SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7782-50-5
Chemical Name	Chlorine
Structural Formula	Cl-Cl

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Chlorine is a gas which when dissolved in water is in a fast equilibrium with hypochlorous acid (HOCl) which is in equilibrium with hypochlorite ion (ClO^{-}). The latter is predominant at alkaline pH values, while Cl_2 is mainly present at pH below 4. Therefore the concentration of chlorine in an aqueous solution is generally expressed as available chlorine which is the sum of Cl_2+HOCl+ ClO^-, regardless whether these species stem from dissolved gaseous chlorine or from dissolved sodium hypochlorite.

Although the ingestion of chlorine gas is unlikely, solutions of chlorine may pose hazard by this route of exposure.

Most of data for chlorine toxicity by oral route come from studies performed with sodium hypochlorite. In biological systems, characterised by pH values in the range 6-8, the most abundant active chemical species is HOCl, in equilibrium with ClO.

Available chlorine is readily absorbed via oral route and distributed into plasma, bone marrow, testis, skin, kidney and lung. Only ca. 50% is excreted mainly with the urine followed by excretion with feces. HOCl is not enzymatically metabolised and its (bio) tranformation readily occurs through direct reactions with organic compounds or with other chemicals present in the cellular environment, leading to the formation of chlorinated organic compounds possessing their own inherent toxicity.

Irrespective of the mode of breathing (either through the nose or the mouth) and respiratory flow rate, > 95% of the inspired Cl_2 was absorbed in the upper airways, whereas the dose delivered to the lower airways was < 5% when a micro-bolus of 3 ppm in air is injected into an airstream. No data are available for a continuous exposure to 3 ppm or more of chlorine.

A large number of studies on acute inhalation toxicity of chlorine have been performed. The results from these studies show that acute inhalation toxicity is high and LC50 values ranges from 250 ppm (900 mg/m^3 /30 min) for mice to 400 ppm (1200 mg/m^3 /30 min) for rats. Asthma-like symptoms following acute inhalation of high-dose irritant gases have also been related to acute chlorine exposure in humans.

No information is available on any potential systemic toxicity that can be caused by dermal route as no dermal acute toxicity studies are available for both chlorine or hypochlorite salts solutions. It can be expected to be low considering the low acute systemic toxicity by the oral route.

Chlorine is corrosive to the skin and severe effects can be expected from exposure to the eyes. Moderate to severe lesions in the respiratory tract after exposure to 9 ppm (27 mg/m^3) chlorine for 6 h/d at 1, 3 and 5 days were reported in rats and mice, mainly in the nasal passage, epithelial necrosis, cellular exfoliation, erosion, ulceration and squamous metaplasia. Skin sensitization studies are not available. No case reports were found showing a sensitization potential in humans.

For repeated dose toxicity, in a two year study, the LOAEL for respiratory irritation has been determined to be 0.4 ppm (1.2 mg/m^3) for rats and mice: an NOAEL for inhalation route could not be established. In none of the available studies any systemic effect was observed.

A NOAEL of 950 ppm available chlorine (59.5 mg/kg bw/day) can be derived from a 13-week rat study with sodium hypochlorite in drinking water. A NOAEL of 14 mg/kg bw/day for rats and a NOAEL of 22.5 mg/kg bw/day for mice can be derived from a two year study with sodium hypochlorite in drinking water.

There are many detailed studies reported for human exposure. An inhalation acute NOEL of 0.5 ppm (1.5 mg/m^3) which excludes tissue lesions and impairment of the pulmonary function can be derived by human experience and control studies in volunteers.

For genetic toxicity the majority of the *in vitro* assays have shown positive or ambiguous responses, suggesting that sodium hypochlorite may be mutagenic *in vitro*, however genotoxic effects were not seen *in vivo* probably due to the cytotoxic properties of chlorine.

No evidence of treatment related carcinogenicity was observed in mice and rats exposed by inhalation to chlorine and orally to sodium hypochlorite, but some equivocal results were reported for female rats by oral route. For human cancer no association between chlorine exposure and tumor incidence was observed.

The absence of reproductive toxic effects was clearly shown up to 5 mg/kg (maximum dose tested) in a one generation oral study in rats. Although limited data are available in animals, there is no evidence of adverse developmental effects. Moreover, epidemiological studies in humans did not show evidence of toxic effects on foetal development.

Environment

Chlorine is a greenish-yellow gas with a pungent odour at ambient temperatures and pressures. Density is 2.5 times higher than air. Its vapour pressure is 6.39 10^6 Pa at 20 °C. Molecular chlorine is a strong oxidiser and a chlorinating agent. Chlorine is moderately soluble in water (~6.5 g/ l). The total amount of chlorine dissolved in water and the relative amounts of the components in equilibrium (Cl_2+HOCl+ ClO^- = free available chlorine) are dependent on ionic strength and pH. Diluted aqueous solution of hypochloric acid will decompose, very slowly in the dark, but more rapidly in the presence of light, particularly rapidly in full sun light, by producing hydrogen chloride and oxygen. Some chlorine and chloric acid may also develop. The physico-chemical properties indicate that chlorine released into the environment is distributed into water and preferably air.

