Chlorite (sodium salt); CASRN 7758-19-2

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR Chlorite

File First On-Line 11/01/1995

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	10/12/2000*
Inhalation RfC (I.B.)	qualitative discussion	10/12/2000*
Carcinogenicity Assessment (II.)	yes	10/12/2000*

*A comprehensive review of toxicological studies was completed (05/27/05) - please see sections I.A.6., I.B.6., and II.D.2. for more information.

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Chlorite (sodium salt)
CASRN — 7758-19-2
Last Revised — 10/12/2000

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without

an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Neurodevelopmental effects **Two-generation rat drinking water study** **CMA, 1996**	NOAEL: 3 mg/kg-day (35 ppm sodium chlorite) LOAEL: 6 mg/kg-day (70 ppm sodium chlorite)	100	1	3×10^{-2} mg/kg-day

*Conversion Factors and Assumptions — MW of sodium chlorite = 90.5; MW of chlorite = 67.5. Doses (mg sodium chlorite/kg-day) were estimated by the study authors using measured water consumption and body weight data. To express doses as the chlorite ion, the estimated doses were multiplied by the molecular weight ratio of sodium chlorite to chlorite.

I.A.2. Principal and Supporting Studies (Oral RfD)

CMA (Chemical Manufacturers Association). (1996) Sodium chlorite: drinking water rat two-generation reproductive toxicity study. Quintiles Report Ref. CMA/17/96.

CMA (1996) conducted a two-generation study to examine reproductive, developmental neurotoxicity, and hematological endpoints in rats exposed to sodium chlorite. Thirty male and 30 female Sprague-Dawley rats (F0) generation received drinking water containing 0, 35, 70, or 300 ppm sodium chlorite for 10 weeks and were then paired for mating. Males were exposed throughout mating and then were sacrificed. Exposure for the females continued through mating, pregnancy, and lactation until necropsy following weaning of their litters. Twenty-five males and females from each of the first 25 litters to be weaned in a treatment group were chosen to produce the F1 generation. The F1 pups were continued on the same treatment regimen as their parents. At approximately 14 weeks of age, they were mated to

produce the F2a generation. Because of a reduced number of litters in the 70 ppm F1-F2a generation, the F1 animals were remated following weaning of the F2a to produce the F2b generation. Pregnant F1 females were allowed to litter and rear the F2a and F2b generations until weaning at postnatal day (PND) 21. Using water consumption and body weight data, the study authors calculated doses (adjusted for molecular weight) of 0, 3.0, 5.6, and 20.0 mg chlorite/kg-day for F_0 males; 0, 3.8, 7.5, and 28.6 mg chlorite/kg-day for F_0 females; 0, 2.9, 5.9, and 22.7 mg chlorite/kg-day for F_1 males; and 0, 3.8, 7.9, and 28.6 mg chlorite/kg-day for F_1 females. Numerous parameters were measured or calculated, including body weight, food and water consumption, estrus cycle in the F0 and F1, hematology and T3 and T4 levels in the F1 (blood samples collected from one male and one female from the first 20 F1 litters at age PND 25 and another group at 13 weeks), reproductive/developmental toxicity parameters (i.e., gestation duration, litter size, pup body weight, pup developmental landmarks), total caudal sperm number and percent motile, sperm morphology in the F0 and F1, and organ weight and histopathological examination (brain, pituitary gland, liver, adrenal, spleen, thymus, kidneys, and reproductive organs) of all F0 and F1 controls and high-dose animals. An additional group of F1 pups was chosen for neurohistopathology on PND 11 (examination of the brain and spinal cord) or PND 60 (sensory ganglia, dorsal and ventral nerve roots, and several peripheral nerves and muscles). Another group of F1 rats was examined for neurotoxicological endpoints (motor activity in a "Figure 8" Activity System and neuropathology on PND 60, auditory startle in the SR-Screening System, learning and memory retention in a water E-maze). A functional observational battery (FOB) was also conducted on the pups undergoing the auditory and learning assessments. This group was composed of 2 males and 2 females from 20 litters, and exposure was discontinued after weaning. A reevaluation of the auditory startle response was conducted in 20 males and 20 females in the F2a and F2b generations.

