CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

DEPARTMENT OF PESTICIDE REGULATION

HUMAN HEALTH ASSESSMENT BRANCH

Summary of Toxicological Data: Sodium Chlorate

Original: 12/8/98
Revised: 7/23/24

[redacted] 7/31/2024

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INTRODUCTION

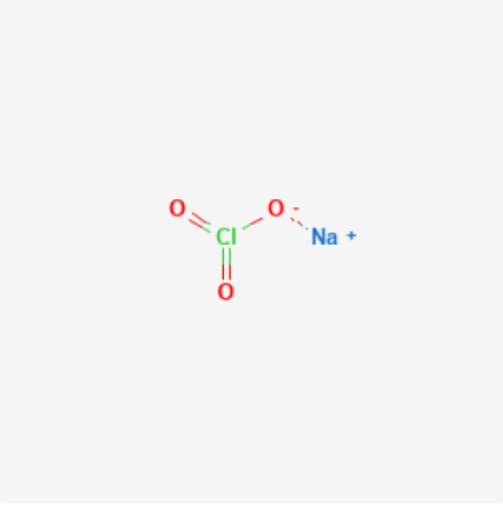
DPR Background

File Name: T240610
DPR Chemical Code: 536
Data Volume Nos.: 1020-0027, -0044, -0047 to -0051, -0089, -0103, -0106 to -0109
SB 950: 317
Original: t981208, 12/8/98
Revised: T240724
About This Document: Toxicology one-liners are attached. All record numbers for the above study types W076609 through W355037, (Data Volume Numbers 1020-0044 through 1020-0109) were examined. This includes all relevant studies indexed by DPR as of 7/23/24. This record contains summaries of studies. Individual worksheets may be useful for detailed assessment. In the 1-liners below: ** indicates an acceptable study, and † indicates a potential health effect was identified in the study.

Chemical Properties

IUPAC Name: sodium chlorate
Synonyms: sodium chlorate
CAS No.: 7775-09-9
Description: Colorless or white odorless solid
Molecular Weight: 106.44 g/mol
pH: Aqueous solution is neutral
Melting Point: 248 °C
Boiling Point: when heated to decomp it emits toxic fumes
Density: 2.5 g/cm³
Dissociation Constant: N/A
Partition Coefficient:
Water Solubility: 100 g/100 g water at 25 °C
Vapor Pressure: Negligible at room temperature

Chemical Structure



Structure from: pubchem.ncbi.nlm.nih.gov/compound/Sodium-Chlorate#section=Structures

HAZARD IDENTIFICATION SUMMARY

Sodium chlorate is a non-selective herbicide and defoliant and is used as a precursor to the generation of chlorine dioxide in the treatment of water. It has strong oxidizing properties. The active ingredient is readily absorbed through the leaves and roots. Both foliar and soil applications are effective means of treatment.

The acute toxicity profile is Category III/IV with no indication of a dermal sensitization potential. In the repeated-dosing longer term studies, the thyroid was the primary target organ. Depletion of colloid in the follicular cells of the thyroid was noted in the rat subchronic dietary toxicity study (dosing through the drinking water). The LOEL was 100 mg/kg/kg/day. Anemia with lower red blood cell count, hemoglobin concentration and hematocrit percentage was observed at a treatment level of 1000

mg/kg/day. In a primate study, after treatment for 8 weeks at 54 mg/kg/day, no apparent treatment-related effect on the serum thyroxine level was evident. Treatment at 150 mg/kg/day in the NTP rat study resulted in a lower serum thyroxine and triiodothyronine levels and elevated thyroid stimulating hormone levels during the first four days of treatment. The effect had largely resolved after 3 weeks of treatment. Follicular cell hypertrophy was noted in the histopathological examination at a treatment level of 90 mg/kg/day after 14 weeks. This effect persisted through the 2-year treatment period at a level as low as 4 mg/kg/day. Histological lesions in the thyroid were evident at treatment levels lower than those for which any disruptions of serum thyroid hormone concentrations were noted. An increased incidence of follicular cell adenoma/carcinoma was observed at a treatment level of 75 mg/kg/day. For mice there was an increased incidence of follicular cell adenoma/carcinomas in the thyroid, of ovarian granulosa cell adenomas/carcinomas and of pancreatic islet cells adenoma/carcinomas at a treatment level of 95 mg/kg/day. A non-neoplastic effect of bone marrow hyperplasia was evident at a treatment level of 5 mg/kg/day. In the genotoxicity battery one of the DNA damage studies indicated a possible positive response. The other six studies in the battery did not demonstrate such a potential.

Sodium chlorate is classified as "not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis".[1] This classification is in accordance with the EPA policy, Assessment of Thyroid Follicular Cell Tumors, which states that non-mutagenic pesticides that induce elevated levels of thyroid-stimulating hormone (TSH) and follicular cell tumors in rats are classified as not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis.

There were no fetal developmental effects noted in the rat and rabbit developmental toxicity studies at maximal treatment levels of 1000 and 475 mg/kg/day, respectively. In the rat-two generation reproductive study, the parental NOEL was 70 mg/kg/day with no effects being noted on the reproductive indices at 500 mg/kg/day.

Sodium chlorate was rapidly absorbed from the gastrointestinal tract with a half-life of 1.74 hours. The excretion demonstrated a biphasic mode with a rapid excretion half-life of 6 hours and a slow excretion phase of 36.7 hours, primarily in the urine. Forty percent was excreted within 72 hours as the radiolabeled moieties, Cl^-, ClO_2^-, and ClO_3^-. Otherwise the radiolabel was distributed throughout the tissues/organs.

No acute and subchronic neurotoxicity studies nor immunotoxicity studies have been performed for sodium chlorate. At this time they have been waived as there are no endpoints noted in the rat subchronic toxicity studies that suggested that the nervous or immune systems were significantly affected by exposure to sodium chlorate.

Particular toxicity endpoints have been noted in human acute poisoning episodes. They are characterized by methemoglobinemia formation, hemolysis, and renal insufficiency. These effects were evident at a treatment level of approximately 3 g/kg.

[1] US EPA. (2016). Six-Year Review 3 Technical Support Document for Chlorate.

