in whole blood following potassium chlorite administration and highest in plasma following potassium chlorate administration. The highest measured radioactivity after the plasma in the chlorate treated rats was in the whole blood followed by stomach, testes, lungs, kidneys,

skin, duodenum, spleen, brain, packed cells, ileum, carcass, liver, and bone marrow. ^{36}Cl- concentration in the plasma was 2 ng/g, and in bone marrow was less than 0.5 ng/g. Significantly high levels of ^{36}Cl- activity after dosing with both compounds were found in the testes. Seventy two hours after dosing with potassium chlorite, 35 percent of the dose was eliminated in the urine and 5% in the feces. Approximately 43% of the potassium chlorate dose was eliminated by the urinary and feces routes. ^{36}Cl- was not detected in exhaled air after dosing with either compound. The administered chlorate was eliminated as chlorate (ca. 13% of the administered dose), chlorite (ca. 4% of the administered dose) and chloride (ca. 20% of the administered dose). The authors suggest that the high levels of ^{36}Cl- activity in the testes after 72 hours suggest possible pharmacological action at this site.

870.7485 Metabolism - Dog

A metabolism study in dogs is reported in the National Research Council 1980 report on Drinking Water and Health and is summarized in California EPA/OEHHA 2002 Report (OEHHA, 2002). In this study, when seven female dogs were given 500 mg/kg doses of chlorate in 500 mL water, 55-70 % of the dose was excreted in the urine in the first 6 hours. By 24 to 48 hours, 76-99% of the dose had been excreted unchanged in urine. The chlorate concentration in the blood peaked at 2 hours and decreased to little or none by 24 hours.

Special/Other Studies

Sodium Chlorate as an Inhibitor of Protein Sulfation

Sodium chlorate has been described as a non-toxic inhibitor of tyrosine sulfation (Beinfeld, 1994). This property is utilized by biochemists to study peptide and protein synthesis, regulation of protein secretion and function (Beinfeld, 1994; Mintz *et al*, 1994). Sodium chlorate is an *in vitro* inhibitor of ATP-sulfurylase, the first enzyme in the biosynthesis of 3'-phosphoadenosine 5'-phosphosulfate which is the ubiquitous co-substrate for sulfation (Baeuerle and Huttner, 1986). Treatment of hybridoma derived cells and rat pheochromocytoma cell cultures with 1 mM sodium chlorate in a medium low in sulfate and sulfur-containing amino acids resulted in more than 95% inhibition of protein sulfation as well as tyrosine and carbohydrate sulfation, but did not inhibit protein synthesis even after prolonged incubation. The authors concluded from this study that sodium chlorate "provides powerful tool for studying the biological significance of protein sulfation" (Baeuerle and Huttner, 1986). The sulfation of polyethylene glycol 200 by the isolated perfused guinea pig liver was inhibited to about 60% by 10 mM of sodium chlorate in the plasma of the perfusate when the concentration of the sulfate ion was 1.18 mM, but in a low sulfate medium (0.1mM), the inhibition was almost complete (94%) (Roy *et al*, 1988). Bile production from isolated perfused livers was not affected by the presence of sodium chlorate in this test, suggesting that chlorate is not a general liver poison according to the authors of this article (Roy *et al*, 1988). When bovine aorta endothelial cells were cultured in a medium containing ^{3}H-glucosamine, ^{35}S-sulfate and various concentrations of sodium chlorate, cell growth and viability was not affected by 10mM chlorate and slight inhibition at 30 mM (Humphries and Silbert, 1988). Chlorate concentrations of 10 mM and greater resulted in significant inhibition of sulfation of chondroitin. With 30 mM chlorate the inhibition was 90% for chondroitin and 65% for heparin, but 3H-glucosamine incorporation was not inhibited. Removal of chlorate from the cell culture medium restored the rapid resumption of sulfation.

Chlorate Toxicity in Humans

In a series of studies by Lubbers *et al* (1984a, 1984b), investigating the physiological impact of human ingestion of chlorine dioxide and its water breakdown byproducts (chlorite and chlorate), reported no effects attributable to the daily consumption of water treated with these products for periods extending to 12 weeks. In these studies normal healthy adult male volunteers (21-35 years of age) divided into groups (10/group) drank daily 500 mL of water containing 5 ppm of chlorite, or chlorate or distilled water (control) for 12 weeks. Subjects were monitored weekly during the 12 week treatment and for 8 additional weeks by conducting physical medical examination, checking vital signs. Special chemical tests for thyroid function, antibody formation, hepatoglobin and methemoglobin concentrations, and blood morphology were repeated regularly to assess physiological functions in areas "suspected to be most sensitive to oxidative challenge". Subjective evaluations of the palatability of the water disinfectant solutions were recorded at regular intervals. A total of 47 quantitative chemical parameters derived from an extensive battery of blood and urine testing were recorded regularly. Abnormalities in the qualitative blood and urine analysis were few and appeared to be randomly distributed. In several cases,

statistically significant trends (mean corpuscular hemoglobin levels) were associated with treatment, but "none of these were judged to have physiological consequence". The authors concluded that the possibility that these trends might achieve proportions of clinical importance cannot be ruled out, but "within the limits of the study, the relative safety of oral ingestion of chlorine dioxide, and its metabolites, chlorite and chlorate, was demonstrated". In their second study (Lubbers *et al*, 1984b), 3 male healthy adult volunteers deficient in glucos-6-phosphate dehydrogenase and receiving 500 mL of water containing 500 ppm of sodium chlorite did not experience any adverse effects demonstrating the safety of this chemical to a susceptible group of the human population.

These data were not deemed useful for dose-response evaluation and were not relied upon in the risk assessment.

Chlorates Mechanism of Toxicity

The mode of action in sodium chlorate poisoning in humans is summarized by Smith and Oehme (1991) in their review article. The chlorate ion initially reacts with thiol groups on the red blood cells and may cause it to lyse, similar to nitrite ions, converting the hemoglobin to methemoglobin. The chlorate ion is a strong oxidizer, and it oxidizes the ferrous ion of the hemoglobin molecule to ferric ion to result in methemoglobin formation. With chlorate, in contrast to nitrite, a concentration dependent lag phase was seen before methemoglobin was formed (Singelmann *et al*, 1984). Sodium chlorate ranked the least potent among six direct-acting methemoglobin agents (French *et al*, 1995). These were (most to least) *p*-dinitrobenzene > *o*-dinitrobenzene > copper = nitrite > chlorite > chlorate. The ranking was based on linear regression analysis of dose-response data, the calculated dose expected to induce a given amount of methemoglobin formation and the calculated percentage methemoglobin response induced by mmole/L of the agent in Dorset sheep erythrocytes. Calbarese *et al*, 1995 also investigated the potency of sodium chlorate to produce methemoglobin in mink erythrocytes and it was the least potent among six other chemicals (a-naphthol>nitrite>copper>p-dinitrobenzene>chlorite>o-dinitrobenzene> chlorate).

Potassium chlorate incubated with washed erythrocytes from human venous blood (0.1 to 6.0 mmol/L) caused a dose-related increase in glutathione activity and mechanical fragility with a parallel increase in Heinz body formation (Hopkins and Tudhope, 1974). There was also a close relationship between increased mechanical fragility and increased inhibition of glutathione peroxidase. Spontaneous hemolysis in this test was less than 10%.

The mechanism of chlorate poisoning was explored in a set of *in vitro* and *in vivo* experiments by Steffen and Wetzel (1993). They found that incubation of human erythrocytes with 5 mM sodium chlorate oxidized hemoglobin to methemoglobin after a lag period of approximately 60 minutes. When after different periods of contact with the 30 mM chlorate, samples of erythrocytes were washed free of the chlorate and incubated with methylene blue, reduction of methemoglobin was only partial during the first hour of incubation (8%) but became nil after 2 hours of incubation.

The catalytic reduction of methemoglobin by methylene blue was found to be dependent on the availability of NADPH formed in the pentose phosphate cycle. Therefore, an intact enzyme system in erythrocytes is required. Incubation of homeliest erythrocytes with 5 mM sodium chlorate showed that glucose-6-phosphate dehydrogenase and glyceraldehyde -3-phosphate dehydrogenase were most sensitive, whereas glutathione reductase was very stable. When human erythrocyte membranes (devoid of hemoglobin) were incubated with 5 mM sodium chlorate, there was a rapid inactivation of glyceraldehyde -3-phosphate dehydrogenase when hemoglobin was added, but not in its absence. This suggests that sodium chlorate does not inactivate the membane-bound glyceraldehyde -3-phosphate dehydrogenase, the key enzyme in the NADPH-dependent methemoglobin reduction. Nearly all membrane proteins were affected by the hemoglobin catalyzed oxidation. Earlier work by Heubner and Jung, 1941 (cited by Steffen and Wetzel, 1993) demonstrated that methemoglobin formation by chlorate was an autocatalytic reaction. Both the lag period and the rate were dependent on the actual methemoglobin concentration.

Steffen and Wetzel (1993) also explored the *in vitro* effects of chlorate on rabbit erythrocytes and compared them to the *in vivo* effects on methemoglobin formation in rabbits. It was discovered in 1888 by Cahn (cited by Steffen and Wetzel, 1993) that rabbits do not develop methemoglobine anemia after chlorate administration. When rabbit erythrocytes were incubated with sodium chlorate at concentrations ranging from 7.5 to 75 mM, methemoglobin was formed in a dose dependent manner. Higher concentrations of the chlorate were needed for rabbit erythrocytes than for the human erythrocytes. No methemoglobin was formed after the oral administration of sodium chlorate (1000 mg/kg body weight) in 50 mL water. The serum concentration of the chlorate was 10 - 20 mM for at least 12 hours. The highest concentration of the chlorate in the serum was reached after 90 minutes (16±4.3 mM) and in the urine after 6 hours (246±99 mM). The elimination half-life was 20 hours. During 7 days of observation period there were no changes in serum values of urea, creatinine, aspartate and alanine aminotransferases. When the animals were killed at the end of the 7 day observation period and kidneys examined histologically, there were no pathologic findings detected, indicating lack of nephrotoxicity in the treated rabbits.

TOXICOLOGY REFERENCES

UNPUBLISHED

MRID: 40444801
Barrett, D. (1987) A Subchronic (3 Month) Oral Toxicity Study of Sodium Chlorate in the Rat Gavage: Final Report: Project No. 86-3112. Unpublished study prepared by Bio/dynamics, Inc. 464 p.

MRID: 40460401
Schroeder, R. (1987) A Teratogenicity Study in Rats with Sodium Chlorate: Project No. 86-3117. Unpublished study prepared by Bio/dynamics, Inc. 372 p.

MRID: 40460402
Barrett, D. (1987) A Subchronic (3 Month) Oral Toxicity Study in the Dog Gavage Administration with Sodium Chlorate: Project No. 86-3114. Unpublished study prepared by Bio/dynamics, Inc. 323 p.

MRID: 41256201
May, K. (1989) Sodium Chlorate: Assessment of Mutagenic Potential in Histidine Auxotrophs of Salmonella Typhimurium (Ames Test): Rept. No. 89/0285. Unpublished study prepared by Life Science Research Limited. 39 p.

MRID: 41256204
May, K. (1989) Sodium Chlorate: Assessment of Its Ability to Cause Lethal DNA Damage in Strains of Escherichia Coli: LSR Report No. 89/SKR004/0341. Unpublished study prepared by Life Science Re- search Ltd. 34 p.

MRID: 41256202
Hudson-Walker, G. (1989) Sodium Chlorate: Investigation of Mutage- nic Activity at the HGPRT Locus in a Chinese Hamster V79 Cell Mutation System: Report No. 89/0631. Unpublished study prepared by Life Science Research. 42 p.

MRID: 41256203
Mackay, J. (1989) Sodium Chlorate: Assessment of Clastogenic Action on Bone Marrow Erythrocytes in the Micronucleus Test: LSR Report No. 89/SKR003/0253. Unpublished study prepared by Life Science Research Ltd. 34 p.

MRID: 41256204
May, K. (1989) Sodium Chlorate: Assessment of Its Ability to Cause Lethal DNA Damage in Strains of Escherichia Coli: LSR Report No. 89/SKR004/0341. Unpublished study prepared by Life Science Re- search Ltd. 34 p.

MRID: 41256205
Seeburg, A. (1989) Unscheduled DNA Synthesis (UDS) in Hela S3 Cells In Vitro: Sodium Chlorate: LSR-RTC Report No. 102002-M-02289. Unpublished study prepared by Life Science Research Roma Toxicology Centre. 50 p.

PUBLISHED

Abdel-Rahman MS, Couri D, Bull RJ. 1982. Metabolism and pharmacokinetics of alternate drinking water disinfectants. Environ Health Perspect. 46:19-23.

Abdel-Rahman MS, Couri D, Bull RJ. 1984a. Toxicity of chlorine dioxide in drinking water. J AM COLL TOXICOL; 3 (4) 277-284.

Abdel-Rahman MS, Couri D, Bull RJ. 1984b. The Kinetics of Chlorite and Chlorate in the Rat. Journal of the American College of Toxicology, 3(4): 261-267.

Abdel-Rahman MS, Couri D, Bull RJ. 1985. The kinetics of chlorite and chlorate in rats. J Environ Pathol Toxicol Oncol. 6(1):97-103.

Aggazzotti G, Righi E, Fantuzzi G, Biasotti B, Ravera G, Kanitz S, Barbone F, Sansebastiano G, Battaglia MA, Leoni V, Fabiani L, Triassi M, Sciacca S. 2004. Chlorination by-products (CBPs) in drinking water and adverse pregnancy outcomes in Italy. J Water Health. 2(4):233-47.

