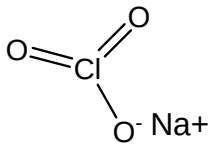
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7775-09-9
Chemical Name	Sodium chlorate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Sodium chlorate is rapidly absorbed and distributed throughout the body where after exerting its oxidative action it will be taken up in the chloride pool. Excretion takes place in the urine mainly in the form of chloride. Excretion of unchanged sodium chlorate is only observed during the first day after uptake.

Animal studies with sodium chlorate show a low acute toxicity after inhalation (LC_{50} > 5.59 mg/l), dermal (LD_{50} > 2000 mg/kg bw) and oral (4950-6250 mg/kg bw) exposure. A handbook reports that doses of 5 to 10 grams can be fatal in adult humans, and doses of 2 grams in children. But also multiple cases are described surviving intakes ranging from 40 g to even 150-200 grams. This is likely related to the possibility of dialysis treatment in case of renal failure after the 1960's. No fatalities were reported in recent years. Despite the low acute toxicity in animals, available data on human lethal effects indicate that sodium chlorate should be classified as harmful.

The primary concern for acute sodium chlorate exposure is oxidative damage to red blood cells and resulting methaemoglobinemia. Acute toxicity of chlorate is mediated by methemoglobin. There are marked species differences in susceptibility to form methemoglobin. Humans are more affected than rodent species.

Experience from exposure of workers in chlorate production plants indicates that eye and respiratory irritation are possible. Also cases were reported of 1st and 2nd grade skin burns related to the possible spontaneous ignition of dried sodium chlorate. Sodium chlorate is only mildly irritating to skin and eyes in rabbit studies. Available data and studies do not indicate that sodium chlorate has a potential for skin sensitization. Concerns for subchronic and chronic chlorate exposures are related to its competitive inhibition of iodide transport through thyroid follicular cells, required for thyroid hormone synthesis. This results in an initial decrease in the T3 and T4 serum levels followed by a compensatory increase of TSH. This in turn results in an increase in thyroid cell proliferation with subsequent restored thyroid hormone production, thus maintaining homeostasis. Thyroid effects were already visible after intake from 4 mg/kg/day in animal (rat) studies. These effects indicate a physiological compensatory mechanism to maintain homeostasis upon the presence of chlorate, and not an adverse effect as such. Human volunteer studies, which also included evaluation of thyroid function parameters, showed no effects up to 36 µg/kg/day for 12 weeks. Sub-chronic and chronic studies do not show a high level of toxicity. A 90-day study on rats resulted in a NOAEL of 100 mg/kg bw/day and a 90-day study on dogs resulted in a NOAEL of 360 mg/kg bw/day, the highest dose tested. In another rat study, a NOAEL of 38 mg/kg was determined when based on the colloid depletion in reaction to decreased iodide transport. In this study, haematological effects (anemia) were also observed at the highest dose (653 mg/kg/day for males and 1021 mg/kg/day for females).

Available studies differ in their reported effects on the thyroid. One study did not show any effect after 90-days up to 1000 mg/kg/day, whereas in NTP studies (2004) hypertrophy was observed from around 40 mg/kg/day. Another 90-day study in rats indicated possible effects of thyroid colloid depletion, and a NOAEL in rats of 38 (males) and 53 mg/kg bw/day (females). A two generation reproduction study on rats indicated a parental NOAEL of 10 mg/kg bw/day for males and 70 mg/kg bw/day for females, based on slight to moderate follicular hyperplasia and signs of slight to moderate hyperactivity of the thyroid gland. Two year chronic NTP studies (2004) in mice and rats indicated thyroid hypertrophy in rats. There seemed to be a concentration related increase in percentage of smaller follicles, often showing colloid depletion, which was visible from 4.5 mg/kg bw/day in males. The seriousness of

long term stimulation of the follicle cells is relatively limited as even at the highest dose levels in this study of 75 to 96 mg sodium chlorate/kg bw/day hypertrophy was clearly present, whereas hyperplasia and follicular cell carcinomas, although exceeding control ranges, were not statistically significant increased.