METABOLISM AND PHARMACOKINETICS

1020-0107; 353043; "Metabolism and Pharmacokinetics of Alternate Drinking Water Disinfectants"; (Abdel-Rahman, M.S., D. Couri and R.J. BulI; Department of Pharmacology, UMDNJ-New Jersey Medical School, Newark, NJ; Department of Pharmacology, College of Medicine, Ohio State University, Columbus, OH; Health Effects Research Laboratory, U.S. Environmental Protection Agency, Cincinnati, OH; Environmental Health Perspectives 46, 19-23 (1982); In the first phase of the study, four male Sprague-Dawley rats were dosed orally by gavage with 0.065 mg/kg of $^{36}Cl0_3^-$ (0.85 µCi). Blood was collected from the retro-orbital sinus at 5, 10, 20, 30 and 60 minutes and 2, 4, 8, 24 and 48 hours post-dose. At 72-hours post-dose, the animals were euthanized and a final blood sample was obtained. The stomach, testes, lung, kidney, duodenum, ileum, spleen, liver, bone marrow, carcass and skin were dissected. The radiolabel content in the blood and tissue samples was determined by liquid scintillation spectrometry. In a second phase of the study, 4 male Sprague-Dawley rats were dosed orally with 0.065 mg/kg of $^{36}Cl0_3^-$ (0.85 µCi). Urine and feces were collected up to 72 hours post-dose. Recovery of radiolabel was determined by liquid scintillation. Radiolabeled moieties, Cl^-, ClO_2^-, and ClO_3^-, were quantified in the urine and fecal samples. In the 3rd phase 9 male Sprague-Dawley rats received 100 mg/l of $Cl0_3^-$ in the drinking water for 20 hours/day, 7 days/week for 12 months. After one year the animals were euthanized and liver and blood were analyzed for the presence of chloroform. In the toxicokinetic phase of the study, the absorption and excretion half-lives for the radiolabel were 1.74 and 36.7 hours, respectively. The radiolabel was widely distributed throughout the body at 72 hours post-dose with the percentage of dose administered ranging from 0.15% in the bone marrow to 0.68% in the plasma. In the excretion and metabolism phase, 40.1 and 3.1% of the administered radiolabel was excreted via the urine and feces, respectively, by 72 hours post-dose. By 72 hours post-dose, 20.5, 3.95 and 8.2% of the administered dose were Cl^-, ClO_2^-, and ClO_3^-, respectively. In the third phase of the study, chloroform was found in the livers of the ClO_3^- treated animals. Summary report ([redacted], 1/25/24)

1020-0107; 353044; "The Kinetics of Chlorite and Chlorate in the Rat"; (Abdel-Rahman, M.S., D. Couri and R.J. BulI; Department of Pharmacology, UMDNJ-New Jersey Medical School, Newark, NJ; Ohio State University, College of Medicine, Department of Pharmacology, Columbus, OH; USEPA, Health Effects Research Laboratory, Cincinnati, OH; J. American Coll. of Toxicol. 3: 261- 267 (1984); J. American Coll. of Toxicol. 3: 261- 267 (1984); In the first phase of the study, four male Sprague-Dawley rats were dosed orally by gavage with 0.065 mg/kg of $^{36}Cl0_3^-$ (0.85 µCi). Blood was collected from the retro-orbital sinus at 5, 10, 20, 30 and 60 minutes and 2, 4, 8, 24 and 48 hours post-dose. At 72-hours post-dose, the animals were euthanized and a final blood sample was obtained. The stomach, testes, lung, kidney, duodenum, ileum, spleen, liver, bone marrow, carcass and skin were dissected. The radiolabel content in the blood and tissue samples was determined by liquid scintillation spectrometry. In the second phase of the study, 4 male Sprague-Dawley rats were dosed orally by gavage with 0.065 mg/kg of $^{36}Cl0_3^-$ (0.85 µCi). Urine and feces were collected up to 72 hours post-dose. Recovery of radiolabel was determined by liquid scintillation. Radiolabeled moieties, Cl^-, ClO_2^-, and ClO_3^-, were quantified in the urine and fecal samples. Note: these data were reported in Abdel-Rahman, M.S. *et. al.,* 1982. In the first phase of the study, a biphasic pattern was observed for the elimination of the chlorate ion from the plasma. The half-lives for the rapid and slower elimination phases were 6 and 36.7 hours, respectively, The radiolabel was widely distributed throughout the body at 72 hours post-dose with the tissue concentrations ranging from 0.5 in the bone marrow to 2 ng/g of tissue in the plasma. In the excretion

profile, urine was the primary route of elimination with 40% of the administered radiolabel being recovered via that route by 72 hours post-dose. Three percent was recovered in the feces. Quantification of the radiolabeled chloride moieties recovered in the urine up to 72 hours post-dose were as follows: Cl^-, 20.5%; ClO_2^-, 3.9% and ClO_3-, 12.2%. Summary Report ([redacted], 1/26/24)

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute Oral Toxicity, Rat

1020-044; 89227; Acute Oral; 811; rat; Product Safety Labs, East Brunswick, NJ; Lab Study No. T-488; 1/24/91; Sodium Chlorate Crystal (Batch No. DL-1), dosed as a 50% (w/w) solution in distilled water; 2.0, 5.0 g/kg; 5 animals/sex/dose level; Mortality- male: 0/5, 0/5, female: 0/5, 1/5; Clinical Observations- hunched posture, lethargic, reduced feces, anogenital stain; Necropsy- intestines green, green fluid in stomach, pink liquid in abdominal cavity, lungs red; LD50 (M and F) > 5.0 g/kg; Toxicity Category IV; Acceptable. ([redacted], 4/5/91)

Acute Dermal Toxicity, Rat

1020-051; 98081; Acute Dermal; 812; rabbit; Product Safety Labs, East Brunswick, NJ; Lab Study No. T-911; 7/15/91; Sodium Chlorate Crystal (Batch No. DL-1), moistened with distilled water (0.2 ml/g test article) before application; 2.0 g/kg; 5 animals/sex; occlusive wrap, 24-hour exposure; no mortality; Clinical Observations- slight to moderate skin irritation at application site; Necropsy- no abnormalities; LD50 (M and F) > 2.0 g/kg; Toxicity Category III; Acceptable. ([redacted], 9/24/91)

1020-044; 76609; Acute Dermal; 812; rabbit; Product Safety Labs, East Brunswick, NJ; Lab Study No. T-491; 1/21/91; Sodium Chlorate Crystal (Batch No. DL-1), applied neat (not moistened); 2 g/kg; 5 animals/sex; occlusive wrap, 24-hour exposure; no mortality; Clinical Observations- diarrhea, anogenital staining; Necropsy- no abnormalities; LD50 and Toxicity Category cannot be determined; Unacceptable and cannot be upgraded because test article was not moistened before application. ([redacted], 4/5/91).

Acute Inhalation Toxicity, Rat

1020-044; 89225; Acute Inhalation; 813; rat; Product Safety Labs, East Brunswick, NJ; Lab Study No. T-493; 2/28/91; Sodium Chlorate Crystal (Batch No. DL-1), tested as a 33.3% (w/w) solution in distilled water; 1.42, 5.59 mg/l (gravimetric); 5 animals/sex/dose level; liquid aerosol inhalation, 4-hour, whole-body exposure; MMAD (GSD) = 2.1 (1.9), 2.2 (2.0) for 1.42 mg/l and 3.0 (1.7), 3.0 (1.8) for 5.59 mg/l w/cascade impactor; no mortality; Clinical Observations- hunched posture, closed eyes, irregular respiration, reduced movement, alopecia, anogenital and facial stains; Necropsy- lungs red, mottled, with uneven surface, cysts on surface, or edematous; jejunum red; reported LC50 (M and F) > 5.59 mg/l; Study originally considered to be acceptable, Category IV ([redacted], 4/4/91); revised to Supplemental (dilution of test article) ([redacted], 8/4/92).