Baeuerle PA, Huttner WB. 1986. Chlorate a potent inhibitor of protein sulfation in intact cells. Biochem biophys res commun; 141 (2). 870-877.

Beinfeld, MC. 1994. Inhibition of Cholecystokinin (CCK) sulfation by treatment with Sodium Chlorate alters its processing and decreases cellular content and secretion of CCK 8. Neuropeptides 26: 195-200.

Bercz, JP, Jones L, Garner L, Murray D, Ludwig DA, Boston J. 1982. Subchronic Toxicity of Chlorine Dioxide and Related Compounds in Drinking Water in Nonhuman Primate. Env. Hlth Perspectives, 46: 47-55.

Chang, S., Crothers, C., Lai, S., Lamm, S. (2003) Pediatric Neurobehavioral Diseases in Nevada Counties with respect to Perchlorate in Drinking Water - An Ecological Inquiry. Birth Defects Res A Clin Mol Teratol. 67(10):886-92.

Cosmetic Ingredient Review Panel. 1995. Final report on the safety-assessment of Potassium Chlorate J Am Coll Toxicol. 14: 221-30

Couri D, Abdel-Rahman MS, Bull RJ. 1982. Toxicological effects of chlorine dioxide, chlorite and chlorate. Environ Health Perspect. 46:13-7.

Dohler, K.D., Wong, C.C., Von Zur Muhlen, A. (1979) The rat as a model for the study of drug effects on thyroid function: Consideration of methodological problems. Pharmacol. Ther. 5, 305-318.

Eckhardt K, Gocke E, King MT, Wild D. 1982. Mutagenic activity of chlorate, bromate, and iodate MUTAT RES 97:185.

French CL, Yaun S-S, Baldwin LA, Leonard DA, Zhao XQ, Calabrese EJ. 1995. Potency Ranking of Methemoglobin-Forming Agents. J. of Appld. Tox., 15(3):167-174.

Gill, MW, Swanson, MS, Murphy SR, Bailey GP . 2000. Two-Generation Reproduction and Developmental Neurotoxicity Study with Sodium Chlorite in the Rat. J. Applied Toxicology. 20(4): 291-203.

Helliwell, M; Nunn J. 1979. Mortality in Sodium Chlorate Poisoning. British Med. J. 1: 1119

Heywood, R, Sortwell, RJ, Kelly, PJ, Street, AE. 1972. Toxicity of sodium chlorate to the dog. Vet. Rec. 90:416-418.

Hooth, MJ, DeAngelo AB, George MH, Gailard ET, Travlos GS, Boorman GA, Wolf DC. 2001. Subchronic Sodium Chlorate Exposure in Drinking Water Results in a Concentration-Depndent Increase in Rat Thyroid Follicular Cell Hyperplasia. Toxicologic Pathology. 29(2):250-259.

Hopkins J and Tudhope GR, 1974. The effects of drugs on erythrocytes *in vitro*: Heinz body formation, glutahione proxidase inhibition, and changes in mechanical fragility. Br. J. Clin Pharmacolo 1:191-195.

Kurokawa Y, Imazawa T, Matsushima M, Takamura N, Hayashi Y. 1985. Lack of promoting effect of sodium chlorate and potassium chlorate in two-stage rat renal carcinogenesis. J Am Coll Toxicol 4:331-337.

Li, F.X., Byrd, D.M., Deyille, G.M., Sesser, D.E., Skeels, M.R., Katkowsky, S.R., Lamm, S.H. (2000) Neonatal Thyroid-Stimulating Hormone Level and Perchlorate in Drinking Water. Teratology 62:429-431.

Li, Z., Li, X.I., Byrd, D., Deyhle, G.M., Sesser, D.E., Skeels, M.R., Lamm, S.H. (2000) Natal Thyroxine Level and Perchlorate in Drinking Water. 42:200-205.

Lubbers JR, Chauhan S, Miller JK, Bianchine JR. 1984a. The effects of chronic administration of chlorine dioxide, chlorite and chlorate to normal healthy adult male volunteers. J Environ Pathol Toxicol Oncol 5(4-5):229-238.

Lubbers JR, Chauhan S, Miller JK, Bianchine JR. 1984b. The effects of chronic administration of chlorite to glucose-6-phosphate dehydrogenase deficient healthy adult male volunteers. J Environ Pathol Toxicol Oncol 5(4-5):239-242.

McCain, R.M. (1992) Thyroid gland neoplasia: non-genotoxic mechanisms. Toxicol. Lett. 64/65, 397-408.

McCauley PT, Robinson M, Daniel FB, Olson GR. 1995. The effects of subchronic chlorate exposure in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2,3):185-199.

Meier JR, Bull RJ, Stober JA, Cimino MC. 1985. Evaluation of chemicals used for drinking water disinfection for production of chromosomal damage and sperm-head abnormalities in mice. Environ Mutagen 7 (2):201-212.

Mintz KP, Fisher LW, Grzesik WJ, Hascall VC, Midura RJ. 1994. Chlorate-induced inhibition of tyrosine sulfation on bone sialoprotein synthesis by a rat osteoblast like cell line (UMR 106-01 BSP). JBiol. Chem. 269(7): 4845-4852.

Moriya M, Ohta T, Watanabe K, Miyazawa T, Kato K, Shirasu Y. 1983. Further mutagenicity studies on pesticides in bacterial reversion assay Systems. MUTAT RES 116:185-216.

NTP (1999a). National Toxicology Program. 21-day toxicity study of sodium chlorate administered in dosed water to B6C3F1 mice. NIEHS/NTP Contract No. N01-ES-85420. Southern Research Institute, February 11, 1999.

NTP (1999b). National Toxicology Program. 21-day toxicity study of sodium chlorate administered in dosed water to Fisher-344 rats. NIEHS/NTP Contract No. N01-ES-85420. Southern Research Institute, February 11, 1999.

NTP (2002). National Toxicology Program. Final Study Report on the Developmental Toxicity Evaluation for Sodium Chlorate (CAS No. 7775-09-9) Administered by Gavage to New Zealand White Rabbits on Gestational Days 6 through 29. Prepared by Julia D. George and Catherine J Price. NIEHS/NTP Contract No. N01-ES-65405. Govt Reports Announcements & Index (GRA&I), Issue 04, 2003 Research Triangle Inst., Research Triangle Park, NC. Center for Life Sciences and Toxicology.

NTP (2004). NTP Technical Report on the Toxicology and Carcinogenesis Studies of Sodium Chlorate (CAS No. 7775-09-9) in F344 rats and B6C3F1 Mice (Drinking Water Studies). Scheduled peer review date: December 9-10, 2004. Draft Report.

OEHHA. 2002. Proposed Action Level for Chlorate. Office of Environmental Health Hazard Assessment, California EPA. Memorandum from Robert A. Howd to David P. Spath. January 7, 2002. http://www.oehha.ca.gov/water/pals/chlorate.html

Olivier P, Marzin D. 1987. Study of genotoxic potential of 48 inorganic derivatives with the SOS chromotest. Mutation Research 189:263-270.

Roy AB, Curtis CG, Powell GM. 1988.. The inhibition by chlorate of the sulfation of polyethyleneglycol in the isolated perfused guinea pig liver. Xenobiotica. 18(9): 1049-1055.

Singelmann E, Wetzel E, Adler G, Steffen C. 1984. Erythrocyte membrane alterations as the basis of chlorate toxicity. Toxicology 30(2):135-147.

Smith EA; Oehme FW. 1991. A review of Selected Herbicides and Their Toxicities. Vet. Hum Toxicol. 33:596-608

Steffen C; Seitz R. 1981. Severe Chlorate Poisoning. Arch. Toxicol. 48:281-288.

Steffen C, Wetzel E. 1993. Chlorate Poisoning: Mechanism of Toxicity. Toxicology 84:217-231.

Suh DH, Abdel-Rahman MS, Bull RJ. 1983. Effect of chlorine dioxide and its metabolites in drinking water on fetal development in rats. J Appl Toxicol 3(2):75-79.

Suh DH Abdel-Rahman MS Bull RJ. 1984. Biochemical Interactions Of Chlorine Dioxide And Its Metabolites In Rats. Archives of Environmental Contamination and Toxicology, 13(2):163-169.

Tellez, R., Chacon, P.M., Abarca, R.C., Blount, B.C., Van Landingham, C.B., Crump, K.S., Lobo, Gibbs, J.P. (2005) Thyroid:15:(in publication)

Tuthill RW, Giusti RA, Moore GS, Calabrese EJ. 1982. Health Effects Among Newborns after Prenatal Exposure to ClO2-Disinfected Drinking Water. Environmental Health Perspectives, 46:39-45.

USEPA. 1994. Final Draft for the Drinking Water Criteria Document on Chlorine Dioxide, Chlorite and Chlorate. Prepared for the Health Effects Division/Office of Science and Technology/Office of Water, March 31, 1994, under contract by Clement International Corp.

USEPA 2000. Toxicological Review of Chlorine Dioxide and Chlorite, EPA/635/R-00/007. http://www.epa.gov/IRIS/toxreviews/0496-tr.pdf

Warrington. P. 2002. Ambient Water Quality Guidelines for Chlorate - technical background report. Government of British Columbia, Ministry of Water, Land and Air Protection. ISBN 0-7726-4734-8. http://wlapwww.gov.bc.ca/wat/wq/BCguidelines/chlorate.html

WHO. 2004. Chlorite and chlorate in Drinking Water. Background document for developing WHO *Guidelines for Drinking-water Quality*,20 pages. WHO/SDE/WSH/03.04/86 http://www.who.int/water_sanitation_health/dwq/chemicals/en/chloratechlorite.pdf

APPENDIX C RESIDUE CHEMISTRY CONSIDERATIONS for Sodium Chlorate (073301) as an active ingredient in conventional (agricultural) pesticides

Preface: Through a series of negotiations between members of SRRD and AD to coordinate Inorganic Chlorates and Chlorine Dioxide and Sodium Chlorite, with regards to the risk assessment for Inorganic Chlorates, the residue of concern from sodium chlorate exposures is chlorate by agreement. See Section 1.0 Executive Summary above.

Sodium chlorate is currently registered for preharvest and foliar applications as a defoliant or desiccant to the following food/feed crops: dry beans, corn, cotton, flax, guar, chili peppers, potatoes, rice, safflower, sorghum (grain), southern peas (*i.e.*, cowpeas), soybeans, and sunflowers. For food/feed uses, sodium chlorate is formulated as a soluble concentrate (SC) with the active ingredient ranging from 18% to 47.2%. Sodium chlorate may be applied using aircraft or ground spray equipment, including high and low volume equipment.

Uses of sodium chlorate as a defoliant or desiccant on cauliflower, cucurbit vegetables, and okra grown for seed only are considered non-food uses. Uses of sodium chlorate on ornamental gourds and fallow lands are also considered non-food uses. These non-food uses will not be discussed further with regards to residue chemistry or dietary exposure/risk considerations.

Under 40 CFR 180.1020 (a) Sodium chlorate is exempt from the requirement of a tolerance for residues in or on the following raw agricultural commodities when used as a defoliant, desiccant, or fungicide in accordance with good agricultural practice: beans (dry, edible), corn (fodder), corn (forage), corn (grain), cottonseed, flaxseed, flax (straw), guar beans, peas (southern), peppers (chili), potatoes, rice, rice (straw), safflower (grain), sorghum (grain), sorghum (fodder), sorghum (forage), soybeans and sunflower seed.

Under 40 CFR 180.1020 (b) A time-limited exemption from the requirement of a tolerance is established for residues of the defoliant/desiccant in connection with use of the pesticide under section 18 emergency exemptions granted by EPA. This exemption has been granted for wheat and will expire on 12/31/04. As requested by the Registration Division (*Sodium Chlorate Use Closure Memo Amendment*; J. Guerry; dated 11/15/2004) the use of sodium chlorate on wheat is also addressed herein with the intention to convert the time-limited exemption status to a permanent exemption from the requirement of a tolerance under 40 CFR.1020 (a). The proposed use rate is for a single application of sodium chlorate to wheat at 6 lbs ai/A with a 3-day PHI.

No plant metabolism data have been submitted in support of the reregistration of sodium chlorate; however, no new plant metabolism data are required to support the established sodium chlorate tolerance exempts. Based on available published information (Loomis *et al.*, J. Am. Soc. Agron.; 25, 724 (1933)), sodium chlorate is highly soluble in water and is expected to readily absorb and translocate throughout plants. However, given the proposed use conditions, the means of translocation in treated plants may be substantially disrupted. Translocation of very small

amounts of chlorate ion (ClO_3^-) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses may occur. Terminal residues are expected to be primarily surface residues.

Since sodium chlorate is a strong oxidizing agent, depending on environmental factors, it is expected to be easily reduced to chloride and possibly chlorite in plants. Total redox conversion to these reduced species is not expected; hence, the terminal residues of sodium chlorate in/on plants are likely chlorate (ClO_3^-), chlorite (ClO_2^-), and chloride (Cl^-).

No ruminant, swine, or poultry metabolism or feeding data have been submitted in support of the reregistration of sodium chlorate; however, no new animal metabolism data are required to support the established sodium chlorate exemptions from the requirement of a tolerance. Based on published rat metabolism data (Abdel-Rahman *et al*, 1982, 1984b and 1985), terminal residues of sodium chlorate in animal tissues are expected to be chlorate (ClO_3^-), chlorite (ClO_2^-), and chloride (Cl^-). Chlorate is readily absorbed from the digestive tract and is excreted as chlorate, chlorite, and chloride in urine primarily and feces. Within 72 hours, about 40% of the administered dose was excreted in the urine as chlorate (ca. 13%), chlorite (ca. 4%), and chloride (ca. 20%) and about 2-4% was excreted in the feces in the same time period. Less than 1% of the administered dose was found in any of the tissues analyzed including kidney, liver, and skin.