There were reductions in water consumption, food consumption, and body weight gain in both sexes in all generations at various times throughout the experiment, primarily in the 70 and 300 ppm groups. The authors attributed these reductions to a lack of palatability of the drinking water solution, but did not show data to support this contention. Significant alterations related to treatment at 300 ppm include reductions in absolute and relative liver weight in F0 females and F1 males and females, reduced pup survival (increase in number of pups found dead and/or killed prematurely during lactation) and reduced body weight at birth and throughout lactation in F1 and F2, lower thymus and spleen weight in both generations, lowered incidence of pups exhibiting a normal righting reflex and with eyes open on PND 15, alteration in clinical condition in F2 animals chosen for neurotoxicity, decreases in absolute brain weight for F1 males and F2 females, delays in sexual development in males (preputial separation) and females (vaginal opening) in F1 and F2, and lower red blood cell parameters in F1. It is possible that the reported alterations in pup sexual maturation measures may be due to reduced pup body weight, but a definitive conclusion cannot be drawn. In the 70 ppm groups, reduced absolute and relative liver weight in F0 females and F1 males was observed.

Minor, statistically significant changes in hematological data at the 35 and 70 ppm concentrations (generally 1%-7%) in the F1 appear to be within normal ranges based on historical data and are, therefore, not considered clinically or biologically significant or adverse. In addition, a significant decrease in maximum response to an auditory startle stimulus was noted in the 70 and 300 ppm groups on PND 24, but not on PND 60. The NOAEL for this study is 35 ppm (3 mg chlorite/kg-day) and the LOAEL is 70 ppm (6 mg chlorite/kg-day) based on lowered auditory startle amplitude and altered liver weights in two generations.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF=100

The composite uncertainty factor (UF) of 100 includes a factor of 10 to account for uncertainties associated with interspecies extrapolation and a factor of 10 for intrahuman variability. Because the critical effect is developmental toxicity in a database that includes chronic studies, it is not necessary to use an additional uncertainty factor to account for use of a less-than-lifetime study.

MF = 1.

I.A.4. Additional Studies/Comments (Oral RfD)

Lubbers et al. (1981, 1982, 1984a) examined the toxicity of chlorite in normal healthy adults. In the single-exposure study (Lubbers et al., 1981, 1982), 10 male adults consumed two (separated by 4 hours) 500 mL solutions containing 2.4 mg/L chlorite (0.034 mg/kg, assuming a reference body weight of 70 kg). In a 12-week study (Lubbers et al., 1984a), groups of 10 men drank 500 mL solutions of 0 or 5 mg/L chlorite (0.04 mg/kg-day assuming a 70 kg body weight). No physiologically relevant alterations in general health (observations and physical examination), vital signs, hematological (including erythrocyte and total and differential leukocyte counts, hemoglobin, hematocrit, and methemoglobin) or serum clinical chemistry (including glucose, electrolytes, calcium, urea nitrogen, enzyme levels, and cholesterol) parameters, or serum T3 or T4 levels were found in either study.

In a companion study, three healthy glucose-6-phosphate dehydrogenase (G6PD) deficient male subjects were given deionized water containing 5 mg/L chlorite (0.04 mg/kg-day, assuming a reference body weight of 70 kg) for 12 weeks (Lubbers et al., 1984b). Compared with the control group in Lubbers et al. (1984a), the chlorite exposure did not alter general health, vital signs, hematological parameters, or serum clinical chemistry parameters.

Michael et al. (1981), Tuthill et al. (1982), and Kanitz et al. (1996) examined communities with chlorine dioxide-disinfected water. Michael et al. (1981) found that chlorine dioxide in drinking water rapidly disappeared from the stored water (within 2-4 hours) and chlorite levels concomitantly increased. In an epidemiological study of a community using chlorite as a drinking water disinfectant, adult exposures ranged from 0 to 39.4 mg/day for chlorite for 10 weeks, and no consistent alterations in hematological parameters were reported (Michael et al., 1981). Tuthill et al. (1982) retrospectively compared morbidity and mortality data for a community that had utilized high levels of chlorine dioxide as a drinking water disinfectant with data from a neighboring community and found a greater postnatal weight loss in infants from the exposed community and no increase in the proportion of premature births when the age of the mother was controlled. The authors reported average monthly levels of 0.32 ppm of chlorine dioxide added post-treatment, but did not report total chlorine dioxide levels in the treated water. Kanitz et al. (1996) followed 598 births to women who lived in a community with filtered water disinfected with chlorine dioxide, sodium hypochlorite, or both, and 128 births to women living in a community with well water that did not undergo disinfection treatment. Levels of chlorine dioxide in the water immediately after treatment were less than 0.3 mg/L, while chlorine residue was less than 0.4 mg/L. The study authors concluded that infants of women who consumed drinking water treated with chlorine compounds during pregnancy were at higher risk for neonatal jaundice, cranial circumference <= 35 cm, and body length <= 49.5 cm. However, these studies as a whole are limited by methodological problems such as lack of characterization of exposure to other agents in the drinking water, drinking water consumption data, and control of potential confounding factors.