Primary Eye Irritation, Rabbit

1020-044; 89226; Primary Eye Irritation; 814; rabbit; Product Safety Labs, East Brunswick, NJ; Lab Study No. T-489; 1/21/91; Sodium Chlorate Crystal (Batch No. DL-1), sifted through a 425 µm sieve before dosing; 0.1 g/eye; 6 animals unwashed; examined at 1, 24, 48, 72 h, and 4, 7, 10, and 14 d (termination); corneal opacity (max. score = 1) which cleared by 24 h, iritis (max. score = 1), and

conjunctivitis (max. scores = 3/redn., 2/chem., 3/disch.); all effects cleared by 14 d; Toxicity Category III; Acceptable. ([redacted], 4/5/91).

Primary Dermal Irritation, Rabbit

1020-051; 98080; Primary Dermal Irritation; 815; rabbit; Product Safety Labs, East Brunswick, NJ; Lab Study No. T-912; 7/12/91; Sodium Chlorate Crystal (Batch No. DL-1), moistened with distilled water (0.2 ml/dose) before application; 0.5 g/site; one intact and one abraded site/animal; 6 animals; occlusive wrap, 4-hour exposure; examined 1, 24, 48, and 72 h (termination) after exposure; INTACT- erythema and edema of 0-1 at 1 h, erythema of 0-1 at 24 h, clear by 48 h; ABRADED- erythema and edema of 0-2 at 1 h, erythema of 0-2 and edema of 0-1 at 24 h, erythema of 0-1 at 48 h, clear by 72 h; Toxicity Category IV; Acceptable. ([redacted], 9/24/91).

Dermal Sensitization, Guinea Pig

1020-0103; 249082; Skin Sensitization; 816; guinea pig; J. Durando; "Dermal Sensitization Study in Guinea Pigs (Buehler Method)"; Eurofins, Product Safety Laboratories, Dayton, NJ; Project #: 26522; 02/18/09; Defol 750; Lot #: not specified; Code #:TWD-0310; composition: a. i., 52.0% sodium chlorate; Buehler Method; induction treatments 1-3: 0.4 mL of 100% test article was applied to the left side of each subject for a 6-hour exposure (1 treatment/week/3 weeks/20 male test subjects), using an occlusive 25-mm, Hill Top Chamber, wrapped with a non-allergenic Durapore adhesive tape; challenge: 0.4 mL of 100% test article was applied for a 6-hour exposure to a naïve site on the right side of each subject, 27 days after the 1st induction treatment; naïve-challenge: 0.4 mL of 100% test article was applied for a 6-hour exposure (10 male subjects); positive control: 0.4 mL of 100% HCA (alpha-hexylcinnamaldehyde technical) was applied for 6-hours for the induction treatments and 100% for both the challenge (10 female subjects) and the positive-control, naïve-challenge treatments (5 female subjects); mortality: none; clinical signs: no systemic toxicity reported; induction treatment 1, erythema, grade 0.5 in 1/20 at 24 hours, with complete clearing by 48 hours; induction treatment 2, erythema, grade 1 in 4/20 at 24 hours (grade 0.5 in 12/20), decreasing to grade 1 in 3/20 at 24 hours (grade 0.5 in 12/20) at 48 hours; induction treatment 3, erythema, grade 1 in 6/20 at 24 hours (grade 0.5 in 11/20), decreasing to grade 1 in 1/20 at 24 hours (grade 0.5 in 13/20) at 48 hours; challenge, erythema, grade 0.5 in 6/20, with complete clearing by 48 hours; naïve challenge, erythema, grade 2 in 1/10 at 24 hours (grade 0.5 in 1/10), decreasing to grade 2 in 1/10 at 48 hours; body-weight gain was positive over the course of the study in all throughout; the positive control, HCA, was positive for dermal sensitization indicating that the test system was effective; test article tested negative for dermal sensitization; Acceptable. ([redacted], 11/25/09)

SUBCHRONIC STUDIES

Rat Subchronic Oral Toxicity Study

** 1020-047 098072 " A subchronic (3 month) oral toxicity study of sodium chlorate in the rat via gavage" (D. S. Barrett, Bio/dynamics, Project 86-3112, 12/4/87) Sodium chlorate, 100% white granular solid, was given to 15 Sprague-Dawley CD® rats/sex/group at 0 (distilled water), 10, 100 or 1000 mg/kg/day by gavage, 7 days per week for 90 days. Hematology, clinical chemistry and ophthalmology were conducted at appropriate intervals but no urinalysis was done. The clinical chemistry/hematology included sodium and chloride levels in the blood and percent methemoglobin found at the end of treatment. There were no treatment-related effects on any of these parameters. The most significant finding was a suggestion of anemia, especially in female rats with slightly lower red blood cell counts,

hematocrit and hemoglobin levels. There were no histological findings after 90 days due to treatment. NOEL = 100 mg/kg/day (hematology). ACCEPTABLE. ([redacted], 11/10/98)

1020-0107; 353038; "The Effects of Subchronic Chlorate Exposure to Sprague-Dawley Rats"; (McCauley, P.T , M. Robinson, F.B. Daniel, G.R. Olson; Risk Reduction Engineering Laboratory, US. Environmental Protection Agency, Cincinnati, OH; Environmental Monitoring Systems Laboratory, US. Environmental Protection Agency, Cincinnati, OH; Pathology Associates, Inc., West Chester, OH; Drug and Chemical Toxicology 18: 185-199 (1995); Five Sprague-Dawley rats/sex/group received 0 (distilled water), 48 mM sodium chloride control, and 3.0, 12.0 or 48 mM of sodium chlorate (purity of the test material was not reported) in the drinking water for 90 days. The sodium content in the 3.0 and 12.0 mM preparations was adjusted to 48 mM using sodium chloride. Based upon the water consumption of each group the dosing levels of chlorate were calculated to be: (M) 0, 30, 100, 513 mg/kg/day, (F) 0, 53, 164, 801 mg/kg/day. No treatment related deaths occurred during the study. The mean final body weights of both sexes in the high dose group were less than those of the control group ($p<0.05$). Food consumption was likewise reduced. In the hematological evaluation, the mean rbc counts, hematocrit percentage and hemoglobin concentrations were lower for both sexes (NS or $p<0.05$). In the clinical chemical evaluation the high dose males demonstrated significantly reduced activity levels in serum for aspartate aminotransferase and alanine aminotransferase, lower serum concentrations of calcium, phosphorus and creatinine and an elevated concentration of cholesterol ($p<0.05$). These parameters were not significantly affected for the females. In the necropsy examination the mean relative liver, kidney and heart weights were reduced and the testis weights were higher for the high dose males in comparison to those values for the control group ($p<0.05$). These effects were not apparent for the females. (Note: the thyroid weights were not recorded). The histological examination revealed lesions in the pars distalis of the pituitary gland which were most pronounced in both sexes in the high dose group. The lesion was characterized by cytoplasmic vacuolation. Thyroid colloid depletion was noted in both the control and treatment groups. The incidence and severity of this lesion was increased in the mid and high dose groups of both sexes. Rat Subchronic Dietary Toxicity NOEL: 3 mM in the drinking water (M) 30 mg/kg/day, (F) 43 mg/kg/day (based upon the increased incidence and severity the colloid depletion in the thyroid of both sexes in the 12 mM treatment group). Summary Report ([redacted], 1/25/24)