Although some previous residue chemistry reviews for specific exemptions from the requirement of a tolerance have concluded that there is no reasonable expectation of transfer of residues to meat, milk, poultry or eggs in specific cases, re-evaluation of the available crop field trial data taken as a whole, indicate that there is the possibility of detectable residues of sodium chlorate on animal feedstuffs at harvest. Hence, secondary residues of concern in meat, milk, poultry, and eggs are possible and; therefore, new ruminant and poultry feeding data are hereby required to support the reregistration of sodium chlorate. These data are considered confirmatory.

The analytical method used to support the established exemptions from the requirement of a tolerance is a non-specific colorimetric method (Branderis, J. Sci. Food Agric., 16, 558 (1965)), deemed acceptable for data collection. The method was originally developed to estimate residual chlorate concentrations in soil and as a rapid diagnostic test for chlorate toxicity in plants. Briefly, the method involves acid extraction, clean-up by shaking with activated charcoal, and filtration. A solution of ortho-toluidine in HCl is then added to the concentrated extract and the resulting color is measured at 448 nm for low concentrations and at 490 nm for higher concentrations of dye. The method is not specific for chlorate since it measures any oxidizing agent capable of oxidizing chloride ion to free chlorine. A standard curve is prepared with sodium chlorate for comparison. The lowest sensitivity of the method is estimated at 1 ppm based on available fortification data from field trials. Chloride does not interfere with the method but residues of chlorite, which might be present, may also be detected with this method. This method is hereby deemed adequate for enforcement of sodium chlorate exemptions from the requirement of a tolerance. [Note: If needed, a more selective HPLC method ("Determination of Residues of

Sodium Chlorate in Potatoes", Method #S57023, 4/2/91) is available for the detection of sodium chlorate residues in or on raw agricultural commodities (RACs).]

New reference standards must be supplied to the EPA National Pesticide Standards Repository.

Only crop field trial data have been submitted to support the reregistration of sodium chlorate. No storage stability or processing data are available. The available crop field trial data have been re-evaluated herein. No additional plant magnitude of the residue or storage stability data are required to support the reregistration of sodium chlorate.

Table C.1. Residue Chemistry Science Assessment for Reregistration of Sodium Chlorate (073301) as an active ingredient in conventional (agricultural) pesticides			
GLN Data Requirements	**Current Tolerances (ppm) [§180.1020]**	**Additional Data Needed?**	**Citations [1]**
860.1200: Directions for Use	NA	No	
860.1300: Nature of the Residue - Plants	NA	No	00062497, 00066805
860.1300: Nature of the Residue - Animals	NA	No	None
860.1340: Residue Analytical Method	NA	No	00049610, 00066802, 00066804, 00066808, 00066809, 00066810, 00123747, 00124680, 00135224
860.1360: Multiresidue Method	NA	No	None
860.1380: Storage Stability Data	NA	No	None
860.1400: Magnitude of the Residue - Water, Fish and Irrigated Crops	None	No	None
860.1460: Magnitude of the Residue - Food Handling	None	No	None
860.1480: Magnitude of the Residue - Meat, Milk, Poultry, Eggs			
- Cattle fat, meat, and meat byproducts	None	Yes [2]	None
- Goat fat, mean and meat byproducts			
- Horse fat, meat and meat byproducts			
- Sheep fat, meat and meat byproducts			
- Milk			
- Eggs and the Fat, Meat and Meat Byproducts of Poultry			
860.1500: Crop Field Trials [3]			
- Beans (dried, edible)	Exempt	No	
- Corn (fodder, forage, grain)	Exempt	No	
- Cottonseed	Exempt	No	
- Flaxseed and Flax (straw)	Exempt	No	00136326
- Guar beans	Exempt	No	00136388

Table C.1. Residue Chemistry Science Assessment for Reregistration of Sodium Chlorate (073301) as an active ingredient in conventional (agricultural) pesticides			
GLN Data Requirements	**Current Tolerances (ppm) [§180.1020]**	**Additional Data Needed?**	**Citations [1]**
-Peas (southern)	Exempt	No	00128727
- Peppers (chili)	Exempt	No	00116554
- Potatoes	Exempt	No	42464201, 42930601
- Rice and Rice straw	Exempt	No	00159210
- Safflower (grain)	Exempt	No	None
- Sorghum (grain, fodder, forage)	Exempt	No	00123727
- Soybeans	Exempt	No	00128727
- Sunflower seed	Exempt	No	00135224
- Wheat	Exempt	No	00136326
860.1520: Processed Food/Feed	NA	No	None
860.1850: Confined Accumulation in Rotational Crops	NA	No	None
860.1650: Submittal of Analytical Reference Standards	NA	Yes [4]	None
860.1900: Field Accumulation in Rotational Crops	NA	No	None

[1] Only data considered primary sources of information to support the reregistration of sodium chlorate are included here. All other available data are considered supplemental.

[2] New ruminant and poultry feeding studies are required.

[3] Sodium chlorate is exempt from the requirement of a tolerance for residues in or on the listed raw agricultural commodities when used as a defoliant, desiccant, or fungicide in accordance with good agricultural practice [40 CFR 180.1020]

[4] Replenish standards as requested by the repository.

860.1300 Nature of the Residue - Plants

No plant metabolism data have been submitted in support of the reregistration of sodium chlorate; however, no new plant metabolism data are required to support the established sodium chlorate tolerance exempts. Based on available published information (Loomis *et al.*, J. Am. Soc. Agron.; 25, 724 (1933)), sodium chlorate is highly soluble in water and is expected to readily absorb and translocate throughout plants. However, given the proposed use conditions, the means of

translocation in treated plants may be substantially disrupted. Translocation of very small amounts of chlorate ion (ClO_3^-) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses may occur. Terminal residues are expected to be primarily surface residues.

Since sodium chlorate is a strong oxidizing agent, depending on environmental factors, it is expected to be easily reduced to chloride and possibly chlorite in plants. Total redox conversion to these reduced species is not expected; hence, the terminal residues of sodium chlorate in/on plants are likely chlorate, chlorite, and chloride.

860.1300 Nature of the Residue - Livestock

No ruminant, swine, or poultry metabolism or feeding data have been submitted in support of the reregistration of sodium chlorate; however, no new animal metabolism data are required to support the established sodium chlorate exemptions from the requirement of a tolerance. Based on published rat metabolism data (Abdel-Rahman *et al*, 1982, 1984b and 1985), terminal residues of sodium chlorate in animal tissues are expected to be chlorate (ClO_3^-), chlorite (ClO_2^-), and chloride (Cl^-). Chlorate is readily absorbed from the digestive tract and is excreted as chlorate, chlorite, and chloride in urine primarily and feces. Within 72 hours, about 40% of the administered dose was excreted in the urine as chlorate (ca. 13%), chlorite (ca. 4%), and chloride (ca. 20%) and about 2-4% was excreted in the feces in the same time period. Less than 1% of the administered dose was found in any of the tissues analyzed including kidney, liver, and skin.

Metabolism - Rat

The metabolism and distribution of chlorine dioxide (ClO_2), chlorite ion (ClO_2^-), and chlorate ion (ClO_3^-) were studied in rats (Abdel-Rahman *et al*, 1982, 1984b, 1985). Three groups of male Sprague-Dawley rats (4/group) were administered a single oral (gavage) dose of one of the compounds which were ^{36}Cl-radiolabeled. Expired air, fecal and urine samples were collected over 72 hours. The $^{36}Cl^-$ activity in these samples was measured and the radioactivity in the urine was identified as chlorate (ca. 13% of the administered dose), chlorite (ca. 4% of the administered dose) and chloride (ca. 20% of the administered dose). At 72 hours, the rats were killed and the distribution of $^{36}Cl^-$ activity in tissues was determined (see Table C.2). Total radioactivity in each of the tissues examined was <1% of the initial dose.

Table C.2.	**Distribution of radioactivity in rat tissues after dosing with ^{36}Cl-labeled chlorine dioxide, potassium chlorite, or potassium chlorate.**		
Tissue	Percentage of initial dose [1]		
	Chlorine dioxide ($^{36}ClO_2$)	Chlorite ($^{36}ClO_2^-$)	Chlorate ($^{36}ClO_3^-$)
Plasma	0.72 ± 0.02	0.55 ± 0.038	0.68 ± 0.09
Packed cells	-- [2]	0.63 ± 0.11	0.23 ± 0.02
Whole blood	--	0.64 ± 0.01	0.57 ± 0.05
Kidney	0.81 ± 0.15	0.30 ± 0.06	0.42 ± 0.07
Lung	0.74 ± 0.15	0.37 ± 0.04	0.45 ± 0.07
Stomach	0.70 ± 0.15	0.43 ± 0.07	0.46 ± 0.05
Duodenum	0.29 ± 0.07	0.31 ± 0.01	0.34 ± 0.04
Ileum	0.48 ± 0.09	0.17 ± 0.03	0.21 ± 0.02
Liver	0.38 ± 0.09	0.06 ± 0.03	0.20 ± 0.03
Spleen	0.25 ± 0.04	0.22 ± 0.02	0.29 ± 0.04
Bone marrow	0.16 ± 0.03	0.09 ± 0.03	0.15 ± 0.03
Testes	--	0.39 ± 0.04	0.45 ± 0.07
Skin	--	0.38 ± 0.06	0.42 ± 0.10
Carcass	--	0.25 ± 0.04	0.21 ± 0.02

[1] Value represents the mean ± SE as percentage of the initial dose from four rats per treatment after 72 hr.
[2] Not Determined

860.1340 Residue Analytical Methods

The analytical method used to support the established exemptions from the requirement of a tolerance is a non-specific colorimetric method (Branderis, J. Sci. Food Agric., 16, 558 (1965)), deemed acceptable for data collection. The method was originally developed to estimate residual chlorate concentrations in soil and as a rapid diagnostic test for chlorate toxicity in plants. Briefly, the method involves acid extraction, clean-up by shaking with activated charcoal, and filtration. A solution of ortho-toluidine in HCl is then added to the concentrated extract and the resulting color is measured at 448 nm for low concentrations and at 490 nm for higher concentrations of dye. The method is not specific for chlorate since it measures any oxidizing agent capable of oxidizing chloride ion to free chlorine. A standard curve is prepared with sodium chlorate for comparison. The sensitivity of the method is estimated at 1 ppm based on available fortification data from field trials. Chloride does not interfere but residues of chlorite, which might be present, may also be detected with this method. This method is hereby deemed adequate

for enforcement of sodium chlorate exemptions from the requirement of a tolerance. A more selective HPLC method ("Determination of Residues of Sodium Chlorate in Potatoes", Method #S57023, 4/2/91) is available for the detection of sodium chlorate residues in or on raw agricultural commodities (RACs).

860.1360 Multiresidue Methods

It does not appear that the registrant has submitted multiresidue method studies. Sodium chlorate is not listed in the FDA PESTDATA database dated 11/01 (PAM Volume I, Appendix I). However, sodium chlorate would not be expected to be recovered by the PAM I multiresidue methods. No additional multiresidue methods data are required to support the reregistration of sodium chlorate.

860.1380 Storage Stability

No storage stability data have been submitted in support of the reregistration of sodium chlorate. However, the available data continue to uphold the established sodium chlorate exemptions from the requirement of a tolerance, and therefore, no new storage stability data are required to support the reregistration of sodium chlorate.

860.1400 Water, Fish, and Irrigated Crops

Sodium chlorate is not presently registered for direct use on water and aquatic food and feed crops other than as a desiccant on rice. Since sodium chlorate is used to desiccate green foliage and weeds present in rice fields to increase harvest efficiency, residues of concern are not expected to be occurred in water, fish, and irrigated crops from the use of sodium chlorate as a desiccant on rice. Therefore, no residue chemistry data are required under these guideline topics.

860.1460 Food Handling

Sodium chlorate is not presently registered for use in food-handling establishments; therefore, no residue chemistry data are required under these guideline topics.

860.1480 Meat, Milk, Poultry, and Eggs

No ruminant, swine or poultry feeding studies have been submitted in support of the reregistration of sodium chlorate. Although some previous residue chemistry reviews for exemptions from the requirement of a tolerance have concluded that there is no reasonable expectation of transfer of residues to meat, milk, poultry or eggs in specific cases, re-evaluation of the available crop field trial data taken as a whole, indicate that there is the possibility of detectable residues of sodium chlorate on animal feedstuffs at harvest. Hence, secondary residues of sodium chlorate in meat, milk, poultry, and eggs are possible and; therefore, new ruminant and poultry feeding data are hereby required to support the reregistration of sodium chlorate.

Table C.3.	**Calculation of the highest average and maximum theoretical dietary burden for beef/dairy cattle and poultry from the maximum registered use rates of sodium chlorate (073301) as an active ingredient in conventional (agricultural) pesticides.**								
Feed Commodity	% Dry Matter	% Diet	Residue Estimate (ppm)		Dietary Contribution [1] (ppm)		Max. Feed Per Day on a Dry Wt. Basis (Kg)	Dietary Exposure Estimate (mg)	
			Highest Ave	Max	Highest Ave	Max		Highest Ave	Max
Beef and Dairy Cattle									
Cowpea forage	30	40	100 [2]	300 [2]	133	400			
Cowpea hay	86	20	100 [2]	300 [2]	23	70			
Sorghum grain	86	40	40 [3]	70 [3]	19	33			
Total Burden					175	500	9.1 [5]	1600	4600
Poultry									
Sorghum grain	Not Used [1]	80	40 [3]	70 [3]	32	56			
Rice bran		20	40 [4]	70 [4]	8	14			
Total Burden					40	70			

[1] Dietary Contribution for Cattle = (Residue Estimate in ppm ÷ %DM) x %Diet
Dietary Contribution for Poultry = Residue Estimate in ppm x %Diet

[2] Based on the available straw (flax, oat, wheat, rice) and forage (guar plants, sorghum stalks, soybean forage) data, **maximum** residues of sodium chlorate in/on straw and forage livestock feedstuffs harvested 3-7 days after treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application) are not expected to exceed 300 ppm at the point of harvest. On **average**, residues in/on straw and forage livestock feedstuffs should not exceed 100 ppm when harvested 7-14 days after foliar treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application).