The subchronic/chronic toxicity of chlorite was investigated by Harrington et al. (1995) and Haag et al. (1949). Harrington et al. (1995) administered via gavage 0, 10, 25, or 80 mg sodium chlorite/kg-day (0, 7.4, 19, or 60 mg chlorite/kg-day) to Sprague-Dawley rats for 13 weeks. At the highest dose, gross effects included increased adrenal, spleen, liver, and kidney weight. Hematological alterations included decreased erythrocyte counts, hemoglobin levels, and hematocrit; increased methemoglobin levels (males) and decreased methemoglobin levels (females). Histologic alterations of the stomach consisted of squamous epithelial hyperplasia, hyperkeratosis, ulceriation, chronic inflammation, and edema. At 19 mg/kg-day, stomach lesions (similar to those in the high-dose group) and increases in absolute and relative spleen weights and relative adrenal weights were observed. No effects were observed at 7.4 mg/kg-day.

In the Haag (1949) study, renal pathology, characterized by distention of the glomerular capsule and appearance of a pinkish staining material in the renal tubules, was observed in rats exposed to 100 or 1,000 mg/L chlorite in drinking water for 2 years (9.3 or 81 mg/kg-day). These effects were also observed in a group of animals administered sodium chlorite at a concentration equimolar to 1,000 mg sodium chlorite/L. No other effects were observed. The

study was limited because there was an insufficient number of animals tested per group, pathology was conducted on a small number of animals, and it did not provide adequate evaluations of more sensitive parameters, which would have been more useful in the overall assessment of chronic toxicity.

Numerous animal studies have examined neurodevelopmental toxicity of chlorine dioxide and chlorite. These studies consistently show a LOAEL of 14 mg/kg-day and NOAEL of 3 mg/kg-day for multiple neurodevelopmental endpoints. Decreases in locomotor activity on PND 18-19, but not on days 15-17 or day 20, were observed in Sprague-Dawley rat pups administered gavage doses of 14 mg/kg-day chlorine dioxide on PND 5-20 (Orme et al., 1985). In in utero-exposed pups (dams exposed to 100 mg/L chlorine dioxide in drinking water [14 mg/kg-day] for 2 weeks prior to mating and throughout gestation and lactation), there was a consistent decrease in locomotor activity, but the activity was not statistically significantly lower than controls. Triiodothryonine (T3) and thyroxine (T4) were significantly decreased in the in utero-exposed pups and T4 levels were decreased in the postnatally exposed pups. No significant alterations in locomotor activity or T3 or T4 levels were observed in the offspring of rats exposed to 2 or 20 mg/L (1 or 3 mg/kg-day; exposure protocol the same as 100 mg/L group). However, there was a significant correlation between T4 levels and locomotor activity in all groups. Thus, this study identifies a NOAEL of 3 mg/kg-day and LOAEL of 14 mg/kg-day.

Mobley et al. (1990) found decreases in exploratory activity on postconception days 36-39, but not on days 39-41, in offspring of Sprague-Dawley rats exposed to 100 ppm chlorine dioxide in the drinking water (14 mg/kg-day) for 10 days prior to mating with unexposed males and during the gestation and lactation periods. A significant decrease in litter weight was also observed. Mobley et al. also found significant decreases in exploratory activity on PND 36-39, but not on days 39-41, in the offspring of Sprague-Dawley rats exposed to 40 ppm chlorine dioxide in the drinking water (6 mg/kg-day) for 10 days prior to mating and during gestation and lactation. T3 and T4 levels were not significantly altered. A slight decrease in activity was also observed in the offspring of rats exposed to 20 ppm (3 mg/kg-day). This study identifies a NOAEL of 3 mg/kg-day and LOAEL of 14 mg/kg-day.