Dog Subchronic Oral Toxicity Study

** 1020-048 098073; "A subchronic (3 month) oral toxicity study in the dog via gavage administration with sodium chlorate" (D. S. Barrett, Bio/dynamics, NJ, 86-3114, 10/19/87) Four beagle dogs/sex/group were given sodium chlorate, 100%, by oral gavage at 0 (distilled water), 10, 60 or 360 mg/kg/day for 3 months. Clinical signs included emesis in 1/4 females during the first 3 weeks of dosing. No other clinical signs or effects on hematology, clinical chemistry (including methemoglobin), ophthalmology, or histopathology were reported. No urinalysis was done. Range-finding study was not included for dose selection but the report contains a statement that doses higher than 360 resulted in emesis. NOEL = 60 mg/kg/day. ACCEPTABLE. ([redacted], 11/12/98).

Primate 60-Day Oral Toxicity Study

1020-027 024093 "Subchronic toxicity of chlorine dioxide and related compounds in drinking water in the nonhuman primate." (J. P. Bercz *et al.*, Environmental Health Perspectives 46: 47-55 (1982)) Sodium chlorate solutions equivalent to 25, 50, 100, 200 and 400 mg/l of ClO_2, was available to African Green Monkeys for 30 - 60 days. Hematology parameters were measured. Red cell count and

hemoglobin were slightly decreased with "dose dependence" with treatment. Other parameters were reported as "no response". No worksheet. ([redacted], 11/12/98).

28-Day Dermal Toxicity

No study on file with DPR. Sodium chlorate is unlikely to be absorbed by the skin based on its high water solubility and ionic nature; therefore, a risk assessment for dermal exposure is not needed and a dermal endpoint was not selected.[1]

[1] US EPA. (2006). Reregistration Eligibility Decision (RED) for Inorganic Chlorates.

CHRONIC STUDIES

Oncogenicity, Rat

1020-0106; 351375; "NTP Technical Report on the Toxicology and Carcinogenesis Studies of Sodium Chlorate (Cas No. 7775-09-9) in F344/N Rats and B6C3F1 Mice (Drinking Water Studies)"; (J.D. Prejean, W.R. Richter, C.D. Hébert; Southern Research Institute, Birmingham, AL; Report No. NTP TR 517; 12/05); F334/N rats of both sexes were treated with Sodium chlorate (lot no. 14019PQ; purity: > 99%) in the drinking water. In the initial study, 20 rats/sex/group were treated with 0, 125, 250, 500, 1000 or 2000 mg/l for 3 weeks (males, 0, 20, 35, 75, 170, 300 mg/kg/day, females, 20, 40 75, 150, 340 mg/kg/day). Ten animals/sex/group were dedicated to clinical assessments. The other 10 animals/sex/group were euthanized and examined for histological lesions. In the 2-year study 50 animals/sex/group were treated with 0. 125, 1000 or 2000 mg/l (males, 0, 5, 35, 75 mg/kg/day, females, 0, 5, 45, 95 mg/kg/day). Specified tissues/organs were examined histologically among the decedents and survivors of the treatment. An additional 20 animals/sex/group were treated for 14 weeks. Blood was collected from 10 animals/sex/group after 4 days, 3 weeks and 14 weeks of treatment and serum T3, T4 and TSH concentrations were determined. For the other 10 animals/sex/group, the thyroid gland was examined histologically after 14 weeks. In the 3-week study there was no treatment-related effect upon body weight gain. Although the hematocrit percentage, hemoglobin concentration and red blood cell count of the 2000 mg/l males were less than the control group values, there was no apparent significant physiological effect. Otherwise the hematological evaluation of the females and the clinical chemical evaluation of both sexes did not reveal any treatment-related effects. In the histopathological examination, follicular cell hypertrophy was noted in the thyroid of both sexes of the 500, 1000 and 2000 mg/l groups. In the 2-year study there was no treatment-related effect upon body weight gain over the course of the study. The thyroid was the primary target organ. The serum T3 and T4 level concentrations were reduced for both sexes in the 1000 and 2000 mg/l after 4 days of treatment. After 3 weeks of treatment, they were significantly reduced for both sexes only in the 2000 mg/l group. By 14 weeks there was no statistically significant effect upon T3 or T4 levels in even this treatment group. Serum TSH levels were elevated for both sexes after 4 days of treatment for the 1000 and 2000 mg/kg treatment groups and for the 2000 mg/kg treatment group after 3 and 14 weeks of treatment. The TSH levels were also increased for the males in the 1000 mg/kg group after 3 weeks of treatment. Histological examination of this cohort revealed the presence of follicular cell hypertrophy in the thyroid gland of both sexes in the 1000 and 2000 mg/l groups. After 2 years of treatment, there was a statistically significant increase in incidence of follicular cell hypertrophy in the thyroid glands of both sexes in the 1000 and 2000 mg/l group and in the males of the 125 mg/l group. An increasing incidence of follicular cell

mineralization was also noted for the females in the 1000 and 2000 mg/l groups. Furthermore, an increased incidence of combined follicular cell adenoma and carcinoma was noted in both sexes in the 2000 mg/l group (M, 0: 1/47 (2.1%) vs. 2000: 6/47 (12.8%), F, 0: 1/47 (2.1%) vs. 2000: 4/46 (8.7%)). The historical control incidence of these tumors in drinking water studies was 2.9% for the males (pg. 95) and 2.8% for the females (pg. 134). Rat 3-week NOEL in drinking water: 250 mg/l (M: 35 mg/kg/day, F: 40 mg/kg/day) (based upon the incidence of follicular cell hypertrophy in the thyroid of both sexes in the 500 mg/l group); Rat Chronic NOEL was not assigned because only the histology was examined in the study; Possible oncogenic potential: Thyroid follicular cell adenoma and carcinoma. Summary Report ([redacted] 10/10/23)

Dog Chronic Toxicity

No study on file with DPR nor required.[1]

[1] US EPA (2006). Length of Dog Toxicity Study(ies) that is Appropriate for Chronic RfD Determinations of Pesticide Chemicals.