[3] Based on the available sorghum field trial data alone, **maximum** residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate for sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 70 ppm. On **average**, residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate on sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 40 ppm.

[4] Translated from sorghum grain estimate.

[5] Cattle eat a maximum of 9.1 kg of feed per day on a dry wt. basis (Update of Livestock Feed Consumption, 1993)

The highest average residues of chlorate (excluding percent crop treated data) in meat, poultry, and eggs are expected to be <4 ppm and in milk are expected to be <0.5 ppm based on the following information and assumptions:

- The highest average theoretical dietary burden for livestock is 175 ppm for cattle feed on a dry wt. basis
- Cattle eat a maximum of 9.1 kg of feed per day on a dry wt. basis (Update of Livestock Feed Consumption, 1993); hence, the highest average theoretical dietary exposure for sodium chlorate to livestock is 1600 mg per day
- Based on the available rat metabolism data, <1% of the initial dose of chlorate is expected to be incurred in animal tissues 72 hours after exposure (Abdel-Rahman *et al*, 1982, 1984b and 1985); hence <16 mg is expected to be incurred in any livestock tissue of interest
- Assuming that kidneys have the lowest weight of the organs/tissues of interest (other than milk) in livestock (*i.e.*, compared to meat, liver, fat, and eggs)
- Assuming that the average weight of cattle kidneys is about 4 kg (Update of Livestock Feed Consumption, 1993; cattle kidneys weigh 3.6-4.5 kg)
- Assuming that the average milk production per day is about 30 kg (Frank, 2002; milk production is 50-90 lb milk/cow/day)

Calculations:

$$\frac{\text{(Highest Average Theoretical Dietary Exposure (1600 mg) x Percent of Dietary Exposure Expected in Organs (< 1\%)}}{\text{Average Weight of the Organ/Tissue of Interest (Kidney at 4 Kg or Milk at 30 Kg)}}$$

Highest Average Residue Estimate in Meat, Poultry, and Eggs = <4 ppm
Highest Average Residue Estimate in Milk = <0.5 ppm

The maximum residues of chlorate (excluding percent crop treated data) in meat, poultry, and eggs are expected to be <12 ppm and in milk are expected to be <2 ppm based on the following information and assumptions:

- The maximum theoretical dietary burden for livestock is 500 ppm for cattle feed on a dry wt. basis
- Cattle eat a maximum of 9.1 kg of feed per day on a dry wt. basis (Update of Livestock Feed Consumption, 1993); hence, the highest average theoretical dietary exposure for sodium chlorate to livestock is 4600 mg per day
- Based on the available rat metabolism data, <1% of the initial dose of chlorate is expected to be incurred in animal tissues 72 hours after exposure (Abdel-Rahman *et al*, 1982, 1984b and 1985); hence <46 mg is expected to be incurred in any livestock tissue of interest
- Assuming that kidneys have the lowest weight of the organs/tissues of interest (other than milk) in livestock (*i.e.*, compared to meat, liver, fat, and eggs)
- Assuming that the average weight of cattle kidneys is about 4 kg (Update of Livestock Feed Consumption, 1993; cattle kidneys weigh 3.6-4.5 kg)
- Assuming that the average milk production per day is about 30 kg (Frank, 2002; milk production is 50-90 lb milk/cow/day)

Calculations:

$$\frac{\text{(Maximum Theoretical Dietary Exposure (4600 mg) x Percent of Dietary Exposure Expected in Organs (< 1\%)}}{\text{Average Weight of the Organ/Tissue of Interest (Kidney at 4 Kg or Milk at 30 Kg)}}$$

Maximum Residue Estimate in Meat, Poultry, and Eggs = <12 ppm
Maximum Residue Estimate in Milk = <2 ppm

860.1500 Crop Field Trials

Available crop field trial data deemed the primary sources of information to support the reregistration of sodium chlorate are briefly discussed below and summarized in Table C.5. All other available crop field trial data are considered supplemental and will not be discussed further. No additional crop field trial data are required to support the reregistration of sodium chlorate.

The subject data, except the potato tuber data, were all collected using the colorimetric method (Branderis, J. Sci. Food Agric., 16, 558 (1965)), deemed acceptable for data collection and enforcement of the established sodium chlorate exemptions from the requirement of a tolerance. The potato tuber data were collected with a more selective HPLC method ("Determination of Residues of Sodium Chlorate in Potatoes", Method #S57023, 4/2/91) deemed adequate for data collection. The lowest limits of quantitation (LOQs) of these methods is estimated at 1 ppm.

Based on the available flax, guar, southern pea, soybean, and sunflower field trial data no detectable residues of sodium chlorate (<1 ppm) are expected in/on dry beans, guar beans, southern peas, soybeans, flaxseed, safflower seed, and sunflower seed at the point of harvest from the maximum use rate of sodium chlorate on dry beans, guar, southern peas, soybeans, flax, safflower, and sunflower (1 application; 7.5 lbs ai/A; 7-day PHI). Furthermore, no detectable residues of sodium chlorate (<1 ppm) are expected in/on cottonseed at the point of harvest from the maximum use rate of sodium chlorate on cotton (2 applications, 7.5 lbs ai/A/application; 7-day PHI). Any residues which might be detected at the point of harvest are expected to be primarily surface residues which would be substantially removed prior to the point of consumption.

Based on the available chili pepper field trial data, it is possible that detectable residues of sodium chlorate (ca. 13 ppm) might be found on the surface of unwashed chili peppers treated with sodium chlorate at the maximum use rate of sodium chlorate on chili peppers (1 application; 12.5 lbs ai/A/application; 10-day PHI). However, these residues are primarily surface residues present at the point of harvest which would be substantially removed by washing (<1 ppm) prior to the point of consumption.

Based on the available potato field trial data, no detectable residue of sodium chlorate (<1 ppm) are expected in/on potato tubers at the point of harvest from the maximum use rate of sodium chlorate on potatoes (1 application; 12.5 lbs ai/A; 7-day PHI). As demonstrated by the chili pepper field trial data, any residues present at harvest are expected to be primarily surface residues which would be substantially removed by washing prior to the point of consumption.

Based on the available oat, rice, sorghum, and wheat field trial data, it is possible that detectable residues of sodium chlorate (ca. 70 ppm (maximum) as demonstrated by sorghum grain) might be found on the surface of cereal grains retaining their outer hulls at harvest (such as oats and sorghum) from the maximum use rate of sodium chlorate on rice and sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) and wheat (1 application; 6 lbs ai/A; 3-day PHI). However, once the outer hulls are removed (either at harvest or during processing), no detectable residues of sodium chlorate

(<1 ppm) are expected in/on cereal grains such as rice and wheat (as demonstrated by rice w/out hulls and wheat grain data).

Based on the available sorghum field trial data alone, **maximum** residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate for sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 70 ppm. On **average**, residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate on sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 40 ppm.

Translating the available sorghum field trial data to corn, residues of sodium chlorate are not expected to exceed 20 ppm (ca. 10 ppm on average) in/on corn grain at the point of harvest from the maximum use rate of sodium chlorate on corn (1 application, 7.5 lbs ai/A; 14-day PHI). As demonstrated by the chili pepper field trial data, any residues present at harvest are expected to be primarily surface residues which would be substantially removed by washing prior to the point of consumption. Hence, residues of sodium chlorate in/on sweet corn after washing and prior to consumption would not be expected to exceed 1 ppm.

Based on the available straw (flax, oat, wheat, rice) and forage (guar plants, sorghum stalks, soybean forage) data, **maximum** residues of sodium chlorate in/on straw and forage livestock feedstuffs harvested 3-7 days after treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application) are not expected to exceed 300 ppm at the point of harvest. On **average**, residues in/on straw and forage livestock feedstuffs should not exceed 100 ppm when harvested 7-14 days after foliar treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application).

Chili peppers: MRID 00116554

Chili pepper plants were treated with a single application of sodium chlorate at 8 or 16 lb ai/A. Chili pepper samples were collected 7-21 days after treatment. Residues of chlorate in/on chili pepper samples were <0.1 to 13 ppm. After washing the treated chili peppers with water, residues of chlorate were all <0.1 ppm.

Flax, Oats, Wheat: MRID 00136326

Flax, oats, and wheat plots were treated with a single application of sodium chlorate at 6 or 12 lbs ai/A. Grain and straw samples were collected 3-10 days after treatment. Residues of chlorate in/on flax grain/straw, wheat grain/straw and oat straw samples were <2 ppm. Residues of chlorate in/on oat grain samples treated at 6 and 12 lbs ai/A were 10-36 ppm (20 ppm average) and <2-125 ppm (80 ppm average), respectively.

Guar: MRID 00136388

Guar plots were treated with a single application of sodium chlorate at 6 or 12 lbs ai/A. Seed and plant samples were collected 2-14 days after treatment. Residues of chlorate in/on seed samples <10 ppm. Residues of chlorate in/on plant samples were 18-266 ppm.

Potatoes: MRID 42464201 (Chromatograms - MRID 42930601)
Potato plants were treated with a single application of sodium chlorate at 9 lbs ai/A. Potato tubers were collected 7-10 days after treatment. Residues of chlorate in/on potato tubers were <1.0 ppm.

Rice: MRID 00159210
Rice plots were treated with a single application of sodium chlorate at 6 or 12 lbs ai/A. Grain w/out hulls, grain with hulls, and straw samples were collected 2-9 days after treatment.

While residues of chlorate in/on grain with hulls collected 8 days after treatment were 7-160 ppm, residues in/on grain w/out hulls collected 7 days after treatment were essentially nil (reported as 0.0 ppm). Detectable residues (0.0-30 ppm) were reported in/on grain w/out hulls collected 2 days after treatment at 12 lbs ai/A.

Residues of chlorate in/on straw samples ranged from <1 ppm to 44 ppm from treatment at 6 lbs ai/A and from <1 ppm to 438 ppm from treatment at 12 lbs ai/A.

Sorghum: MRID 00123727
Sorghum plots were treated with a single application fo sodium chlorate at 3, 6, and 12 lbs ai/A. Grain and stalk samples were collected 2-14 days after application.

Residues of chlorate in/on grain samples collected 7 and 14 days after treatment at 6 lbs ai/A were 44-69 ppm (59 ppm average) and 8-21 ppm (13 ppm average), respectively. Residues of chlorate in/on grain samples collected 7 and 14 days after treatment at 12 lbs ai/A were 83-132 ppm (106 ppm average) and 13-40 ppm (30 ppm average), respectively.

Residues of chlorate in/on stalk samples collected 7-14 days after treatment at 6 lbs ai/A were essentially nil (0.0 ppm) to 51 ppm (21 ppm average). Residues of chlorate in/on stalk samples collected 7-14 days after treatment at 12 lbs ai/A were essentially nil (0.0 ppm) to 352 ppm (117 ppm average).

Southern Peas (cowpeas): MRID 00128727
Southern pea plots were treated with a single application of sodium chlorate at 6 lbs ai/A. Shelled pea samples were collected 4 or 5 days after treatment. Some of the raw shelled peas were processed into frozen peas. Residues of sodium chlorate were <0.3 ppm in/on all samples.

Soybeans: MRID 00128727
Soybean plots were treated with a single application of sodium chlorate at 6 or 12 lbs ai/A. Soybean and foliage samples were collected 2-14 days after treatment. Residues of chlorate in/on soybeans collected 7-14 days after treatment were <5.0 ppm. Residues of chlorate in/on soybean foliage collected 7 days after treatment at 6 or 12 lbs ai/A were as high as 153 ppm and 526 ppm, respectively. Residues of chlorate in/on soybean forage collected 14 days after treatment at 6 or 12 lbs ai/A were as high as 100 ppm and 318 ppm, respectively.

Sunflower Seeds: MRID 00135224

Sunflower plots were treated with a single application of sodium chlorate at 3, 6, or 12 lbs ai/A. Seed samples were collected 2-14 days after treatment. Residues of sodium chlorate in/on all samples were essentially nil (reported as 0 ppm) except 1 seed sample collected 4 days after treatment at 12 lbs ai/A which showed residues of 10 ppm (average of 3 replicates; one replicate showed residues of 30 ppm).

