SIDS INITIAL ASSESSMENT PROFILE

CAS No.	Sodium chlorite 7758-19-2 Chlorine dioxide 10049-04-4
Chemical Name	Category Sodium chlorite and chlorine dioxide
Molecular Formula	Sodium chlorite $NaClO_2$  Chlorine dioxide ClO_2 

SUMMARY CONCLUSIONS OF THE SIAR

Category justification

Chlorine dioxide and sodium chlorite are characterized together in this dossier because studies conducted with chlorite, the predominant reduction product of chlorine dioxide, are considered to be relevant in characterizing the toxicity of chlorine dioxide. In addition, studies conducted with chlorine dioxide may be relevant to characterize the toxicity of chlorite. Chlorine dioxide is fairly unstable and dissociates predominantly into chlorite (ClO_2^-) and chloride (Cl^-), and to a lesser extent, chlorate (ClO_3^-). There is a ready interconversion among these species in both water and the human gut. Therefore, what exists in water or the body is a mixture of these chemical species. Toxicity information on sodium chlorite is also relevant and appropriate for assessing the effects of chlorine dioxide in man and the environment and *vice versa.* This category approach does not take into account local effects that would occur by dermal or inhalation exposure as they are specific to each substance.

Human Health

Both sodium chlorite and chlorine dioxide are rapidly absorbed following ingestion with chlorine dioxide being converted into chlorite and chloride ions with chlorate as a minor by-product.

Both oral and dermal acute studies on sodium chlorite suggest that it is of moderate acute toxicity while chlorine dioxide gas is a potent respiratory toxicant. The oral LD_{50} for sodium chlorite in rats was 284 mg/kg body weight and the 24-hour dermal LD_{50} in rabbits was 134 mg/kg body weight. Acute oral and inhalation studies conducted with chlorine dioxide showed marked local toxicity and corrosive properties: The oral LD_{50} for chlorine dioxide was 94 mg/kg body weight while the inhalation LC_{50} was 0.089 mg/l. Two clinical acute oral studies of sodium chlorite and chlorine dioxide in humans gave no observed adverse effect levels (NOAELs) of 0.034 mg/kg body weight and 0.34 mg/kg body weight, respectively.

Sodium chlorite is non-sensitising to skin and is at worst, mildly irritating to skin (34.5%) and severely irritating to the eye (31% solution). Chlorine dioxide gas is classified as corrosive.

No repeat dose dermal and inhalation studies were available. In repeated-dose oral studies in rats and mice, the main target for both sodium chlorite and chlorine dioxide was the haematological system. Sodium chlorite was shown to induce a reduction in red blood cells, including decreased haemoglobin levels and haematocrit. This change was associated with morphological changes in the red blood cells, namely, polychromasia, poikilocytosis and macrocytosis. The NOAEL for sodium chlorite based on haematological effects observed in rats was 10 mg/kg body weight/day. Chlorine dioxide was also shown to induce decreased red blood cell counts, haemoglobin concentration and packed cell volume in addition to increased erythocyte fragility and blood glutathione levels based on a limited study. Although this latter study with chlorine dioxide was limited in the number of animals, it gives important information in terms of comparable effects with sodium chlorite. The other specific toxicity observed in monkeys and in some reproductive studies was an effect on the thyroid system (with decreased T3 and T4), which was demonstrated to be reversible. A lower oral LOAEL (1.9 mg/kg bodyweight/day) for chlorine dioxide based on nasal inflammation in male rats only, was probably caused by chlorine dioxide gas being released from the solution.

There were no reliable *in vitro* mutagenicity tests for sodium chlorite while those for chlorine dioxide were inconclusive. There were however, a number of negative *in vivo* tests for sodium chlorite and chlorine dioxide and it is considered that they have a low potential for genotoxicity.

In a carcinogenicity drinking water study in mice, there were no significant dose-related increases in tumour incidence with sodium chlorite, and it was concluded that sodium chlorite had no carcinogenic potential.

In a two-generation oral study with sodium chlorite in rats, haematotoxic effects occurred at all dose-levels and no significant fertility, reproductive or developmental effects were observed at the highest concentration tested. The NOAEL for haematotoxicity was 3 mg/kg bodyweight/day. A rabbit developmental study in drinking water concluded that sodium chlorite was not considered to be teratogenic or a selective developmental toxicant.

Chlorine dioxide did not affect fertility in a one-generation study performed on rats by gavage. The NOAEL was 10 mg/kg bodyweight/day (highest dose tested).

Experiments on human volunteers suggest no effects in humans exposed in drinking water to 0.036 mg/kg of bodyweight/day of chlorine dioxide or sodium chlorite during a period of 12 weeks. An epidemiological study of 198 people exposed for 3 months to drinking water disinfected with chlorine dioxide (concentration of chlorite ion averaged 5 mg/l) also suggested no effects in humans.