Mouse Oncogenicity

1020-0106; 351375; "NTP Technical Report on the Toxicology and Carcinogenesis Studies of Sodium Chlorate (Cas No. 7775-09-9) in F344/N Rats and B6C3F1 Mice (Drinking Water Studies)"; (J.D. Prejean, W.R. Richter, C.D. Hébert; Southern Research Institute, Birmingham, AL; Report No. NTP TR 517; 12/05); B6CF1 mice of both sexes were treated in the drinking water with Sodium chlorate (lot no. 14019PQ; purity: > 99%). In the initial study, 10 mice/sex/group were treated with 0, 125, 250, 500, 1000 or 2000 mg/l for 3 weeks (males, 0, 20, 45, 90, 175, 350 mg/kg/day, females, 20, 45, 95, 190, 365 mg/kg/day). All of the animals survived the treatment. There was no treatment-related effect upon the mean body weights. The hematological evaluation did not reveal any treatment-related effects. In the necropsy there were no treatment-related effects on the organ weights. The histological examination did not reveal any treatment-related lesions. In the 2-year study, 50 B6CF1 mice/sex/group received 0, 500, 1000 or 2000 mg/l of the test material in the drinking water for at least 105 weeks (males: 0, 5, 35, 75 mg/kg/day, females: 0, 5, 45, 95 mg/kg/day). There was no apparent treatment-related effect on survival of the study animals or the mean body weights over the course of the study. In the histopathology no apparent treatment-related neoplastic or non-neoplastic lesions in the male mice were identified. For the females a significant incidence of pancreatic islet cells adenoma and carcinoma was noted for the 2000 mg/l group (0: 0/46, 2000: 4/49) (historical control data, drinking water as the dosing route: 1.4%). In the ovaries there was an increased incidence of granulosa cell tumors, benign and malignant (0: 1/45, 2000: 6/50) (historical control data, ovarian granulosa cell carcinoma, 0.2%*). An increased incidence of follicular cell hypertrophy in the thyroid gland was only noted in the 2000 mg/l group (0: 3/48, 500: 2/50, 1000: 5/49, 2000: 14/50). The incidence of bone marrow hyperplasia was increased in all of the treatment groups (0: 14/50, 500: 28/50, 1000: 29/50, 2000: 31/50). Mouse 3-week NOEL in drinking water: 2000 mg/l (M: 350 mg/kg/day, F: 365 mg/kg/day) (based upon the lack of treatment-related effects in the 2000 mg/l treatment group); Mouse Chronic NOEL was not assigned because only the histology was examined in the study; Possible oncogenic potential: pancreatic islet cell adenoma and carcinoma, ovarian granulosa cell tumors. Summary report ([redacted] 10/13/23).

GENOTOXICITY

Gene Mutation

** 1020-050 098075 "Sodium chlorate: Investigation of mutagenic activity at the HGPRT locus in a Chinese hamster V79 cell mutation system." (G. Hodson-Walker, Life Science Research, UK, Report No. 89/SKR002/0631, 9/18/89) Chinese hamster V79 4-1 clone 9 3/12 cells were exposed for 3 hours with and without rat liver activation to concentrations of 0 (distilled water), 8, 40, 200, 1000 or 5000 ug/ml. There were triplicate cultures per concentration with two trials. EMS was the positive control without activation and DMBA, the positive control with activation. Both were functional. There was no concentration-dependent cytotoxicity as determined by plating efficiency compared with the solvent control. There was no increase in the mutation frequency as measured by resistance to 6-thioguanine after a 7-day expression period. No adverse effect. ACCEPTABLE. ([redacted], 11/12/98)

** 1020-050 098077 " Sodium chlorate: Assessment of mutagenic potential in histidine auxotrophs of *Salmonella typhimurium* (the Ames test)." (K. May, Study Director, Life Science Research Limited, UK, LSR report 89/SKR001/0285, 8/14/89) Sodium chlorate, 99.9%, was tested with and without Aroclor 1254-induced rat liver activation at 0 (distilled water), 50, 158, 500, 1580 and 5000 ug/plate in two trials, triplicate plates per trial. *Salmonella* strains used were TA1535, TA1537, TA1538, TA100 and TA98. Positive controls were functional. There was no evidence of cytotoxicity or induction of revertants at any concentration tested under conditions of the assay. No adverse effect. ACCEPTABLE. ([redacted], 12/8/98)

1020-0106; 351375; "NTP Technical Report on the Toxicology and Carcinogenesis Studies of Sodium Chlorate (Cas No. 7775-09-9) in F344/N Rats and B6C3F1 Mice (Drinking Water Studies)"; (J.D. Prejean, W.R. Richter, C.D. Hébert; Southern Research Institute, Birmingham, AL; Report No. NTP TR 517; 12/05); In two trials, *S. typhimurium* strains TA 97, TA 98, TA 100, TA 102, TA 104, and TA 1535 were treated by a 20-minute preincubation followed by plate incorporation with Sodium chlorate (lot no. 14019PQ; purity: > 99%) at concentrations ranging from 100 to 10000 µg/plate with or w/o activation for 2 days at 37° C. Each treatment level was plated in triplicate. An Arochlor 1254-induced rat or hamster liver S-9 fraction was used to metabolize the test material. There was no treatment-related increase in reverse mutations with or w/o activation. The positive controls were functional. Summary report. ([redacted], 10/16/23)

Chromosome Damage

** 1020-050 098076 "Sodium chlorate: Assessment of clastogenic action on bone marrow erythrocytes in the micronucleus test." (J. M. Mackay, Life Science Research Limited, UK, LSR 89/SKR003/0253, 8/25/89) CD-1 mice, 5/sex/group, were given an oral dose of 0 (distilled water), 200, 1000 or 5000 mg/kg. Chlorambucil, 30 mg/kg, was the positive control at 24 hours. Animals were sacrificed at 24, 48 or 72 hours after dosing. 2000 polychromatic erythrocytes were scored per animal and the ratio of polychromatic:mature cells was calculated for each animal. Five males at 5000 mg/kg had clinical signs of hunched posture and piloerection on day 4. The frequencies of micronucleated erythrocytes in treated animals was similar to controls. No significantly toxic effect. ACCEPTABLE. ([redacted], 12/7/98).

1020-0106; 351375; "NTP Technical Report on the Toxicology and Carcinogenesis Studies of Sodium Chlorate (Cas No. 7775-09-9) in F344/N Rats and B6C3F1 Mice (Drinking Water Studies)"; (J.D. Prejean, W.R. Richter, C.D. Hébert; Southern Research Institute, Birmingham, AL; Report No. NTP TR

517; 12/05); Ten B6CF1/sex/group were treated in the drinking water with 0, 125, 250, 500, 1000 or 2000 mg/l of Sodium chlorate (lot no. 14019PQ; purity: > 99%) for 3 weeks (males, 0, 20, 45, 90, 175, 350 mg/kg/day, females, 20, 45, 95, 190, 365 mg/kg/day). At the conclusion of the treatment period, blood samples were obtained from each study animal. Smears were prepared, fixed, and stained with acridine orange. The frequency of micronuclei in 2000 normochromatic erythrocytes (NCE) was determined. The percentage of polychromatic erythrocytes (PCE) in a population of 1000 erythrocytes was also measured in order to assess bone marrow toxicity. The study results did not indicate any treatment related effect upon the presence of micronuclei in the NCEs. Summary report. ([redacted], 10/16/23).