Although no haematological effects were observed in the chronic NTP studies, the incidence of bone marrow hyperplasia was possibly increased in male rats and female mice, but lowered in male mice.

In a two generation study, there was no indication of either reproductive toxicity of sodium chlorate or developmental toxicity up to 500 mg/kg bw/day in rats. No indication of developmental toxicity was observed up to 475 mg/kg bw/day in rabbits

Sodium chlorate was not mutagenic in the majority of in vitro studies and in all in vivo systems tested. Sodium chlorate did not induce gene mutations in either bacteria or mammalian cells but the results in *Escherichia coli* are suggestive of a primary DNA damage with no requirement for metabolic activation. This effect was not confirmed in mammalian HeLa S3 cells. Sodium chlorate was not considered to be genotoxic.

In the NTP carcinogenicity study, sodium chlorate resulted in a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma in female mice. NTP concluded that it was an equivocal effect. An increase of thyroid neoplasia in male rats (at 75 mg/kg bw/day) was seen. Taking into account the mechanism of action, available data suggest hormone imbalance leads to thyroid tumor formation in rats. The human thyroid is much less sensitive than the rat thyroid for this TSH stimulated effect. Therefore, sodium chlorate was not considered to be a potential human carcinogen.

Environment

Ecotoxicity: Sodium chlorate is a white, odorless, crystalline solid and is highly water soluble. It is a strong oxidant, not combustible but reacts violently with combustible and reducing materials. There is a risk of fire and explosion in dry mixtures with other substances, especially certain organic materials.
Sodium chlorate has a melting point of 255.0 –259.5 ± 1°C, and decomposes upon further heating. The solubility in water at 20 °C is about 802 g/L.

Distribution: Sodium chlorate does not adsorb to soil and will end up in the surface water where it dissociates. Due to its chemical structure, sodium chlorate is considered as stable in water regardless of the pH. Bioaccumulation is not expected. A representative average upon delivery of industrial hypochlorite to bleach formulators is 3 to 5 g/L sodium chlorate in commercial concentrated (15% w/w) hypochlorite product. The total chlorate level amounts to 1.8 g/L in domestic bleach. The predicted environmental input of chlorate from bleach in surface waters is 12.5 µg/l (range 0.4-30 µg/l) for Europe. There are few data on chlorate levels in brackish or marine waters. In the Baltic Sea, mean values of up to 53 mg ClO_3-/L were recorded in kraft pulp mill effluent discharged into coastal waters in the early 1980s. A few years later the system was improved and the concentration in the Baltic Sea decreased to 2 µg/l at a distance of 3 - 4 km from the diffuser.

Fate: As sodium chlorate is an inorganic substance, it cannot be defined as biodegradable on the basis of mineralization of organic matter. However biotic degradation occurred within anaerobic niches in the soil where anaerobic biodegradation occurred via non-obligate anaerobes which mineralise chlorate to chloride generally using the same pathway as for nitrate reduction. In a water-sediment system the DT_{50}s under anaerobic- and aerobic conditions were 8 days in water and less than 3 days in sediment. In soil, sodium chlorate is rapidly degraded under anaerobic conditions, the half-life is 7.5 days. Under aerobic conditions the half-life was at least 39 days. In the presence of glucose or sucrose at a concentration of 10 g carbon/kg soil potassium chlorate is rapidly degradable under aerobic conditions. A concentration of 341 mg chlorate/kg soil was almost completely decomposed within 4 weeks. In 30 cm soil columns sodium chlorate was found in the leachate, but more than half of the total amount was degraded over a period of 34 days.

Freshwater organisms were not found to be particularly sensitive to sodium chlorate. In the acute studies aquatic algae were found to be most sensitive species tested. For *Selenastrum capricornutum* the E_rC_{50} at 72h was 129 mg/l. The EC_{50} for invertebrates (*Daphnia magna*) was greater than 1000 mg/l. For several fish species an LC_{50} greater than 1000 mg/l was found. Of the chronic aquatic endpoints, the macrophyte, *Lemna minor* was found to be the most sensitive species to sodium chlorate with a NOEC of 10 mg/l. The NOEC for fish (*Danio rerio*) and invertebrates (*Daphnia magna*) were greater than or equal to 500 mg/l (the highest concentration tested in each case). The EC_{50} for aquatic microorganisms was greater than 1000 mg/l.