Environment

Sodium chlorite at atmospheric pressure is solid with a melting point of 234°C, a vapour pressure of 1.1×10^{-7} Pa at 25°C and its relative density is 2.432 at 20°C. It is soluble in water (571 g/1) with a dissociation constant of 141 equating to a pKa of 2.15. Under laboratory conditions in pure water and using very high levels of UV radiation, sodium chlorite solutions have a photodegradation half-life of about 30 minutes with major products being identified as chlorine dioxide, hydroxide and chloride ions with chlorate and hypochlorite as minor products. The radiation dose required to degrade sodium chlorite suggest that doses required for drinking water disinfection would not significantly reduce chlorite concentrations. Sodium chlorite is expected to be rapidly reduced to sodium chloride in the environment especially in anaerobic conditions.

Chlorine dioxide at atmospheric pressure is a gas with a melting point of -59^{o}C, vapour pressure of 975.9 hPa at 10^{o}C, a relative density of 1.6 at 0^{o}C (relative vapour pressure 2.3) and it is soluble in water (7.5 g/l). A number of physicochemical parameters for chlorine dioxide cannot be directly measured owing to its explosive potential when air concentrations exceed 10%. Solutions are stable when kept cold and in the dark. These chemicals are

strong oxidising agents.

Sodium chlorite, in general, shows low acute toxicity to fish with LC_{50} values above 100 mg/l for zebrafish, sheepshead minnow and rainbow trout and slightly lower for bluegill sunfish while chlorine dioxide appears to be highly toxic to fish. Due to extremely low lipophilicity and high instability in water, sodium chlorite is not expected to bioaccumulate in fish.

Sodium chlorite and chlorine dioxide are more toxic to invertebrates with high toxicity to *Daphnia magna* (sodium chlorite and chlorine dioxide, LC_{50} 48-hour = 0.063 and 0.026 mg/l, respectively) and the crustacean, *Mysidopsis bahia* (sodium chlorite LC_{50} 96-hour = 0.65 mg/l). However, the mollusc, *Crassostrea virginica* was much less sensitive (sodium chlorite 96 hours NOEC was 70.6 mg/l and the EC_{50} (shell growth) was 129 mg/l). The green algae were more sensitive to sodium chlorite than fish or oyster and toxicity increased with time (ECr50 value at 72 hours was recorded as 1.2 mg/l). At present there are no data on the stability and exposure of sodium chlorite in the environment. However, the instability of these chemicals suggests that it would not be relevant to perform chronic experiments.

Studies on the effects of sodium chlorite on terrestrial species were not of sufficient quality to form conclusions on its toxicity. Sodium chlorite would be expected to rapidly reduce to sodium chloride in the environment.

Exposure

The commercial production of sodium chlorite is carried out in two steps: first, sodium chlorate is reacted with an acid to generate chlorine dioxide, and then, chlorine dioxide is reacted with caustic soda, catalysed by hydrogen peroxide, to form sodium chlorite. The industrial product formed is a solution of about 34.5% sodium chlorite; the commercial grades are obtained by dilution with water.

The total amount of sodium chlorite (as 100%) sold on average in the EU member countries (15) for the years 1998-2000 was 11 800 tonnes per year. This includes use as preservatives for liquid cooling and processing systems; food and feed area disinfectants; food or feedstocks; molluscicides; and slimicides and other non-defined biocidal use. The estimated total consumption of sodium chlorite in Japan is 4000 tonnes per year.

In the European Union, the total amount of chlorine dioxide produced per year (averaged from the years, 1998-2000) from sodium chlorite is 7859 metric tonnes and the amount for biocidal use is 6105 metric tonnes, approximately 78% of the total production.

Occupational exposure may occur during manufacturing, in the paper and pulp bleaching industries, during use as a sterilizing agent in hospitals, as a biocide in water treatment and as an improving agent in flour. Sodium chlorite and chlorine dioxide may also occur in foodstuffs as a result of their use in processing.

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

Human Health: The chemicals in this category are candidates for further work. The chemicals possess properties indicating a hazard for human health (corrosivity, haematological toxicity). Member countries are invited to perform an exposure assessment for consumers and workers, and if then indicated, a risk assessment.

Environment: The chemicals in this category are candidates for further work**.** The chemicals possess properties indicating a hazard to the environment (acute toxicity to aquatic invertebrates). An exposure assessment, and if indicated, an environmental risk assessment are recommended, especially since the substances have widespread uses as biocides. However, the fact that these substances are considered to be unstable in the environment and rapidly degrade to the non-toxic chloride ion should be taken into account.

Note: For both human health and environment, a risk assessment will be carried out under the European Union Biocidal Products Directive. (dossiers on biocidal products should be submitted at latest by July 2007).

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