DNA Damage or Miscellaneous Effects

** 1020-050 098078, 098079 "Unscheduled DNA synthesis (UDS) in HeLa S3 cells in vitro." (A. H. Seeberg, Study Director, Life Science Research, Roma Toxicology Centre, Report 102002-M-02289, 9/27/89) HeLa S3 cells in monolayer were treated with sodium chlorate (99.9%) for three hours in the presence of hydroxyurea and tritiated thymidine. Concentrations were 0 (distilled water), 100, 316, 1000, 3160 and 10000 ug/ml. There were triplicate cultures and two independent trials with and without rat liver activation (phenobarbital and beta-naphthoflavone induced). DNA was extracted from the cells and quantitated as ug. Radioactivity was determined by liquid scintillation counting and the results were expressed as DPM/ug DNA. 4-Nitroquinoline-N-oxide and benzo(a)pyrene were functional as positive controls. The incorporation of thymidine decreased with increasing concentrations of sodium chlorate indicating toxicity. There was no evidence of the induction of UDS with treatment. ACCEPTABLE. ([redacted], 12/9/98)

** 1020-0089; 184877; "Sodium chlorate: Assessment of its ability to cause lethal DNA damage in strains of *Escherichia coli*." (K. May, Life Science Research Limited, LSR report no. 89/SKR004/0341, 9/5/89) Sodium chlorate, 99.9%, was tested with *Escherichia coli* strains WP2 (repair proficient), WP67 (repair deficient) and CM871 (repair deficient) with and without rat liver activation. Cells were incubated for 2 or 18 hours in liquid culture with shaking, then diluted and plated for viable colony counts. Concentrations of sodium chlorate were 0 (distilled water), 100, 316, 1000, 3160 or 10000 ug/ml. Positive controls were mitomycin C (- S9) and 2-aminoanthracene (+ S9), and ampicillin as a negative control for toxicity without DNA damage. The coefficients of survival (C_s) were calculated, comparing survival of treated cultures with relevant controls and repair proficient cells with repair deficient cells. Values less than 0.3 were considered indicative of DNA damage. The results indicated that sodium chlorate caused DNA damage without (as well as with) activation after 2 hours of incubation at $\geq$ 1000 ug/ml but not after 18 hours. Mitomycin C was effective with both repair deficient strains but 2-aminoanthracene was effective only with CM871. The absence of differential toxicity at 18 hours was suggested as due to a "feeder" effect of lysing cells in nutrient-exhausted medium. Possible adverse effect. ACCEPTABLE. ([redacted], 12/8/98)

REPRODUCTIVE TOXICITY

Rat

1020-0109; 355037; "Two-Generation Reproduction Study (Reproduction and Fertility Effects) by Oral (Gavage) Route in Rats"; (W. Gaoua; CIT, BP 563-27005 Evreux, France; Study No. 22824 RSR; 8/19/04); Twenty five Sprague-Dawley rats/sex/group of the P generation were dosed orally by gavage with 0, 10, 70 or 500 mg/kg/day of Sodium chlorate technical (batch no. 1E012IUM; purity: 99.68%) for 10 weeks during the premating period, mating period, and 3 weeks both for the gestation and lactation

periods; upon the weaning of the F1 generation pups, 25 animals/sex/group were selected and dosed for a 10-week premating period, mating, and the gestation and lactation period. There were no treatment-related deaths in either generation of parental animals. The mean body weights and food consumption of both parental generations were not affected by the treatment over the course of the treatment periods. Hematological evaluation of the P generation adults revealed lower red blood cell counts, hemoglobin concentrations and hematocrit percentages for both sexes in the 500 mg/kg group. There was no treatment-related effect on mating and reproduction parameters or offspring development for either the F1 or F2 generations. The sexual maturation of the F1 pups was not affected by the treatment. No treatment-related effect was evident in the reflex and growth development of the F1 and F2 pups. The spontaneous motor activity of the F1 pups was not affected by the treatment. In the necropsy examinations of the parents, the mean relative liver weight of the 500 mg/kg females was greater than the control group value for the P generation. For the F1 generation, the mean relative spleen and thyroid weights of the 500 mg/kg males were greater than those of controls. For the F1 females, the mean relative adrenal weight of the 500 mg/kg group was less than the control group value. The mean relative liver weight of these females was greater than the value for the control group. For the pups of the F2 generation, the mean relative thyroid weight of the 500 mg/kg males was greater than that of the control. Histological examination of the parents revealed thyroid follicular cell hyperplasia in both sexes in the 500 mg/kg groups of both generations. An increased incidence of thyroid hypervascularization was also noted for the 500 mg/kg males of both generations. Parental NOEL: (M/K) 70 mg/kg/day (based upon the histological lesions noted in the thyroid and the hematological effects identified for both sexes of the 500 mg/kg group); Reproductive NOEL: 500 mg/kg/day (based upon the lack of a treatment-related effect on the reproductive indices); Developmental NOEL: 70 mg/kg/day (based upon the increased relative thyroid weight of the 500 mg/kg F1 and F2 males); No significantly toxic effect was evident. Study acceptable. ([redacted], 6/6/24)

DEVELOPMENTAL TOXICITY

Rat

** 1020-049 098074 "A teratogenicity study in rats with sodium chlorate." (R. E. Schroeder, Bio/dynamics, Project 86-3117, 9/24/87) Sprague-Dawley CD® rats, 24/dose group, were given sodium chlorate, 100% purity, at 0 (distilled water), 10, 100 or 1000 mg/kg/day by oral gavage in 5 ml/kg, days 6 - 15 of gestation. No treatment-related effects were reported on body weight, food consumption, clinical signs or developmental parameters. Maternal and developmental NOEL = 1000 mg/kg/day. No adverse effects. ACCEPTABLE. ([redacted], 11/12/98).

Rabbit

** 1020-0108; 353908; "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"; (J. D. George, and C.J. Price; Center for Life Sciences & Toxicology, RTI, Research Triangle Park, NC; Study No. TER-97-005; 11/6/02); Twenty four time-mated female New Zealand White rabbits/group were dosed orally by gavage with 0 (vehicle: deionized/distilled water), 100, 250 or 475 mg/kg/day of (lot no. 03623LR01; purity: 99.2%) from gestation day 6 through gestation day 29. Of the rabbits on study, a number of does in each group were either found dead, misdosed, euthanized for humane reasons, or gave birth prior to having a caesarean section. There were 19/21, 17/19, 18/18 and 20/20 rabbits for which litter examinations were successfully completed for the 0, 100, 250 and 475 mg/kg groups, respectively. No treatment-related deaths occurred during the study. Discolored urine (orange to dark orange) was noted for does in the 250 and 475 mg/kg groups as the study progressed. There was no substantive treatment-related effect on the does' body weight gain or mean daily

food consumption. The treatment did not affect fetal development. No significantly toxic effects were evident. Maternal NOEL: 475 mg/kg/day (based upon the lack of a treatment-related effect at 475 mg/kg); Developmental NOEL: 475 mg/kg/day (based upon the lack of treatment-related effects on the fetuses in the 475 mg/kg group); Study acceptable. ([redacted], 4/5/24)

NEUROTOXICITY

Acute Neurotoxicity, Rat

No study on file with DPR nor is required at this time. The active ingredient does not have a putative neurotoxicity mechanism of action nor does the acute toxicity study identify toxicity endpoints indicative of a neurotoxic effect.[1]

90-Day Neurotoxicity, Rat

No study on file with DPR nor is required at this time. The active ingredient does not have a putative neurotoxicity mechanism of action nor do acute toxicity and longer-term studies identify toxicity endpoints indicative of a neurotoxic effect.[1]

Developmental Neurotoxicity, Rat

No study on file with DPR.