Table C.4.	**Summary of available crop field trial data. Note: Guar, rice, sorghum, soybean, and sunflower data are truncated in this table. Data, except wheat grain data, collected less than 7 days after treatment have been intentionally excluded in this table but may be included in the brief discussions above.**				
Matrix	**Crop**	**Application Rate (lbs ai/A)**	**PHI (days)**	**Residues (ppm)**	
				Maximum [1]	**Estimated Average [2]**
Vegetable	Chili pepper (raw)	8 or 16	7-21	13	Not Calculated
	Chili pepper (washed)			<0.1	<0.1
	Potato tuber	9	7-10	<1	<1
Seed/Bean	Flax	6	10	<2	<2
	Guar		7	<10	<10
	Southern pea		4-5	<0.3	<0.3
	Soybean		7-14	<5	<5
	Sunflower		7-14	essentially nil (zero)	essentially nil (zero)
	Flax	12	10	<2	<2
	Guar		7-14	<10	<10
	Soybean		7-14	<5	<5
	Sunflower		7-14	essentially nil (zero)	essentially nil (zero)
Cereal Grain	Oat	6	8	36	20
	Rice w/out hulls		7-9	essentially nil (zero)	essentially nil (zero)
	Rice with hulls		8	13	9.7
	Sorghum		7	69	59
			14	21	13
	Wheat		3-9	<2	<2
	Oat	12	8	125	80
	Rice w/out hulls		7-9	essentially nil (zero)	essentially nil (zero)
	Rice with hulls		8	160	93

	Sorghum		7	132	106
			14	40	30
	Wheat		3-9	<2	<2
Straw	Flax, Oat, Wheat	6 or 12	3-10	<2	<2
	Rice	6	7-9	44	11
		12	7-9	438	75
Forage	Guar plants	6	7	58	40
		12	7-14	106	70
	Sorghum stalk	6	7-14	51	21
		12	7-14	352	117
	Soybean forage	6	7	153	Reviewer Cannot Determine
			14	100	
		12	7	526	
			14	318	

[1] **Maximum residue as reported in the data submission.**
[2] **Estimated Average calculated by the reviewer.**

860.1520 Processed Food and Feed

No processing data have been submitted regarding residues of sodium chlorate in/on processed food/feed commodities (corn, cotton, flaxseed, potato, rice, safflower, sorghum, and wheat). However, since no significant residues were found in the raw agricultural commodities subject to processing, it is unlikely that significant residues will occur in the processed fractions.

860.1650 Submittal of Analytical Reference Standards

As of 8/11/04, an analytical reference standard for sodium chlorate is not available at the EPA National Pesticide Standards Repository.

860.1850 Confined Accumulation in Rotational Crops

No data have been submitted regarding residues of sodium chlorate in/on confined accumulation in rotational crops.

860.1900 Field Accumulation in Rotational Crops

No data have been submitted regarding residues of sodium chlorate in/on field accumulation in rotational crops.

RESIDUE CHEMISTRY REFERENCES

Studies Considered Primary Sources of Information and Used in the Assessment

PUBLISHED

Abdel-Rahman MS, Couri D, Bull RJ. 1982. Metabolism and pharmacokinetics of alternate drinking water disinfectants. Environ Health Perspect. 46:19-23.

Abdel-Rahman MS, Couri D, Bull RJ. 1984b. The Kinetics of Chlorite and Chlorate in the Rat. Journal of the American College of Toxicology, 3(4): 261-267.

Abdel-Rahman MS, Couri D, Bull RJ. 1985. The kinetics of chlorite and chlorate in rats. J Environ Pathol Toxicol Oncol. 6(1):97-103.

Frank, G. 2002. Cost of Milk Production per Hundredweight Equivalent in Milk Sold per Cow Ranges. Wisconsin Dairy Data. Fact Sheet 2002-01. Center for Dairy Profitability. Univ. Wisconsin Extension Service. Oct. 2002.

UNPUBLISHED

49610 Rhone-Poulenc Chemical Company (1959) Method of Analysis for Chlorates. (Unpublished study received Jan 4, 1962 under 359-400; CDL:119511-B)

62497 Pernert, J.C. (1960) On the Possibility of Toxic Residues following Cotton Defoliation by Chlorate. (Unpublished study received Dec 18, 1969 under 0F0926; prepared by Hooker Chemical Corp., submitted by Fenrich-Vincent Associates, Manhasset, N.Y.; CDL: 093232-G)

66802 Fenrich-Vincent Associates (1969) Analytical Methods and Results of Tests on the Amount of Residue Remaining in or on Raw Cottonseed When an (Inert Ingredient) has Been Used on the Cotton Plant. Unpublished study; 14 p.

66804 Gauditz, I. (1959) The Results of Tests on the Amount of Residue Remaining, Including a Description of the Analytical Methods Used: (Penco De-fol-ate). (Unpublished study received May 30, 1970 under 0F0926; submitted by Fenrich-Vincent Associates, Manhasset, N.Y.; CDL:091580-O)

66805 Banderis, A. (1965) Colorimetric Determination of chlorate in soil and plant extracts. Journal of the Science of Food and Agriculture 16(Sep):558-564. (Also In unpublished submission received May 30, 1970 under 0F0926; submitted by Fenrich-Vincent Associates, Manhasset, N.Y.; CDL:091580-P)

66808 Peniston, Q.P. (1968) Letter sent to E.H. Karr dated Jan 3, 1968: Determination of sodium chlorate residues on cottonseed: Report # 3. (Unpublished study received May 30, 1970 under 0F0926; prepared by Food, Chemical & Research Laboratories, Inc., submitted by Fenrich-Vincent Associates, Manhasset, N.Y.; CDL:091580-T)

66809 Peniston, Q.P. (1968) Letter sent to E.H. Karr dated Jul 30, 1968: Determination of sodium chlorate residues in ground cottonseed--report # 4: Lab. No. 5639. (Unpublished study received May 30, 1970 under 0F0926; prepared by Food, Chemical & Re- search Laboratories, Inc., submitted by Fenrich-Vincent Associates, Manhasset, N.Y.; CDL:091580-U)

66810 Peniston, Q.P. (1969) Letter sent to E.H. Karr dated Feb 18, 1969: Further studies on determination of sodium chlorate residues in ground cottonseed--report #5: Lab. No. 5879; prepared by Food, Chemical & Research Laboratories, Inc. Unpublished study; 2 p.

116554 California, Dept. of Agriculture (1971) Application of Shed-A-Leaf on Chili Peppers: Results. (Compilation; unpublished study received Oct 13, 1972 under 2E1286; CDL:091822-A)

123747 Banderis, A. (1965) Colorimetric determination of chlorate in soil and plant extracts. J. Sci. Ef. Agric. 16(Sep):558. (Also In unpublished submission received 1965 under 3E1386; submitted by Interregional Research Project No. 4, New Brunswick, NJ; CDL: 093699-B)

124680 Roth, F. (1967) A test for chlorate residues. Bulletin of Environmental Contamination & Toxicology 2(4):251-254. (Also In unpublished submission received Jun 23, 1972 under 2E1286; submitted by California, Dept. of Agriculture, Sacramento, CA; CDL:094665-A)

128727 Interregional Research Project No. 4 (1983) The Results of Tests on the Amount of Residues Remaining in or on Southern Peas, Including a Description of the Analytical Method Used. (Compilation; unpublished study received Jun 10, 1983 under 3E2910; CDL:071699-A)

135224 Interregional Research Project No. 4 (1975) The Results of Tests on the Amount of Sodium Chlorate Residue Remaining in or on Sunflower Seeds, Including a Description of the Analytical Method Used. (Compilation; unpublished study received Jul 1, 1976 under 6E1825; CDL:097356-A)

136326 Interregional Research Project No. 4 (1978) The Results of Tests on the Amount of Sodium Chlorate Residue Remaining in or on Flax, Oats, and Wheat Including a Description of the Analytical Method Used. (Compilation; unpublished study received Oct 20, 1978 under 9E2142; CDL:097460-A)

136388 Interregional Research Project No. 4 (1979) Results of Tests Concerning the Amount of Sodium Chlorate Residue Remaining in or on Guar Including a Description of the Analytical Method Used. (Compilation; unpublished study received Jun 15, 1979 under 9E2220; CDL:098331-A)

159210 Kerr-McGee Chemical Corp. (1975) Sodium Chlorate on Rice: Summary of Experimental Conditions and Data from Texas and Louisiana in 1975. Unpublished study. 12 p.

42464201 McGaughey, R. (1992) Determination of the Magnitude of Residues of Sodium Chlorate in Potatoes Treated with DEFOL6: Final Report: Lab Project Number: DREX-9002: 9006-010X: 04-9012. Unpublished study prepared by Compliance Services Intl. 112 p.

42930601 McGaughey, R. (1993) Determination of the Magnitude of Residues of Sodium Chlorate in Potatoes Treated with DEFOL 6: Lab Project Number: DREX-9002. Unpublished study prepared by Minnesota Valley Testing Labs. 22 p.

Study Citations Considered Supplemental Sources of Information

5620 United States Borax & Chemical Corporation (1967) Residue Data. (Unpublished study received Apr 1, 1969 under 9F0783; CDL: 091347-A)

48007 Abernathy, J.; Miller, C.S.; Richard, J. (1975) Sodium chlorate on Sunflowers. Prepared in cooperation with Texas A & M Univ., Agricultural Experiment Station and Iowa State Univ., Ames Laboratory. Unpublished study; 17 p.

48009 Smith, D.T.; Eastin, E.F.; Wiese, A.F.; et al. (1976) Summary of Experimental Conditions and Data from Texas and Oklahoma in 1975. (Unpublished study received Aug 12, 1980 under 2342-964; prepared in cooperation with Texas A & M Univ., Agricultural Experiment Station and others, submitted by Kerr-McGee Chemical Corp., Oklahoma City, Okla.; CDL:243078-I)

48064 Abernathy, J.; Scrib, J.; Miller, C.S.; et al. (1975) Sodium chlorate on Sunflowers: Summary of Experimental Conditions and Data from Texas in 1975; prepared in cooperation with Texas A & M Univ. Agricultural Experiment Station and Iowa State Univ., Ames Laboratory E.R.D.A. Unpublished study; 17 p.

48065 Smith, D.T.; Eastin, E.F.; Wiese, A.F.; et al. (1975) Summary of Experimental Conditions and Data from Texas and Oklahoma in 1975. (Unpublished study received Aug 12, 1980 under 2342-964; prepared in cooperation with Texas A & M Univ., Agricultural Ex- periment Station and others, submitted by Kerr-McGee Chemical Corp., Oklahoma City, Okla.; CDL:243079-E)

49609 Chipman Chemical Company, Incorporated (1962) Progress Report: Residue Data following the Field Use of Shed-a-Leaf on Tomatoes as a Defoliant/Desiccant in California and New York State from Applications Made Fall of 1961. (Unpublished study received Jan 4, 1962 under 359-400; submitted by Rhone-Poulenc Chemical Co., Monmouth Junction, N.J.; CDL:119511-A)

53626 Chipman Chemical Company, Incorporated (1961) Residue Data Sheet. (Unpublished study received Jan 4, 1962 under 359-400; submitted by Rhone-Poulenc Chemical Co., Monmouth Junction, N.J.; CDL: 119510-A)

58490 Pennwalt Corporation (1975) Efficacy of Sodium chlorate--Rice. (Reports by various sources; unpublished study, including published data, received Oct 14, 1976 under 4581-328; CDL:232133-T)

66803 Walaski, L.J. (1960) Residue Analysis and Reports. (Unpublished study received May 30, 1970 under 0F0926; prepared by Chipman Chemical Co., Inc., submitted by Fenrich-Vincent Associates, Manhasset, N.Y.; CDL:091580-N)

74958 Rhone-Poulenc Chemical Company (1964) Tests with Shed-a-leaf L. (Compilation; unpublished study received Apr 16, 1964 under 359- 399; CDL:023331-A)

74967 Walaski, L.J. (1962) Analyses of Dry Edible Beans, Stalks, and Pods for Possible Residues of Borate and Chlorate: BB/9/62. (Unpublished study received Dec 3, 1962 under 359-399; prepared by Chipman Chemical Co., Inc., submitted by Rhone-Poulenc Chemical Co., Monmouth Junction, N.J.; CDL:101365-B)

75021 Chipman Chemical Company, Incorporated (1960) Results of Analyses for Chlorate and Borate Residues on Cottonseed from 1959 & 1960 California Cotton Samples. (Unpublished study received Jan 19, 1961 under 359-399; submitted by Rhone-Poulenc Chemical Co., Monmouth Junction, N.J.; CDL:119545-A)

75023 Rhone-Poulenc Chemical Company (1963) Residues in Sorghum and Rice. (Compilation; unpublished study, including letter dated Jul 1, 1963 from L.R. Reed to Commissioner of Food & Drugs, Food & Drug Administration, Department of Health, Education, & Wel- fare, received Jul 2, 1963 under unknown admin. no.; CDL: 119636-A)

75025 Walaski, L.J. (1963) Analysis of Potatoes for Possible Residues of Borate following Applications of Chlorate/Sodium Metaborate Combinations for Vinekilling: BB/1/63. (Unpublished study received May 21, 1963 under 359-399; prepared by Chipman Chemical Co., Inc., submitted by Chipman Chemical Co., Bound Brook, NJ; CDL: 119640-A)

123745 Interregional Research Project No. 4 (1973) The Results of Tests on the Amount of Sodium Chlorate Residue Remaining on or in Grain Sorghum, Including a Description of the Analytical Method Used. (Compilation; unpublished study received Apr 13, 1973 under 3E1386; CDL:093698-C)

140109 Interregional Research Project No. 4 (1975) The Results of Tests on the Amount of Sodium Chlorate Residue Remaining in or on Sunflower Seeds, Including a Description of the Analytical Method Used. (Compilation; unpublished study received Jul 1, 1976 under 6E1825; CDL:095932-A)

140483 Interregional Research Project No. 4 (1977) The Results of Tests on the Amount of Sodium Chlorate Residue Remaining in or on Corn Including a Description of the Analytical Method Used. (Compilation; unpublished study received Jun 24, 1977 under 7E1972; CDL:097261-A)

140486 Interregional Research Project No. 4 (1976) The Results of Tests on the Amount of Sodium Chlorate Residue Remaining on or in Rice and Rice Straw Including a Description of the Analytical Method Used. (Compilation; unpublished study received Apr 6, 1976 under 6E1996; CDL:097358-A)

159211 Ladd, R. (1976) Meat and Milk Residue Study with Antor Herbicide in a Dairy Cow [Dosing Information Only]: Project No. 76-12: IBT No. 8580-09096. Unpublished study prepared by Industrial Bio- Test Laboratories, Inc. 21 p.