Sodium chlorate is considered as practically non-toxic to freshwater species (EC/LC_{50}s > 100 mg/l). In addition, there is no potential risk of bioaccumulation of sodium chlorate (estimated log P_{ow} < -2.9).

For marine organisms the following tests were performed. The LC_{50} to marine fish was greater than 1000 mg/l. For *Nitzschia closterium* a test with potassium chlorate gave an EC_{50} of 2.8 mg $KClO_3$/l. This was found to be due to the low nitrate concentration used in the study (<0.005 mg NO_3^-/l).

For terrestrial organisms, several data were found. The 14-day LC50 for oligogaetes > 750 mg/kg soil dw. The lowest acute value for arthropods was found for *Typhlodromus pyri* Scheuten with a LR_{50} of 84.4 kg/ha. For worker honey bees, the oral toxicity LD_{50} was greater than 75 µg/bee. Acute and chronic toxicity to birds was tested. The NOAEL (NOEL) in a 14-day study with ducks was higher than 2510 mg/kg. A 135-day study with *Colinus virginianus* gave a NOEC of 300 ppm (equal to 31.6 mg/kg bw/day).

Exposure

Production: Between 1990 and 2002, the North American sodium chlorate capacity increased from 1,100 to 2,100 ktons/year. The total production capacity in Western Europe was about 700 ktons/year in 2002. Eastern Europe had a production capacity of less than 100 ktons/year in 2002. The total use in the Nordic countries is estimated at 260 to 270 ktons/year. In Japan the total volume consumed in 2005 was 100 ktons.

Use: Up to 95% of all sodium chlorate produced worldwide goes into the pulp and paper industry where it is used to generate chlorine dioxide, a key bleaching agent. The other 5% is mainly used as a herbicide and for uranium manufacture. Use as a non-selective herbicide and defoliant has strongly declined. Sodium chlorate is further used as intermediate in making rocket propellants and dyes, in refining for vanadium and uranium and often as intermediate for other chlorates, in matches, explosives, cosmetics and the pharmaceutical industry. Chlorate is present as a by-product in domestic hypochlorite bleach. In the chlor-alkali industry, producers are switching from mercury-based to membrane cell technology, resulting in the discharge of chlorates instead of mercury. Furthermore it is used as oxidizing agent for acrylic fiber.

Release: Releases into the environment may occur during production, further processing and use of chlorates, as well as from by-product formation during water disinfection with chlorine dioxide, from chlorine production from membrane electrolysis, and presence in hypochlorite bleach.

Occupational exposure: Exposure can occur during production and handling of sodium chlorate. The use of protective suits, boots, gloves, goggles and hardhat with safety visor are mandatory when handling sodium chlorate. Dried sodium chlorate is an ignition hazard in the presence of organic material. The packaging of sodium chlorate powder leads to dust exposure even if workers use personal protective equipment. Epidemiological exposure assessments were not available. A recent survey on the medical status among workers from European sodium chlorate production sites reported no evidence of important health effects related to occupational exposure to sodium chlorate.

Consumer products: Chlorate is present as a by-product in domestic hypochlorite bleach. Sodium chlorate does not form a vapor, therefore exposure of the general public is limited to indirect intake via drinking water and food. From recent literature studies, this intake is expected to be below the WHO TDI of 0.03 mg/kg/day (2005).

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical possesses properties indicating a hazard for human health. For acute exposure, the oxidative damage to red blood cells and resulting methaemoglobinemia are of concern. For long-term exposure the potential critical effect is on thyroid function. Exposure to humans is anticipated to be low. Therefore, this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by Sponsor country.

Environment: The chemical is currently of low priority for further work because of its low hazard profile to freshwater organisms. However, marine tests indicate that chlorate toxicity increases when nitrate concentrations are low. The substance has a high potential of biodegradation in sediment and soil and low potential for

bioaccumulation.