IMMUNOTOXICITY

No study is on file with DPR nor is required at this time. No specific treatment-related effects on the total and/or differential leucocyte counts or the immunocompetent organs, spleen and thymus, were evident in the rat subchronic studies.[1]

[1] US EPA (2013). Part 158 Toxicology Data Requirements: Guidance for Neurotoxicity Battery, Subchronic Inhalation, Subchronic Dermal and Immunotoxicity Studies.

ENDOCRINE DISRUPTOR STUDIES

No study on file with DPR. The available toxicity studies on sodium chlorate demonstrate the thyroid gland to be its target of toxicity. The endpoints selected to assess chronic dietary risk and short- and intermediate-term oral and inhalation risks in this document are protective of the observed thyroid effects seen in the available toxicity studies.[1]

[1] US EPA. (2006). Reregistration Eligibility Decision (RED) for Inorganic Chlorates.

SUPPLEMENTAL STUDIES

1020-034 039955 "The effects of repeated administration of the chlorates and chlorides of potassium and sodium in massive doses." (I. S. Kleiner and L. B. Dotti, Bulletin of N. Y. Medical College and Flower Hospital, 3: 309 - 322 (1940)) Rabbits were given 1 g/kg 6 days/week for 4 weeks by gavage. There was no consistent effect on methemoglobin or body weight. Rats were fed diets containing 2.5% salt with a slight inhibition of growth. No inhibition of growth at 0.85% extra salt. No worksheet. ([redacted] 11/12/98).

MECHANISTIC STUDIES

1020-0107; 353036; "Chlorate Poisoning: Mechanism of Toxicity"; (Steffen, C. and E.Wetzel; Federal Health Office, Institut fur Arzneimittel, Seestraβe 10, D-13353, Germany and Department of Pharmacology, University of Marburg, D-35043, Marburg, Germany; Toxicology 84: 217-231 (1993)); *In vitro* assays were performed in order to determine the mechanisms by which the chlorate ion exerts its toxic effects by oxidizing hemoglobin. Human erythrocytes were incubated with 30 mM sodium chlorate for up to 360 minutes at 37° C. Total oxidation of the hemoglobin to methemoglobin was observed by 240 minutes after initiation of the incubation. At each time assessed, the cells were subsequently washed free of chlorate and incubated with 25 µM methylene blue for 180 minutes. Treatment with methylene blue reversed hemoglobin oxidation only minimally. In a second assay, human erythrocytes were hemolyzed and specified enzymes were assayed in the presence of 5 mM sodium chlorate at 37° C for up to 180 minutes. Glucose-6-dehyrodenase was fully inhibited by 100 minutes into the assay. Glyceraldehyde-3-phosphate dehydrogenase was largely inhibited by 150 minutes. For adenosine triphosphate phosphohydrolase and glutathione peroxidase, inhibition was partially observed up to the 180-minute time point (70% and 40%, respectively). In another assay the inhibition of glyceraldehyde-3-phosphate dehydrogenase was observed only in the presence of hemoglobin. This was demonstrated by incubating erythrocyte membranes with 5 mM sodium chlorate in the absence and presence of hemoglobin (2.4 mg/ml) for 180 minutes at 37° C. In order to examine a dose-dependency for methemoglobin formation, rabbit erythrocytes were incubated with concentrations of sodium chlorate which ranged from 7.5 to 75 mM for up to 240 minutes at 37° C. At 75 mM the hemoglobin was fully oxidized by 120 minutes. As the concentration of the sodium chlorate concentration was reduced, a longer time was required to oxidize a comparable concentration of hemoglobin. At 7.5 mM less than 10% of the hemoglobin was converted to methemoglobin after 240 minutes. In a follow-up assay, both human and rabbit erythrocytes were incubated with 30 mM of sodium chlorate for up to 240 minutes at 37° C. In this instance 100% oxidation of human hemoglobin was achieved by 180 minutes. For the rabbit erythrocytes, 100% formation of methemoglobin was barely achieved at 240 minutes. In a toxicokinetic evaluation, the rabbits were dosed orally by gavage with 1 g/kg of sodium chlorate. Blood and urine samples were collected up to 48 hours post-dose. A Cmax in the blood of 16 mM was achieved at 90 minutes post-dose. A maximal concentration of chlorate in the urine was achieved at 6 hours post-dose. The $T_{1/2}$ for urinary excretion was 16 hours. No methemoglobin was observed. At 7 days post-dose the animals were euthanized. No treatment-related lesions were identified. Summary report. [redacted], 2/1/24)

1020-0107; 353040; "A Mixture of Ammonium Perchlorate and Sodium Chlorate Enhances Alterations of the Pitutary-Thyroid Axis Caused by the Individual Chemicals in Adult Male F344 Rats"; (Khan, M.A., S.E. Fenton, A.E. Swank, S.D. Hester, A. Williams, and D.C. Wolf; National Research Council, Health Canada, Ottawa, Ontario, Canada, Reproductive Toxicology and Environmental Carcinogenesis Divisions, U.S. Environmental Protection Agency, Research Triangle Park, NC; Toxicologic Pathology 33:776–783 (2005)); Ten Fischer 344 rats/group received 0, 10, 100 or 1000 mg/l of sodium chlorate (purity>99%) in the drinking water for 7 days (calculated sodium chlorate uptake: 0.07, 3.31, 15.7, 119.8 mg/kg/day). At the time of euthanasia, blood was collected from each animal by cardiac puncture. The hypothalamus, pituitary gland, thyroid gland and liver were dissected and examined for gross lesions. The serum concentrations of T3, T4 and TSH were determined. The dissected organs were examined histologically. For the serum thyroid hormone and TSH concentrations, treatment with sodium chlorate resulted in a slight decrease in T4 at the highest treatment level (0: 4.74 vs. 1000 mg/l: 4.00 µg/ml, NS)

and an increase in the TSH level (0: 3.09 vs. 1000 mg/l: 4.51 ng/ml, $p<0.05$). In the histological examination of the thyroid, a dose-response for the incidence of colloid depletion was observed (0: 0/6, 10: 0/6, 100: 1/6 and 1000 mg/ml: 4/6). An increased incidence of hypertrophy was noted at all of the treatment levels with the severity of the lesion demonstrating a treatment-related increase. Any treatment-related effect for hyperplasia was less apparent. Summary report. [redacted], 2/2/24)