APPENDIX D TOLERANCE REASSESSMENT SUMMARY
For Inorganic Chlorates as active or inert ingredients in conventional (agricultural) pesticides

NOTE: Tolerances and/or exemptions from the requirement of a tolerance for inorganic chlorates as active or inert ingredients in antimicrobial agents is not the purview of HED and should be addressed by AD.

Existing exemptions from the requirement of a tolerance for sodium chlorate (073301) as an active ingredient in conventional (agricultural) pesticides listed under 40 CFR 180.1020

Sodium chlorate is currently registered for preharvest and foliar applications as a defoliant or desiccant to the following food/feed crops: dry beans, corn, cotton, flax, guar, chili peppers, potatoes, rice, safflower, sorghum (grain), southern peas (*i.e.*, cowpeas), soybeans, and sunflowers.

Under 40 CFR 180.1020 (a) Sodium chlorate is exempt from the requirement of a tolerance for residues in or on the following raw agricultural commodities when used as a defoliant, desiccant, or fungicide in accordance with good agricultural practice: beans (dry, edible), corn (fodder), corn (forage), corn (grain), cottonseed, flaxseed, flax (straw), guar beans, peas (southern), peppers (chili), potatoes, rice, rice (straw), safflower (grain), sorghum (grain), sorghum (fodder), sorghum (forage), soybeans and sunflower seed.

Under 40 CFR 180.1020 (b) A time-limited exemption from the requirement of a tolerance is established for residues of the defoliant/desiccant in connection with use of the pesticide under section 18 emergency exemptions granted by EPA. This exemption has been granted for wheat and will expire on 12/31/04. As requested by the Registration Division (*Sodium Chlorate Use Closure Memo Amendment*; J. Guerry; dated 11/15/2004) the use of sodium chlorate on wheat is also addressed herein with the intention to convert the time-limited exemption status to a permanent exemption from the requirement of a tolerance under 40 CFR.1020 (a). The proposed use rate is for a single application of sodium chlorate to wheat at 6 lbs ai/A with a 3-day PHI.

Sodium chlorate exemptions under 40 CFR 180.1020 (a) from the requirement of a tolerance should be amended as follows to: (1) specify defoliant and desiccant use only, (2) specify use on crops rather than raw agricultural commodities, (3) include wheat concomitant with the revocation of wheat under 40 CFR 180.1020 (b).

40 CFR 180.1020 (a) Sodium chlorate is exempt from the requirement of a tolerance for residues when used as a defoliant or desiccant in accordance with good agricultural practice on the following crops: Bean (dry), Corn, Cotton, Cowpeas, Flax, Guar, Pepper (non-bell), Potato, Rice, Safflower, Sorghum (grain), Soybeans, Sunflower, and Wheat.

Table D.1. Tolerance Reassessment Summary for Sodium Chlorate Listed under 40 CFR 180.1020(a)			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	[*Correct Definition*] Comments
beans, dry, edible	Exempt	Exempt	[*Bean (dry)*]
corn, fodder	Exempt	Exempt	[*Corn*]
corn, forage	Exempt		
corn, grain	Exempt		
cottonseed	Exempt	Exempt	[*Cotton*]
flaxseed	Exempt	Exempt	[*Flax*]
flax, straw	Exempt	Revoke	Flax straw is not listed in Table 1 of OPPTS 860.1000
guar beans	Exempt	Exempt	[*Guar*]
peas, southern	Exempt	Exempt	[*Cowpea*]
potatoes	Exempt	Exempt	[*Potato*]
peppers, chili	Exempt	Exempt	[*Pepper (nonbell)*]
rice	Exempt	Exempt	[*Rice*]
rice, straw	Exempt	Exempt	
safflower, grain	Exempt	Exempt	[*Safflower*]
sorghum, grain	Exempt	Exempt	[*Sorghum (grain)*]
sorghum, fodder	Exempt		
sorghum, forage	Exempt		
soybeans	Exempt	Exempt	[*Soybeans*]
sunflower seed	Exempt	Exempt	[*Sunflower*]
Wheat	None	Exempt	[*Wheat*] Concomitant with the revocation of wheat under 40 CFR 180.1020 (b)

Needed exemptions from the requirement of a tolerance for sodium chlorate (873301) and potassium chlorate (900583) as inert ingredients in conventional pesticides

Sodium chlorate (873301) as an inert ingredient in herbicide formulation products can be applied professionally to agricultural (corn, guava, macadamia nuts, sorghum grain, sugarcane, wheat), commercial (non-agricultural), and residential sites. These conventional pesticide products contain < 1 % sodium chlorate and can be applied at rates no greater than 0.07 lb (as sodium chlorate) per acre.

Potassium chlorate (900583) as an inert ingredient in airborne fungicide products can be applied in poultry premises. These conventional pesticide products contain < 20% potassium chlorate and can be applied at rates not greater than 0.01 lb (as potassium chlorate) per 500 ft^3.

Table D.2. Tolerance Exemption Needed

Tolerance Exemption Expression	PC Code	CAS Reg No.	40 CFR §	Use (Pesticidal)	List Classification
Sodium chlorate	873301	7775-09-9	180.920 [1]	Stabilizer	3
Potassium chlorate	900583	3811-04-9	180.930 [2]	Oxidizer	3

1 Residues listed in 40 CFR §180.920 [formerly 40 CFR§ 180.100(d)] are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.

2 Residues listed in 40 CFR §180.930 [formerly 40 CFR§ 180.100(e)] are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to animals.

Codex/International Harmonization

There are no Codex maximum residue limits (MRLs) for sodium chlorate; therefore, no questions of compatibility with U.S. tolerances exist.

APPENDIX E CHLORATE (ClO_3^-) DIETARY EXPOSURE ESTIMATES in FOOD

Exposure estimates for chlorate residues in food are considered conservative and the dietary (food only) risk assessments are deemed upper bound estimates.

Dietary exposure (food only) to inorganic chlorates as the chlorate ion (ClO_3^-) may be expected from the following dietary exposure routes: (1) from sodium chlorate (073301) as an active ingredient in conventional (agricultural) pesticides used on food crops; (2) from sodium chlorate (873301) and potassium chlorate (900583) as inert ingredients in conventional pesticides used on food crops or in poultry premises; (3) from secondary residues in meat/milk/poultry/eggs due to residues in animal feedstuffs; (4) from sodium chlorate (873301) and calcium chlorate (875606) as inert ingredients in antimicrobial agents used as fruit, vegetable, and egg sanitizing washes, on mushrooms to control bacterial blotch, as treatments to seed used for sprouting, for conditioning live oysters, in poultry drinking water, in fish filleting, and in pecan cracking/dyeing; (5) as a potential redox of chlorine dioxide and sodium chlorite in conventional and antimicrobial pesticides; (6) from degradation of hypochlorites in antimicrobial agents used as fruit and vegetable washes; and, (7) from translocation of very small amounts of chlorate ion (ClO_3^-) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present as a result of inorganic chlorate pesticide uses. These dietary (food) routes of exposure are discussed below. Dietary exposure estimates for food only to be incorporated into the dietary risk assessments for inorganic chlorate are summarized in Table E.1 below.

No food monitoring data are available for this risk assessment; only limited, chemical-specific field trial data are available. Exposure estimates in food were based on field trial data or, in the case of fruit/vegetable/other washes, was derived from a film thickness model. No Chemical-specific livestock metabolism or feeding data are available; exposure estimates in meat, milk, poultry, and eggs were derived from rat metabolism data, field trial data, and livestock reference information concerning feed consumption, tissue weights, and milk production. In some cases, due to raw data limitations, food exposure estimates are calculated as sodium chlorate. The effects of washing after foliar treatments and, in some cases such as meat, milk, poultry and eggs estimates, percent crop treated data were also incorporated into these exposure estimates.

Table E.1. Summary of Chlorate Dietary (Food) Exposure Estimates for the Dietary Risk Assessments							
Food Group	Food Crop	Acute Dietary Screen - Do Not Use % Crop Treated Data in DEEM	Chronic Dietary				Comments
			From Agricultural Uses Only		From All Uses		
		Exposure Estimate (ppm)	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	
Vegetables	chili peppers	0.5	0.5	√	0.2		Maximum/Average Exposure Estimate from agricultural use: Based on chili pepper, potato, and cereal grain field trial data and considering the effects of washing field treated RACs as demonstrated by the chili pepper washing data, residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm. Note: Incorporating available sodium chlorate percent crop treated data would result in an estimated residue level below that from sanitizing fruit and vegetable wash. Maximum/Average Exposure Estimate from sanitizing fruit and vegetable wash: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.
	potatoes	0.5	0.5	√	0.2		
	sweet corn	0.5	0.5	√	0.2		
	dry beans, guar beans, southern peas, soybeans	0.5	0.5	√	0.2		Maximum/Average Exposure Estimate from agricultural use: Based on seed/bean field trial data taken as a whole, residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm. Note: Incorporating available sodium chlorate percent crop treated data would result in an estimated residue level below that from sanitizing fruit and vegetable wash. Maximum/Average Exposure Estimate from sanitizing fruit and vegetable wash: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.
	all others	0.2	N/A	N/A	0.2		Maximum/Average Exposure Estimate from sanitizing fruit and vegetable wash: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.

Food Group	Food Crop	Acute Dietary Screen - Do Not Use % Crop Treated Data in DEEM	Chronic Dietary				Comments
			From Agricultural Uses Only		From All Uses		
		Exposure Estimate (ppm)	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	
Fruits	guava	0.5	0.5		0.5		Maximum/Average Exposure Estimate from agricultural use: Based on the exposure estimates for sodium chlorate, as an active ingredient, in conventional (agricultural) pesticides used on food crops and considering the effects of washing field treated RACs as demonstrated by the chili pepper washing data, residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm. Note: No percent crop treated data are currently available. Maximum/Average Exposure Estimate from sanitizing fruit and vegetable wash: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.
	citrus fruits (except peels), bananas, plantains, and coconuts	zero	N/A	N/A	zero		Maximum/Average Exposure Estimate from sanitizing fruit and vegetable wash: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm. For citrus fruits, bananas/plantains, and coconuts which have substantial outer peels/husks which are removed prior to consumption and processing, residues are expected to be essentially nil; the exposure estimate is zero. Residues in citrus fruit peels are estimated at 0.2 ppm.
	citrus fruit peel	0.2			0.2		
	all others	0.2			0.2		
Seeds	cottonseed, flaxseed, safflower seed, sunflower seed	0.5	0.5	√	0.5	√	Maximum/Average Exposure Estimate from agricultural use: Based on seed/bean field trial data taken as a whole, residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm.

Food Group	Food Crop	Acute Dietary Screen - Do Not Use % Crop Treated Data in DEEM	Chronic Dietary				Comments
			From Agricultural Uses Only		From All Uses		
		Exposure Estimate (ppm)	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	
Cereal grains	rice	0.5	0.5	√	0.5	√	Maximum/Average Exposure Estimate from agricultural use: Based on rice field trial demonstrating residues in/on rice w/out outer hulls, residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm.
	wheat	0.5	0.5	√	0.5	√	Maximum/Average Exposure Estimate from agricultural use: Based on wheat and other cereal grain field trial data, residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm.
	corn (except sweet)	20	10	√	10	√	Maximum/Average Exposure Estimate from agricultural use: Translated from sorghum field trial data, maximum and average residues in/on corn grain are not expected to exceed 20 ppm and 10 ppm, respectively, at the point of harvest (14-day PHI).
	sorghum	70	40	√	40	√	Maximum/Average Exposure Estimate from agricultural use: Based on sorghum field trial data, maximum and average residues in/on sorghum grain are not expected to exceed 70 ppm and 40 ppm, respectively, at the point of harvest (7-day PHI).
Nuts	Macadamia Nuts	0.5	0.5		0.5		Maximum/Average Exposure Estimate from agricultural use: Based on the exposure estimates for sodium chlorate, as an active ingredient, in conventional (agricultural) pesticides used on food crops, residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm. Note: No percent crop treated data are currently available.
	Pecans	0.2	N/A	N/A	0.2		Maximum/Average Exposure Estimate from pecan cracking and dyeing: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.

Food Group	Food Crop	Acute Dietary Screen - Do Not Use % Crop Treated Data in DEEM	Chronic Dietary				Comments
			From Agricultural Uses Only		From All Uses		
		Exposure Estimate (ppm)	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	
Animal Tissues	Meat, Poultry, and Eggs	10	0.1		0.1		Maximum/Average Exposure Estimates from Agricultural uses: Conservative estimates based on the rat metabolism data that demonstrated that <1% of a single initial dose of chlorate is expected to be incurred in any animal tissue 72 hours after oral exposure. Maximum residues are expected to be <12 ppm; the maximum exposure estimate is 10 ppm and is based on: • Maximum theoretical dietary burden for livestock (500 ppm) • Maximum feed rate for livestock (9.1 kg/day) • Average weight (4 kg) of the smallest (by weight) organ of interest (kidney) • Percent crop treated data is not incorporated into the estimate Average residues are expected to be <0.2 ppm; the average exposure estimate is 0.1 ppm and is based on: • Highest average theoretical dietary burden for livestock (175 ppm) • Maximum feed rate for livestock (9.1 kg/day) • Average weight (4 kg) of the smallest (by weight) organ of interest (kidney) • Incorporates highest percent crop treated data (cotton 5%) into the estimate Maximum/Average Exposure Estimates from sanitizing washes: Covered by estimates from agricultural uses.