Decreases in exploratory activity (PND 60) were also observed by Taylor and Pfohl (1985) in offspring of Sprague-Dawley rats exposed to 100 ppm chlorine dioxide in the drinking water (14 mg/kg-day) for 14 days prior to breeding and throughout gestation and lactation. A nonsignificant decrease in locomotor activity was noted in PND 10-20. Decreases in home cage or wheel-running activity occurred on PND 10 and 18-19 in pups (not exposed in utero) administered gavage doses of 14 mg/kg-day on PND 5-20. In addition to the decreases in motor activity, decreases in brain weight (primarily due to a decrease in cerebellar weight) and

total cell numbers in the cerebellum were observed in the in utero-exposed pups. A LOAEL of 14 mg/kg-day was identified in this study; a NOAEL was not identified.

Toth et al. (1990) found decreases in forebrain weight, accompanied by decreases in protein content, on PND 21 and 35 in Long-Evans hooded rat pups receiving gavage doses of 14 mg/kg-day on PND 1-20. Dendritic spine counts in Krieg's area 18 (a visual association region of the cortex) were also significantly decreased. No gross lesions, loss of myelin, or changes in cells staining positive for Nissl substance in the forebrain, cerebellum, or brainstem were observed. T3, T4, and free T4 index were not significantly altered on PND 11, 21, and 35. The 14 mg/kg-day dose is a LOAEL for neurodevelopmental effects.

For more detail on Susceptible Populations, exit to the toxicological review, Section 4.7 (PDF).

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — High
RfD — Medium-to-High

The overall confidence in this RfD assessment is medium-to-high. Confidence in the CMA (1996) principal study is medium. Although the study design and analytical approaches are consistent with EPA testing guidelines, some limitations in the design and conduct of the study exist. These limitations include (1) lack of pair-watered and -fed controls, which confounds the results and precludes definitive conclusions on whether the alterations in food and water consumption and body weight are related to water palatability or are a direct toxic effect of the agent; (2) developmental landmarks (e.g., vaginal opening in F2a group) were not reported for all groups; (3) grip strength and landing foot splay were not included in the FOB; and (4) discontinuation of exposure for the animals undergoing neurotoxicity testing minimizes the likelihood of finding a positive effect and precludes comparison of the data with those of other rats with continued exposure. Discontinuation of exposure after weaning reduces the opportunity to detect neurological effects from continuous or lifetime exposures similar to those expected from lifetime drinking water exposure in humans. Confidence in the database is high because there are studies in multiple species, chronic duration studies in males and females, reproductive/developmental toxicity studies, and a multigenerational study. The threshold for adverse effects is consistently defined among the animal studies.

For more detail on Characterization of Hazard and Dose Response, exit to the toxicological review, Section 6 (PDF).

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — This assessment is presented in the Toxicological Review of Chlorine Dioxide and Chlorite (CAS No. 10049-04-4 and 7758-19-2) (U.S. EPA, 2000).

This assessment was peer reviewed by external scientists. Their comments have been evaluated carefully and incorporated in finalization of this IRIS Summary. A record of these comments is included as an appendix to U.S. EPA, 2000. ***To review this appendix, exit to the toxicological review, Appendix A, Summary of and Response to External Peer Review Comments (PDF)***.

Agency Consensus Date — 9/20/2000

A comprehensive review of toxicological studies published through May 2005 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing RfD for Chlorite (sodium salt) and a change in the RfD is not warranted at this time. For more information, IRIS users may contact the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX), or hotline.iris@epa.gov (Internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Chlorite (sodium salt)
CASRN — 7758-19-2
Last Revised — 10/12/2000

The inhalation reference concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for the respiratory system (portal-of-entry) and effects peripheral to the respiratory system (extrarespiratory effects). It is generally expressed in units of mg/m^3. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of

Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.B.1. Inhalation RfC Summary

An RfC for chlorite is not recommended at this time. No human or animal studies examining the toxicity of inhaled chlorite were located. Although the available human and animal data on inhaled chlorine dioxide support the derivation of an RfC for this chemical, these data cannot be used to derive an RfC for chlorite. Under ambient conditions, airborne chlorite is likely to exist as a particulate, whereas inhalation exposure to chlorine dioxide is as a gas. On the basis of their physical and chemical properties, it is anticipated that inhaled chlorine dioxide and chlorite would have very different modes of exposure, and the potential hazard associated with exposure to these two chemicals is also very different. In the absence of data demonstrating parallels in pharmacokinetic behavior following inhalation exposure, as is present following oral exposure, derivation of an RfC for chlorite from the available data for chlorine dioxide is not recommended.