1020-0107; 353041; "Subchronic Sodium Chlorate Exposure in Drinking Water Results in a Concentration-Dependent Increase in Rat Thyroid Follicular Cell Hyperplasia"; (Hooth, M.J., A.B. DeAngelo, M.H. George, E.T. Gaillard, G.S. Travalos, G.A. Boorman and. D. C. Wolf; Environmental Carcinogenesis Division, National Health and Environmental Effects Research Laboratory, Research and Development, US Environmental Protection Agency, Research Triangle Park, NC, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC and Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT; Toxicologic Pathology 29, 250–259 (2001)); Four studies were presented in this report. In the first study ten F344 rats and B6C3F1 mice/sex/group received 0, 0.125, 0.25, 0.5, 1.0, or 2.0 g/l sodium chlorate (purity: >99%) in the drinking water for 21 days. In the second study 10 F344 rats/sex/group received 0, 0.125, 1.0, or 2.0 g/l of the test material in the drinking water for 4, 21 or 90 days. The third study entailed dosing 10 male F344 rats/group receiving 0, 0.001, 0.01, 0.1, 1.0 or 2.0 g/l of the test material in the drinking water for 90 days. In the final study 6 female F344 rats and 6 female B6C3F1 mice/group received 0, 0.5, 1.0, 2.0, 4.0, or 6.0 g/l of the test material in the drinking water for 105 days. In the 2nd study blood was collected at the time of sacrifice and serum triiodothyronine (T3) and thyroxine (T4) concentrations and thyroid stimulating hormone (TSH) levels were analyzed after 4, 21, or 90 days of treatment. The animals were euthanized by carbon dioxide asphyxia after the completion of the designated time of treatment. Blood was recovered from each animal prior to necropsy. The thyroid gland was among the tissues/organs dissected from each animal. After fixation the thyroid glands were processed, embedded in paraffin, sectioned and stained with hematoxylin and eosin for histological examination. Thyroid hormone analysis revealed that both T3 and T4 serum concentrations were lower than the control values for both sexes in the 1.0 and 2.0 g/l treatment groups after 4 days of treatment. After 21 days only the T3 and T4 serum concentrations of both sexes in the 2.0 g/l group and the males in the 1.0 g/l group were significantly lower than those of the control group. By 90 days any effect on either of these hormones was quite minimal. The TSH serum levels were elevated for both sexes in the 1.0 and 2.0 g/l treatment groups at 4 days in a dose-related manner. The effect was less evident after 21 and 90 days of treatment. Histopathological examination of the rat thyroid gland revealed follicular cell hyperplasia in both sexes of the 1.0 and 2.0 g/l treatment groups after 21 days of treatment (Study No. 2). However a more comprehensive examination of the thyroid tissue from the rats in Study No. 1 identified a significantly increased depletion of colloid and/or follicular cell hyperplasia at a treatment level of 0.5 g/l for the males after 21 days of treatment. In Study No. 3 the thyroid glands of the males at the lowest treatment level of 0.001 g/l demonstrated an increased incidence of colloid depletion, hypertrophy, and follicular cell hyperplasia after 90 days of treatment. In contrast after 105 weeks of treatment, lesions were only identified in the thyroid of the female rats at 2.0 g/l. The mice did not give any evidence of thyroid gland alterations at the treatment levels included in either of the studies for which they were included. In summary, the male rats were more affected by the treatment and seemed to sustain thyroid lesions over the 3-month treatment period at much lower treatment levels than the females did. Summary report ([redacted] 1/26/24)

HUMAN TOXICITY

1020-0107; 353037; "Severe Chlorate Poisoning: Report of a Case"; (Steffen, C. and R. Seitz; Pharmakologisches Institut, Lahnberge, D-3550 Marburg and Zentrum fiir Innere Medizin, Medizinische Klinik der Universitiit, D-3550 Marburg, Federal Republic of Germany; Arch Toxicol 48:281-288 (1981)); A patient presented at the clinic approximately 5 hours after having ingested 150 to 200 grams of sodium chlorate (approximately 3 g/kg for a 60 kg woman). At the time of admission they were cyanotic, suffering from 50% methemoglobinemia. Methylene blue was provided intravenously. At 19 hours post-ingestion the hemoglobin concentration had improved 10%. However the erythrocyte count had diminished from $4.7x10^6$ to $2.4x10^6$ cells/µl which was indicative of severe hemolysis. Intravascular coagulation was apparent with a concurrent reduction in thrombocytes. Anticoagulation therapy was undertaken with heparin infusion. Exchange transfusions with blood and hemodialysis were provided. Blood gases demonstrated a continued deterioration with pO_2 at 40 mm at 24 hours after admission. Renal function was absent for the first 10 days of hospitalization and recovered slowly. The patient required peritoneal dialysis for 40 days and was only discharged after 3 months. Summary Report. ([redacted], 2/1/24).

1020-0107; 353039; "The Effects of Chronic Administration of Chlorine Dioxide, Chlorite and Chlorate to Normal Healthy Adult Male Volunteers"; (Lubbers J.R., S. Chauhan, J.K. Miller, and J.R. Bianchine; The College of Pharmacology, The Ohio State University, Columbus, OH; J Environ Pathol Toxicol Oncol:229-238 (1984)); Ten healthy male volunteers drank 500 ml/day of a 5 ppm sodium chlorate solution (2.5 mg/day, approximately 35 µg/kg/day for a 70 kg man) for 12 weeks. Each participant received a weekly physical examination. These examinations included recording of vital signs (blood pressure, pulse rate, respiration rate and body temperature), electrocardiograms and medical history. Clinical tests of a standard blood panel, thyroid function, antibody formation, haptoglobin and methemoglobin concentrations, and blood morphology were periodically performed. During the study, certain parameters did demonstrate a statistically significant difference for the treated individuals from that of the control group, particularly that of mean corpuscular hemoglobin levels. However, upon further examination, this was not deemed to be of physiological importance. Summary report ([redacted], 1/26/24)

DATA GAP STATUS TABLE

Study Type	Data Gap Status
Combined Chronic Toxicity/ Carcinogenicity, Rat	No data gap, possible oncogenic effect
Subchronic Toxicity, Dog[1]	No data gap, no toxicologically significant effect
Oncogenicity, Mouse	No data gap, possible oncogenic effect
Reproduction, Rat	No data gap, no toxicologically significant effect
Developmental Toxicity, Rat	No data gap, no toxicological significant effect
Developmental Toxicity, Rabbit	No data gap, no toxicologically significant effect
Gene Mutation	No data gap, no toxicologically significant effect
Chromosome Effects	No data gap, no toxicologically significant effect
DNA Damage	No data gap,-possible DNA damage
Neurotoxicity	No study on file with DPR nor required[2]

[1] US EPA (2006). Length of Dog Toxicity Study(ies) that is Appropriate for Chronic RfD Determinations of Pesticide Chemicals.

[2] US EPA (2013). Part 158 Toxicology Data Requirements: Guidance for Neurotoxicity Battery, Subchronic Inhalation, Subchronic Dermal and Immunotoxicity Studies