Food Group	Food Crop	Acute Dietary Screen - Do Not Use % Crop Treated Data in DEEM	Chronic Dietary				Comments
			From Agricultural Uses Only		From All Uses		
		Exposure Estimate (ppm)	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	
	Milk	1	0.01		0.01		Maximum/Average Exposure Estimates from Agricultural uses: Conservative estimates based on the rat metabolism data that demonstrated that <1% of a single initial dose of chlorate is expected to be incurred in any animal tissue 72 hours after oral exposure. Maximum residues are expected to be <2 ppm; the maximum exposure estimate is 1 ppm and is based on: • Maximum theoretical dietary burden for cattle(500 ppm) • Maximum feed rate for cattle (9.1 kg/day) • Average milk production per day (ca. 30 kg) • Percent crop treated data are not incorporated into the estimate Average residues are expected to be <0.03 ppm; the average exposure estimate is 0.01 ppm and is based on: • Highest average theoretical dietary burden for cattle (175 ppm) • Maximum feed rate for (9.1 kg/day) • Average milk production per day (ca. 30 kg) • Incorporates highest percent crop treated data (cotton 5%) into the estimate

Food Group	Food Crop	Acute Dietary Screen - Do Not Use % Crop Treated Data in DEEM	Chronic Dietary				Comments
			From Agricultural Uses Only		From All Uses		
		Exposure Estimate (ppm)	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	Exposure Estimate (ppm)	√ = Use % Crop Treated Data in DEEM	
Misc.	Fish fillets	0.2	N/A	N/A	0.2		Maximum/Average Exposure Estimate from sanitizing fish fillet wash: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.
	Oysters	0.2	N/A	N/A	0.2		Maximum/Average Exposure Estimate from conditioning live oysters: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.
	Mushrooms	0.2	N/A	N/A	0.2		Maximum/Average Exposure Estimate from use to control bacterial blotch on mushrooms: Estimate derived from film thickness model developed by FDA for sanitizing non-porous surfaces. Residues are expected to be <0.3 ppm; the exposure estimate is 0.2 ppm.
	Sugarcane	0.5	0.5		0.5		Maximum/Average Exposure Estimate from agricultural use: Based on exposure estimates from sodium chlorate, as an active ingredient, in conventional (agricultural) pesticides used on food crops. Residues are expected to be <1 ppm; the exposure estimate is 0.5 ppm. Note: No percent crop treated data are currently available.

Note: According to the Usage Report in Support of Reregistration for Sodium Chlorate (Chemical Code 073301/Case No. 4049) dated 10/27/2004, the highest average Percent Crop Treated (PCT) for any crop reported is 5% PCT for cotton; all others are reported as <1% PCT except processed lima beans and safflower which are reported as 2% PCT.

Dietary Exposure Route 1. Chlorate (ClO_3^-) dietary exposure estimates from sodium chlorate (073301) as an active ingredient in conventional (agricultural) pesticides used on food crops

Sodium chlorate is currently registered for preharvest and foliar applications as a defoliant or desiccant to the following food/feed crops: dry beans, corn, cotton, flax, guar, chili peppers, potatoes, rice, safflower, sorghum (grain), southern peas (*i.e.*, cowpeas), soybeans, and sunflowers. For food/feed uses, sodium chlorate is formulated as a soluble concentrate (SC) with the active ingredient ranging from 18% to 47.2%. Sodium chlorate may be applied using aircraft or ground spray equipment, including high and low volume equipment.

Uses of sodium chlorate as a defoliant or desiccant on cauliflower, cucurbit vegetables, and okra grown for seed only are considered non-food uses. Uses of sodium chlorate on ornamental gourds and fallow lands are also considered non-food uses. These non-food uses will not be discussed further with regards to dietary exposure/risk considerations.

Under 40 CFR 180.1020 (a) Sodium chlorate is exempt from the requirement of a tolerance for residues in or on the following raw agricultural commodities when used as a defoliant, desiccant, or fungicide in accordance with good agricultural practice: beans (dry, edible), corn (fodder), corn (forage), corn (grain), cottonseed, flaxseed, flax (straw), guar beans, peas (southern), peppers (chili), potatoes, rice, rice (straw), safflower (grain), sorghum (grain), sorghum (fodder), sorghum (forage), soybeans and sunflower seed.

Under 40 CFR 180.1020 (b) A time-limited exemption from the requirement of a tolerance is established for residues of the defoliant/desiccant in connection with use of the pesticide under section 18 emergency exemptions granted by EPA. This exemption has been granted for wheat and will expire on 12/31/04. As requested by the Registration Division (*Sodium Chlorate Use Closure Memo Amendment*; J. Guerry; dated 11/15/2004) the use of sodium chlorate on wheat is also addressed herein with the intention to convert the time-limited exemption status to a permanent exemption from the requirement of a tolerance under 40 CFR.1020 (a). The proposed use rate is for a single application of sodium chlorate to wheat at 6 lbs ai/A with a 3-day PHI.

Based on the available flax, guar, southern pea, soybean, and sunflower field trial data no detectable residues of sodium chlorate (<1 ppm) are expected in/on dry beans, guar beans, southern peas, soybeans, flaxseed, safflower seed, and sunflower seed at the point of harvest from the maximum use rate of sodium chlorate on dry beans, guar, southern peas, soybeans, flax, safflower, and sunflower (1 application; 7.5 lbs ai/A; 7-day PHI). Furthermore, no detectable residues of sodium chlorate (<1 ppm) are expected in/on cottonseed at the point of harvest from the maximum use rate of sodium chlorate on cotton (2 applications, 7.5 lbs ai/A/application; 7-day PHI). Any residues which might be detected at the point of harvest are expected to be primarily surface residues which would be substantially removed prior to the point of consumption.

Based on the available chili pepper field trial data, it is possible that detectable residues of sodium chlorate (ca. 13 ppm) might be found on the surface of unwashed chili peppers treated with

sodium chlorate at the maximum use rate of sodium chlorate on chili peppers (1 application; 12.5 lbs ai/A/application; 10-day PHI). However, these residues are primarily surface residues present at the point of harvest which would be substantially removed by washing (<1 ppm) prior to the point of consumption.

Based on the available potato field trial data, no detectable residue of sodium chlorate (<1 ppm) are expected in/on potato tubers at the point of harvest from the maximum use rate of sodium chlorate on potatoes (1 application; 12.5 lbs ai/A; 7-day PHI). As demonstrated by the chili pepper field trial data, any residues present at harvest are expected to be primarily surface residues which would be substantially removed by washing prior to the point of consumption.

Based on the available oat, rice, sorghum, and wheat field trial data, it is possible that detectable residues of sodium chlorate (ca. 70 ppm as demonstrated by sorghum grain) might be found on the surface of cereal grains retaining their outer hulls at harvest (such as oats and sorghum) from the maximum use rate of sodium chlorate on rice and sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) and wheat (1 application; 6 lbs ai/A; 3-day PHI). However, once the outer hulls are removed (either at harvest or during processing), no detectable residues of sodium chlorate (<1 ppm) are expected in/on cereal grains such as rice and wheat (as demonstrated by rice w/out hulls and wheat grain data).

Based on the available sorghum field trial data alone, **maximum** residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate for sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 70 ppm. On **average**, residues in/on sorghum grain harvested 7-14 days after treatment with sodium chlorate at the maximum use rate on sorghum (1 application; 7.5 lbs ai/A; 7-day PHI) are not expected to exceed 40 ppm.

Translating the available sorghum field trial data to corn, residues of sodium chlorate are not expected to exceed 20 ppm (ca. 10 ppm on average) in/on corn grain at the point of harvest from the maximum use rate of sodium chlorate on corn (1 application, 7.5 lbs ai/A; 14-day PHI). As demonstrated by the chili pepper field trial data, any residues present at harvest are expected to be primarily surface residues which would be substantially removed by washing prior to the point of consumption. Hence, residues of sodium chlorate in/on sweet corn after washing and prior to consumption would not be expected to exceed 1 ppm.

Based on the available straw (flax, oat, wheat, rice) and forage (guar plants, sorghum stalks, soybean forage) data, **maximum** residues of sodium chlorate in/on straw and forage livestock feedstuffs harvested 3-7 days after treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application) are not expected to exceed 300 ppm at the point of harvest. On **average**, residues in/on straw and forage livestock feedstuffs should not exceed 100 ppm when harvested 7-14 days after foliar treatment with sodium chlorate at the maximum use rate permitted on forage crops (1 or 2 applications; 7.5 lbs ai/A/application).

Dietary Exposure Route 2. Chlorate (ClO_3^-) dietary exposure estimates from sodium chlorate (873301) and potassium chlorate (900583) as inert ingredients in conventional (agricultural) pesticides used on food crops or in poultry premises

Sodium chlorate (873301) as an inert ingredient in herbicide formulation products can be applied professionally to agricultural (corn, guava, macadamia nuts, sorghum grain, sugarcane, wheat), commercial (non-agricultural), and residential sites. These conventional pesticide products contain < 1 % sodium chlorate and can be applied at rates no greater than 0.07 lb (as sodium chlorate) per acre.

Taking into account the small percentage of sodium chlorate (873301) in the product(s) and the application rate(s) of the product(s) at issue, chlorate dietary exposure estimates in/on corn, guava, macadamia nuts, sorghum grain, sugarcane, and wheat are expected to be <1 ppm based on the exposure estimates for sodium chlorate (073301) as an active ingredient used in conventional (agricultural) pesticides which are used at higher rates (6-12.5 lb ai/A).

Specifically, based on the available chili pepper and potato data, residues of chlorate in/on guava, macadamia nuts, and sugarcane are expected to be primarily surface residues leaving <1 ppm in/on these commodities after washing and/or removal of outer surfaces prior to consumption, as demonstrated by the available chili pepper washing data and the rice with and w/out hulls field trial data.

Potassium chlorate (900583) as an inert ingredient in airborne fungicide products can be applied in poultry premises. These conventional pesticide products contain < 20% potassium chlorate and can be applied at rates not greater than 0.01 lb (as potassium chlorate) per 500 ft^3.

No chlorate residues are expected in egg commodities from the use of potassium chlorate (900583) as an inert ingredient in poultry premises.

Dietary Exposure Route 3. Chlorate (ClO_3^-) dietary exposure estimates from secondary residues incurred in meat, milk, poultry and eggs from consumption of feedstuffs treated with sodium chlorate (073301 or 873301) as an active or inert ingredient in conventional (agricultural) pesticides

The maximum residues (excluding percent crop treated data) in meat, poultry, and eggs are estimated at 10 ppm and in milk is estimated at 1 ppm based on the following information and assumptions:

- The maximum theoretical dietary burden for livestock is 500 ppm for cattle feed on a dry wt. basis
- Cattle eat a maximum of 9.1 kg of feed per day on a dry wt. basis (Update of Livestock Feed Consumption, 1993); hence, the highest average theoretical dietary exposure for sodium chlorate to livestock is 4600 mg per day
- Based on the available rat metabolism data, <1% of the initial dose of chlorate is expected to be incurred in animal tissues 72 hours after exposure (Abdel-Rahman *et al*, 1982, 1984b and 1985); hence <46 mg is expected to be incurred in any livestock tissue of interest
- Assuming that kidneys have the lowest weight of the organs/tissues of interest (other than milk) in livestock (*i.e.*, compared to meat, liver, fat, and eggs)
- Assuming that the average weight of cattle kidneys is about 4 kg (Update of Livestock Feed Consumption, 1993; cattle kidneys weigh 3.6-4.5 kg)
- Assuming that the average milk production per day is about 30 kg (Frank, 2002; milk production is 50-90 lb milk/cow/day)

Calculations:

(Maximum Theoretical Dietary Exposure (4600 mg) x Percent of Dietary Exposure Expected in Organs (< 1%)
Average Weight of the Organ/Tissue of Interest (Kidney at 4 Kg or Milk at 30 Kg)

Maximum Residue Estimate in Meat, Poultry, and Eggs = <12 ppm; estimated at 10 ppm
Maximum Residue Estimate in Milk = <2 ppm; estimated at 1 ppm

The highest average residues (including percent crop treated data) in meat, poultry, and eggs are estimated at 0.1 ppm and in milk is estimated at 0.01 ppm based on the following information and assumptions:

- The highest average theoretical dietary burden for livestock is 175 ppm for cattle feed on a dry wt. basis (excluding percent crop treated data)
- Cattle eat a maximum of 9.1 kg of feed per day on a dry wt. basis (Update of Livestock Feed Consumption, 1993); hence, the highest average theoretical dietary exposure for sodium chlorate to livestock is 1600 mg per day (excluding percent crop treated data)
- The maximum percent crop treated is 5% on cotton all other feed crops are <1% (Usage Report from A. Halvorson to B. Cropp-Kohlligian and J. Guerry dated 10/27/2004)

hence, the highest average theoretical dietary exposure for sodium chlorate to livestock is 80 mg per day (including percent crop treated data at 5%).