I.B.2. Principal and Supporting Studies (Inhalation RfC)

None

I.B.3. Uncertainty and Modifying Factors (Inhalation RfC)

Not applicable.

I.B.4. Additional Studies/Comments (Inhalation RfC)

Not applicable

I.B.5. Confidence in the Inhalation RfC

Not applicable

I.B.6. EPA Documentation and Review of the Inhalation RfC

Source Document — U.S. EPA, 2000

This assessment was peer reviewed by external scientists. Their comments have been evaluated carefully and incorporated in finalization of this IRIS Summary. A record of these comments is included as an appendix to U.S. EPA, 2000.

Agency Consensus Date — 9/20/2000

A comprehensive review of toxicological studies published through May 2005 indicated that there is insufficient health effects data to derive an RfC for Chlorite (sodium salt) at this time. For more information, IRIS users may contact the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

I.B.7. EPA Contacts (Inhalation RfC)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (fax), or hotline.iris@epa.gov (Internet address).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Chlorite (sodium salt)
CASRN — 7758-19-2
Last Revised — 10/12/2000

Section II provides information on three aspects of the carcinogenic assessment for the substance in question, the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per µg/L drinking water or risk per $\mu g/m^3$ air breathed. The third form in which risk is presented is a concentration of the chemical in drinking water or air associated with cancer risks of 1 in 10,000, 1 in 100,000, or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in the Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since

the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Under the current guidelines (U.S. EPA, 1986), chlorite is classified as Group D; not classifiable as to human carcinogenicity because of inadequate data in humans and animals. Under the draft Carcinogen Assessment Guidelines (U.S. EPA, 1996), the human carcinogenicity of chlorite cannot be determined because of a lack of human data and limitations in animal studies. Chronic oral studies in rats showed no evidence of carcinogenic activity of chlorite (Kurokawa et al., 1986). The short exposure duration (85 weeks) and high incidence of Sendai viral infection in control and exposed rats limit the use of this study to assess carcinogenicity. The mouse studies (Kurokawa et al., 1986; Yokose et al., 1987) showed an increase in liver and lung tumors in treated male mice. However, relatively short exposure duration (80 weeks) and the high incidence of early mortality in the concurrent control males from excessive fighting make statistical comparisons between concurrent controls and treated animals difficult to interpret. No increases in tumor incidence were seen in female mice in this study. Chlorite did not act as a complete carcinogen in a 51-week dermal carcinogenicity assay in mice (Kurokawa et al., 1984). In the same study, chlorite induced skin tumors following initiation by DMBA, but the increase was not statistically significant. Chlorite has shown both positive and negative results in in vitro and in vivo genotoxicity assays.

For more detail on Characterization of Hazard and Dose Response, exit to the toxicological review, Section 6 (PDF).

For more detail on Susceptible Populations, exit to the toxicological review, Section 4.7 (PDF).

II.A.2. Human Carcinogenicity Data

None

II.A.3. Animal Carcinogenicity Data

Inadequate. Kurokawa et al. (1986) exposed groups of 50 male and 50 female F344 rats to 0, 300, or 600 ppm sodium chlorite in drinking water for 85 weeks. Using water consumption and body weight data, the study authors estimated the doses to be 18 and 32 mg/kg-day in male rats and 28 and 41 mg/kg-day in female rats. All groups of rats were infected with the Sendai virus. No adverse effect on survival was observed. A slight dose-related decrease in body weight gain was observed (body weight gain in the high-dose group was within 10% of controls). No chlorite-related increases in tumor incidence were observed.