In water and in atmosphere chlorine/hypochlorite undergoes photolysis with an estimated half-life of 1-4 hours, depending on the time of the day. In natural water, in the presence of organic or inorganic compounds, the free available chlorine immediately reacts forming various chlorinated by-products e.g. chloramines and chloromethanes which are mainly distributed to the hydrosphere, but are also able to transfer to some extent to the atmosphere depending on their intrinsic properties. A potential for bioaccumulation or bioconcentration of active chlorine species can be disregarded, because of their water solubility and their high reactivity.

Valid freshwater short-term toxicity data are available only for invertebrates: the LC50 for *Ceriodaphnia dubia* is 5 µg FAC/l (FAC=Free available chlorine). Adequate standard acute tests with fish are not available, but from many reliable studies performed under intermittent exposure conditions a 96h LC50 of 60 µg TRC/l and a 168h LC50 of 33 µg TRC/l can be derived (TRC= total residual chlorine= the sum of combined end free residual available chlorine). Due to the intermittent regime (three 40 minutes pulses per day) a 96h LC50 << 60µg TRC/l can be expected for fish in a standard test.

For freshwater long-term toxicity, no valid NOEC values from standard long-term tests are available, but data can be derived by some microcosm and field studies: 7d -NOEC for algae 3 µg TRC/l, corresponding to 2.1 µg FAC.

For salt water short-term toxicity valid data are available for molluscs (48h EC50 = 26 µg TRC/l) and for fish (*Oncorhynchus kisutch* 96 h LC50 = 32 µg TRO/l) (TRO = Total Residual Oxidant) showing comparable sensitivity.

For long term toxicity the molluscs are more sensible than fish showing a 15d NOEC = 7 µg TRO/l, while a NOEC of 40 µg CPO/l was calculated for fish fry survival (CPO = Chlorine Produced Oxidants).

Exposure

Total annual world-wide chlorine production capacity was 46.5 million metric tonnes in 1999. Chlorine is produced from sodium chloride by three different processes: diaphragm, mercury and membrane. Chlorine is mainly used as a chemical intermediate to produce raw materials for chemical, pharmaceutical and crop protection industries. There are also wide dispersive use applications of elemental chlorine in water such as drinking water, pulp and paper, swimming pool, sewage treatment, cooling water and textile industry. It can be estimated that less than 1.8‰ of the production volume was released into the environment in the year 1999 and the world wide total antropogenic chlorine release can be estimated to be 71,000 metric tonnes.

Gaseous compounds such as hydrogen chloride (HCl), molecular chlorine (Cl_2), hypochlorous acid (HOCl), and nitryl chloride ($ClNO_2$) occur in nature in sea-salt aerosols arising from the oceans. Volcano eruptions release 400,000-11,000,000 tonnes/year hydrogen chloride into the atmosphere.

All systems for production of chlorine as well as the loading and unloading systems are closed systems. Chlorine is supplied in gaseous form to the destination plants mainly by pipeline. To a minor extent, it is distributed in liquefied form in bottles or tank cars (road and railway). Exposure to chlorine can occur through accidental events in industry (e.g. during filling operations of chlorine gas, in the pulp and paper industry using chlorine, HCl or chlorine dioxide as bleaching agents), in transport and storage, in professional water purification and disinfection measures for swimming-pools.

For workers an indicative limit of 0.5 ppm for short term exposure (15 minutes) to chlorine is proposed in a draft of European Directive on occupational exposure limits.

Since chlorine/ hypochlorite can be irritating or corrosive depending on the concentrations, exposure control should be provided and protective equipment for eyes and skin, masks with filters or self contained breathing apparatus should be worn during specific situations (filling operations, sampling for laboratory purposes) and kept always ready to use.

For consumers exposure to chlorine can occur through accidental events during the use of chlorine for disinfection of swimming-pools and the use of hypochlorite-containing cleaning products, e.g. through mixing of household cleaning agents, such as hypochlorite and acids eventually associated with chlorine release and inhalation.

General population can be exposed by indirect exposure via drinking water and by inhalation of natural occurring sources in the atmosphere.

RECOMMENDATION

Human Health: The chemical is currently of low priority for further work.

Environment: The chemical is a candidate for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical possesses corrosive properties and is an acute respiratory toxicant, indicating a hazard for human health. Based on data presented by the Sponsor country risk management measures are being applied. Countries may desire to check their own risk management measures to find out whether there is a need for

measures beyond those which are being applied.

Environment: The substance has hazardous properties for the environments. As there are some open uses of the substance (e.g. cooling water disinfection) an exposure assessment and if necessary risk assessment should be performed for these uses. The formation of chlorinated by-products should be taken into account.

Work to that effect is being or has been performed in many countries and also within the framework of the EU Existing Substances Regulation.

The substance is under risk assessment following the EU Existing Substances Regulation EC No.793/93.