- Based on the available rat metabolism data, <1% of the initial dose of chlorate is expected to be incurred in animal tissues 72 hours after exposure (Abdel-Rahman *et al*, 1982, 1984b and 1985); hence <0.8 mg is expected to be incurred in any livestock tissue of interest
- Assuming that kidneys have the lowest weight of the organs/tissues of interest (other than milk) in livestock (*i.e.*, compared to meat, liver, fat, and eggs)
- Assuming that the average weight of cattle kidneys is about 4 kg (Update of Livestock Feed Consumption, 1993; cattle kidneys weigh 3.6-4.5 kg)
- Assuming that the average milk production per day is about 30 kg (Frank, 2002; milk production is 50-90 lb milk/cow/day)

Calculations:

$$\frac{\text{Highest Average Theoretical Dietary Exposure (80 mg)} \times \text{Percent of Dietary Exposure Expected in Organs (< 1\%)}}{\text{Average Weight of the Organ/Tissue of Interest (Kidney at 4 Kg or Milk at 30 Kg)}}$$

Highest Average Residue Estimate in Meat, Poultry, and Eggs = <0.2 ppm; estimated at 0.1 ppm
Highest Average Residue Estimate in Milk = <0.03 ppm; estimated at 0.01 ppm

Dietary Exposure Route 4. Chlorate (ClO_3^-) dietary exposure estimates from sodium chlorate (873301) and calcium chlorate (875606) as inert ingredients in antimicrobial agents used: (1) as fruit, vegetable, and egg sanitizing washes; (2) to control bacterial blotch on mushrooms; (3) as treatment to seed used for sprouting; (4) for conditioning live oysters; (5) in poultry drinking water; (6) in fish filleting; and (7) pecan cracking/dyeing

Fruit and vegetable sanitizing washes:
Using a film thickness model, residues of chlorate in/on fruits and vegetables treated at the maximum use rate are expected to be <0.3 ppm; estimated at 0.2 ppm.

This estimate will also be used for seed sprouting, mushrooms, oysters, fish fillets, and pecans.

This estimate will also cover estimates on fruits and vegetables from Dietary Exposure Routes 5, 6, 7, and 8 identified below.

Since these residues are expected to be primarily surface residues in fruits which have substantial outer peels which are removed prior to consumption, residues of chlorate in citrus fruits, bananas and plantains are expected to be essentially nil (zero) once the peels are removed.

No chlorate residues are expected in egg commodities from surface sanitizing washes. Chlorate residue estimates in poultry commodities from chlorate in antimicrobial agents use in poultry drinking water are covered by the secondary residue estimates for meat/milk/poultry/egg addressed above under Dietary Exposure Route 3.

Calculation for percent chlorate in the sanitizing washes:

For the active ingredient(s) the maximum use rate is 500 ppm as total chlorine in the sanitizing wash water. Exposure time is 1-2 minutes.

Percent of chlorate as an inert in the product is at most 2%.
This is equivalent to ca. <15 ppm or <0.0015% chlorate in the sanitizing wash water.

Note: The maximum or peak concentration of chlorate ion (ClO_3^-) in drinking water is estimated at 9 mg/L and is based on the available AwwaRF (1995) survey study report data.

Calculation of the surface and weight of treated fruits and vegetables:

As a model a small fruit with high surface to volume ratio such as a blueberry was selected to represent all fruits and vegetables.

Information Provided by Cassi Walls of AD:
Diameter of one blueberry = 20 mm

Source: Blueberry Research at the University of Georgia
http://www.ces.uga.edu/ES-pubs/RR662.htm#CPPU%20Enhances%20Fruit%20Set

Surface area of one blueberry = 12.56 cm^2

Based on surface area of a sphere where $A = 4\pi r^2$ (where r = 10mm = 1cm)

$A = 4(3.14)(1\ cm^2) = 12.56\ cm^2$

Information Provided by Cassi Walls of AD:

Mass of one blueberry = 0.00136 kg (where 50 berries = 68 g or 0.068 kg)

Source: USDA's nutrient database
http://www.nal.usda.gov/fnic/foodcomp/search/

Calculation of chlorate residues on blueberries

Information Provided by Cassi Walls of AD:

Assumes the film thickness of the sanitizing solution on the surface of the berry is 0.0023 g (2.3 mg) sanitizing solution/cm^2

Source: Proctor and Gamble exposure assessment for ingestion of dishwashing product residues - based on the amount of rinse water in contact with dishware surfaces
http://www.scienceinthebox.com/en_UK/safety/ingestionfromsurface_en.html

$$\frac{2.3\ mg/cm^2\ \text{(film thickness)} \times 12.56\ cm^2\ \text{(surface area)} \times <0.0015\%\ \text{chlorate in solution}}{0.00136\ kg\ \text{blueberry}}$$

Chlorate residues on blueberry = < 0.3 ppm; estimated at 0.2 ppm

Dietary Exposure Route 5. Chlorate (ClO_3^-) dietary exposure estimates from potential redox of chlorine dioxide as the antimicrobial agent in fruit and vegetable washes and water used in poultry processing

These dietary exposure concerns are covered by the estimates from Dietary Exposure Routes 3 and 4 discussed above.

Under 173.300 concerning secondary direct food additives permitted in food for human consumption chlorine dioxide (CAS Reg. No. 10049-04-4) may be safely used in food in accordance with the following prescribed conditions: (a) The additive is generated by one of the following methods: Treating an aqueous solution of sodium chlorite with either chlorine gas or a mixture of sodium hypochlorite and hydrochloric acid, or treating an aqueous solution of sodium chlorate with hydrogen peroxide in the presence of sulfuric acid. In either case, the generator effluent contains at least 90 percent (by weight) of chlorine dioxide with respect to all chlorine species as determined by Method 4500- ClO2 E in the ``Standard Methods for the Examination of Water and Wastewater," 18th ed., 1992, or an equivalent method. Method 4500- ClO2 E is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The additive may be used as an antimicrobial agent in water used in poultry processing in an amount not to exceed 3 parts per million (ppm) residual chlorine dioxide as determined by Method 4500- ClO2 E, referenced in paragraph (a) of this section, or an equivalent method. (2) The additive may be used as an antimicrobial agent in water used to wash fruits and vegetables that are not raw agricultural commodities in an amount not to exceed 3 ppm residual chlorine dioxide as determined by Method 4500-ClO2 E, referenced in paragraph (a) of this section, or an equivalent method. Treatment of the fruits and vegetables with chlorine dioxide shall be followed by a potable water rinse or by blanching, cooking, or canning.

Dietary Exposure Route 6. Chlorate (ClO_3^-) dietary exposure estimates from degradation of sodium hypochlorite or calcium hypochlorite as antimicrobial agents in fruit and vegetable washes

These dietary exposure concerns are covered by the estimates from Dietary Exposure Route 4 discussed above.

Under 40 CFR 180.2 sodium hypochlorite is generally regarded as safe

Under 40 CFR 180.1054 (a) Calcium hypochlorite is exempted from the requirement of a tolerance when used preharvest or postharvest in solution on all raw agricultural commodities. (b) Calcium hypochlorite is exempted from the requirement of a tolerance in or on grapes when used as a fumigant postharvest by means of a chlorine generator pad.

Under 21 CFR 173.315 concerning secondary direct food additives permitted in food for human consumption, chemicals used in washing or to assist in the lye peeling of fruits and vegetables ... sodium hypochlorite ... The use of the chemicals is followed by rinsing with potable water to remove, to the extent possible, residues of the chemical.

Dietary Exposure Route 7. Chlorate (ClO_3^-) dietary exposure estimates from potential redox of acidified sodium chlorite as an antimicrobial agent used in fruit and vegetable washes and poultry carcass and red meat processing water

These dietary exposure concerns are covered by the estimates from Dietary Exposure Routes 3 and 4 discussed above.

Under 21 CFR 173.325 concerning secondary direct food additives permitted in food for human consumption, acidified sodium chlorite solutions may be safely used in accordance with the following prescribed conditions: (a) The additive is produced by mixing an aqueous solution of sodium chlorite (CAS Reg. No. 7758-19-2) with any generally recognized as safe (GRAS) acid. (b)(1) The additive is used as an antimicrobial agent in poultry processing water in accordance with current industry practice under the following conditions: (i) As a component of a carcass spray or dip solution prior to immersion of the intact carcass in a prechiller or chiller tank; (ii) In a prechiller or chiller solution for application to the intact carcass; (iii) As a component of a spray or dip solution for application to poultry carcass parts; (iv) In a prechiller or chiller solution for application to poultry carcass parts; or (v) As a component of a post-chill carcass spray or dip solution when applied to poultry meat, organs, or related parts or trim. (2) When used in a spray or dip solution, the additive is used at levels that result in sodium chlorite concentrations between 500 and 1,200 parts per million (ppm), in combination with any GRAS acid at a level sufficient to achieve a solution pH of 2.3 to 2.9. (3) When used in a prechiller or chiller solution, the additive is used at levels that result in sodium chlorite concentrations between 50 and 150 ppm, in combination with any GRAS acid at levels sufficient to achieve a solution pH of 2.8 to 3.2. (c) The additive is used as an antimicrobial agent in accordance with current industry practice in the processing of red meat, red meat parts, and organs as a component of a spray or in the processing of red meat parts and organs as a component of a dip. Applied as a dip or spray, the additive is used at levels that result in sodium chlorite concentrations between 500 and 1,200 ppm in combination with any GRAS acid at levels sufficient to achieve a solution pH of 2.5 to 2.9. (d) The additive is used as an antimicrobial agent in water and ice that are used to rinse, wash, thaw, transport, or store seafood in accordance with current industry standards of good manufacturing practice. The additive is produced by mixing an aqueous solution of sodium chlorite with any GRAS acid to achieve a pH in the range of 2.5 to 2.9 and diluting this solution with water to achieve an actual use concentration of 40 to 50 parts per million (ppm) sodium chlorite. Any seafood that is intended to be consumed raw shall be subjected to a potable water rinse prior to consumption. (e) The additive is used as an antimicrobial agent on raw agricultural commodities in the preparing, packing, or holding of the food for commercial purposes, consistent with section 201(q)(1)(B)(i) of the act, and not applied for use under section 201(q)(1)(B)(i)(I), (q)(1)(B)(i)(II), or (q)(1)(B)(i)(III) of the act, in accordance with current industry standards of good manufacturing practice. Applied as a dip or a spray, the additive is used at levels that result in chlorite concentrations of 500 to 1200 parts per million (ppm), in combination with any GRAS acid at levels sufficient to achieve a pH of 2.3 to 2.9. Treatment of the raw agricultural commodities with acidified sodium chlorite solutions shall be followed by a potable water rinse, or

by blanching, cooking, or canning. (f) The additive is used as an antimicrobial agent on processed, comminuted or formed meat food products (unless precluded by standards of identity in 9 CFR part 319) prior to packaging of the food for commercial purposes, in accordance with current industry standards of good manufacturing practice. Applied as a dip or spray, the additive is used at levels that result in sodium chlorite concentrations of 500 to 1200 ppm, in combination with any GRAS acid at levels sufficient to achieve a pH of 2.5 to 2.9. (g) The additive is used as an antimicrobial agent in the water applied to processed fruits and processed root, tuber, bulb, legume, fruiting (*i.e.*, eggplant, groundcherry, pepino, pepper, tomatillo, and tomato), and cucurbit vegetables in accordance with current industry standards of good manufacturing practices, as a component of a spray or dip solution, provided that such application be followed by a potable water rinse and a 24-hour holding period prior to consumption. However, for processed leafy vegetables (*i.e.*, vegetables other than root, tuber, bulb, legume, fruiting, and cucurbit vegetables) and vegetables in the Brassica [Cole] family, application must be by dip treatment only, and must be preceded by a potable water rinse and followed by a potable water rinse and a 24-hour holding period prior to consumption. When used in a spray or dip solution, the additive is used at levels that result in sodium chlorite concentrations between 500 and 1,200 ppm, in combination with any GRAS acid at a level sufficient to achieve a solution pH of 2.3 to 2.9. (h) The concentration of sodium chlorite is determined by a method entitled ``Determination of Sodium Chlorite: 50 ppm to 1500 ppm Concentration," September 13, 1995, developed by Alcide Corp., Redmond, WA, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51.

Dietary Exposure Route 8. Chlorate (ClO_3^-) dietary exposure estimates from potential redox of sodium chlorite as the active ingredient in conventional (agricultural) pesticides used in seed-soak treatments

These dietary exposure concerns are covered by the estimates from Dietary Exposure Route 4 discussed above.

Under 40 CFR 180.1070, sodium chlorite is exempted from the requirement of a tolerance for residues when used in accordance with good agricultural practice as a seed-soak treatment in the growing of the raw agricultural commodities crop group Brassica (cole) leafy vegetables and radishes.

Dietary Exposure Route 9. Chlorate (ClO_3^-) dietary exposure estimates from translocation of very small amounts of chlorate ion (ClO_3^-) by plants (translocation of significant amounts would be phytotoxic to plants) from the environment which may be present due to inorganic chlorate pesticide uses

These dietary exposure concerns are covered by the estimates from Dietary Exposure Routes 1, 2, and 4 discussed above.

REFERENCES

Abdel-Rahman MS, Couri D, Bull RJ. 1982. Metabolism and pharmacokinetics of alternate drinking water disinfectants. Environ Health Perspect. 46:19-23.

Abdel-Rahman MS, Couri D, Bull RJ. 1984b. The Kinetics of Chlorite and Chlorate in the Rat. Journal of the American College of Toxicology, 3(4): 261-267.

Abdel-Rahman MS, Couri D, Bull RJ. 1985. The kinetics of chlorite and chlorate in rats. J Environ Pathol Toxicol Oncol. 6(1):97-103.

Frank, G. 2002. Cost of Milk Production per Hundredweight Equivalent in Milk Sold per Cow Ranges. Wisconsin Dairy Data. Fact Sheet 2002-01. Center for Dairy Profitability. Univ. Wisconsin Extension Service. Oct. 2002.