Kurokawa et al. (1986) also exposed groups of 50 male and 50 female B6C3F1 mice to 0, 250, and 500 ppm sodium chlorite in the drinking water for 80 weeks followed by a 5-week recovery period. The results of this study are also presented in Yokose et al. (1987). Daily doses of 0, 48, and 95 mg sodium chlorite/kg-day (0, 36, and 71 mg chlorite/kg-day) were calculated by U.S. EPA (1994). In the mice, there were no significant chlorite-related alterations in survival or body weight gain; increased mortality observed in the male control group was attributed to severe fighting. Significant increases in liver and lung tumors were observed in the male mice. The incidence of hyperplastic nodules in the liver was significantly increased in the low- and high-dose groups relative to controls (3/35 [reported as 6/35 in Yokose et al., 1987], 14/47, 11/43, in the control, low-, and high-dose groups, respectively) and the combined incidence of liver hyperplastic nodules and hepatocellular carcinoma was increased in the low-dose group (7/35, 22/47, and 17/43, respectively). The incidences of lung adenoma (0/35, 2/47, and 5/43, respectively) and the combined incidence for lung adenoma and adenocarcinoma (0/35, 3/47, and 7/43, respectively) were significantly increased in the high-dose group when compared with the controls. The study authors noted that the incidences of liver hyperplastic nodules and lung adenomas in the treated animals were within the range of historical controls in their laboratory and in the National Toxicology Program laboratories. The high mortality in the control males due to fighting may have contributed to the low tumor incidence in the concurrent control group. In the female mice, the only significant alteration in tumor incidence was a significantly lower incidence of malignant lymphoma/leukemia in the high-dose group (7/47, 5/50, 1/50, respectively).

II.A.4. Supporting Data for Carcinogenicity

Kurokawa et al. (1984) also conducted dermal carcinogenicity studies. In a study to assess the ability of chlorite to act as a complete carcinogen, groups of 20 female SENCAR mice were exposed twice weekly for 51 weeks to 20 mg sodium chlorite/mL in acetone. The solution (0.2 mL; 100 mg sodium chlorite/kg per application) was applied to the shaved backs of the mice. The sodium chlorite exposure did not result in increased tumor incidence. To test the ability of chlorite to act as a tumor promoter, a single initiating dose of 20 µM of

dimethylbenzanthracene (DMBA) was applied to the skin of 20 SENCAR mice. The DMBA application was followed by a 51-week exposure to sodium chlorite (as described for the complete carcinogen study). The tumor incidence was 6/20 (30%) compared with 0/20 in mice that received DMBA followed by acetone treatments for 51 weeks. Squamous cell carcinomas were observed in 5/20 animals in the chlorite group. However, these changes failed to reach statistical significance.

The genotoxicity of chlorite has been assessed in several in vitro and in vivo assays. In in vitro assays, chlorite induced reverse mutations in *Salmonella typhimurium* (with activation) and chromosome aberrations in Chinese hamster fibroblast cells (Ishidate et al., 1984). In general, the results of the in vivo assays have been negative. In the micronucleus assays, negative results were found in ddY mice following an oral gavage dose of 37.5-300 mg/kg single injection (Hayashi et al., 1988) and in Swiss CD-1 mice administered 0.25-1 mg via gavage for 5 consecutive days (0, 8, 20, and 40 mg/kg-day) (Meier et al., 1995). Using the same dosages, Meier et al. (1985) also reported negative results in the bone marrow chromosomal aberration assay in Swiss CD-1 mice and in the sperm-head abnormality assay in B6C3F1 mice. Positive results were found in the micronucleus assay in ddY mice when the chlorite was administered via intraperitoneal injection (7.5-60 mg/kg) (Hayashi et al., 1988).

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

None

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

None

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA, 2000

This assessment was peer reviewed by external scientists. Their comments have been evaluated carefully and incorporated in finalization of this IRIS Summary. A record of these comments is included as an appendix to U.S. EPA, 2000. ***To review this appendix, exit to the***

toxicological review, Appendix A, Summary of and Response to External Peer Review Comments (PDF).

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Consensus Date — 9/20/2000

A comprehensive review of toxicological studies published through May 2005 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing carcinogenicity assessment for Chlorite (sodium salt) and a change in the assessment is not warranted at this time. For more information, IRIS users may contact the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (fax), or hotline.iris@epa.gov (Internet address)

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Chlorite (sodium salt)
CASRN — 7758-19-2

VI.A. Oral RfD References

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VII. Revision History

Substance Name — Chlorite (sodium salt)
CASRN — 7758-19-2

Date	Section	Description
11/01/1995	II.	Carcinogenicity assessment on-line
10/12/2000	I., II., VI.	Oral RfD on-line, RfC discussion, revised carcinogenicity assessment
10/28/2003	I.A.6., I.B.6., II.D.2.	Screening-Level Literature Review Findings message has been added.
06/22/2005	I.A.6., I.B.6., II.D.2.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — Chlorite (sodium salt)
CASRN — 7758-19-2
Last Revised — 10/12/2000

- 14998-27-7
- Chlorite
- Chlorous acid, ion (1-)
- Clorito [Spanish]