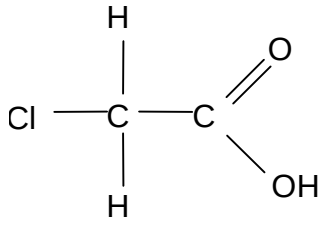
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	79-11-8
Chemical Name	2-Chloro-ethanoic acid
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analogue Rationale

The SIAR contains information on MCAA and SMCA, monocloroacetic acid and its sodium salt. For SMCA a SIAR already exists. Therefore, the present SIAP is only based on MCAA.

Human Health

Most of the studies on the toxicokinetics, metabolism, and distribution of MCAA are very briefly reported and were performed with relatively high doses. After oral exposure of rats and mice the absorption from the gastro-intestinal tract amounted to 90% and 60%, respectively. Based on the high toxicity in one inhalation study and the low molecular weight, inhalation absorption of 100% is indicated, in this limited study. Toxicity data also indicate a high and rapid absorption via the skin of rats, rabbits and humans (100%). The major metabolic pathway of MCAA is an initial formation of S-carboxymethyl glutathione, which is converted to S-carboxymethylcysteine, part of which is further metabolized to thiodiacetic acid. The other route involves hydrolysis of the carbon-chlorine bond resulting in the formation of glycolic acid, which is mainly oxidized to carbon dioxide. MCAA can inhibit different enzymes: acetate oxidation, aconitase, pyruvate carboxylase, pyruvate-dehydrogenase, a-ketoglutarate dehydrogenase and glutathione S-transferase (GST).

The acute toxicity (LD_{50}) of MCAA was between 55 and 277.5 mg/kg bw in rats after oral exposure and circa 300 mg/kg bw after oral exposure in mice. After dermal exposure to MCAA in 0.9% NaCl the LD50 for rabbits was around 250 mg/kg bw and is clearly concentration dependent. The LC_{50} after 1- and 4-hour inhalation exposure of rats was >259 and 180 mg/m^3, respectively. MCAA induced acute neurotoxic effects after exposure by different routes. Also human data indicate a high acute toxicity of MCAA.
MCAA is corrosive to the skin and eyes. Respiratory irritation was observed at 23.7 mg/m^3 in a limited study with rats. The threshold for respiratory (sensory) irritation in humans was reported to be 5.7 mg/m^3. Based on wide practical experience with MCAA in the absence of any case reports on allergy, it is concluded that no indications for sensitizing effects exist.

No suitable dermal and inhalation repeated-dose toxicity studies are available. Oral repeated-dose toxicity studies with 16-day, 13-week, and chronic exposure to MCAA were available. Within the limited study design of the 16-day toxicity studies (by gavage), the NOAEL in rats was 7.5 mg/kg bw/day, and in mice 60 mg/kg bw/day, both based on lacrimation. A NOAEL could not be derived from the results of a 13-week repeated-dose toxicity study with rats (by

gavage). Changes in the weight of the heart, liver, kidneys, and clinical chemistry values were observed at the lowest dose level tested, i.e., 30 mg/kg bw/day. An increased liver weight and decreased activity of serum cholinesterase were observed in mice exposed during 13-weeks by gavage. The NOAEL for mice was 100 mg/kg bw/day. Main target organs of MCAA after prolonged oral administration are liver in both rats and mice, and heart and kidneys in rats. In the chronic toxicity studies, effects on the nasal mucosa, growth depression, and decreased survival became more apparent. The effects on the heart disappeared at lower dose levels in repeated-dose toxicity studies with longer study duration. Based on the data available, rats appeared to be more sensitive for the toxic effects of MCAA than mice. A NOAEL of 3.5 mg/kg bw/day was derived from a 2-year drinking water carcinogenicity study in rats. At this level, no effect on survival, body weight, liver, kidneys, or (non-)neoplastic lesions was found.

MCAA does not induce point mutations or primary DNA damage in bacteria, or chromosome aberrations or DNA strand breaks in mammalian cells in *vitro*. MCAA gave positive results in several TK+/TK- assays with mammalian cells *in vitro*. *In vivo* MCAA did not induce DNA strand breaks in spleen, liver, stomach or duodenum of mice or in liver of rats.

No evidence of carcinogenic activity of MCAA was found in rats and mice after oral administration in drinking water or by gavage. A NOAEL of 3.5 mg/kg bw/day was derived from the 2-year drinking water study in rats (see above for systemic effects). At this level, no (non-)neoplastic lesions were found. Besides, no evidence for carcinogenic activity after repeated dermal exposure (during 580 days) was found in female mice. Carcinogenicity studies by inhalation exposure were not available.

A reproductive toxicity study with MCAA was not available. However, in the oral (sub)chronic repeated-dose toxicity studies with rats and mice, no effects were found on the male and female reproductive organs. With respect to developmental toxicity, in a study, aimed at the investigation of fetal cardiac teratogenicity, in rats exposed to 193 mg/kg bw/day the only effect observed was a decrease in maternal average weight gain during pregnancy. No developmental toxicity was observed in this study. Developmental toxicity of MCAA is indicated based on a limited reported developmental test with rats, on a Hydra regeneration assay, and a whole CD-1 mouse embryo culture test. Indications for effects on the heart of the embryo were found.

Environment

MCAA is a solid with a melting point of about 62 ºC. The solubilities of MCAA and the sodium salt (SMCA) in water are reported as 4210 and 820 g/l at 20 °C, respectively. The vapor pressure for MCAA is 8.7 Pa at 25 °C. The partition coefficient log P_{OW} was measured and calculated as ≤ 0.2. The acid-base constant (pKa) is 2.85 at 25 °C.

MCAA will be completely ionized at environmentally relevant pHs. MCAA hydrolyses very slowly. Direct photolysis of MCAA in air and water is not expected, because it does not absorb UV radiation above 290 nm. The photo-oxidation rate of MCAA with OH-radicals was estimated with a QSAR (DT50 of 58 days). The direct photolysis competes with the dissolution of MCAA in the atmosphere and further with wet deposition. The wet deposition of MCAA was estimated to take about 10 days. Dry deposition of MCAA from air can also take place. MCAA is readily degradable. Bioaccumulation is not expected to occur in view of the low log Kow and ionizing properties. A Henry's Law constant of $1.9*10^{-4}$ $Pa.m^3/mol$ at 20 ºC can be calculated for MCAA. The calculated Henry's Law constants indicate that volatilization of MCAA from surface water will not occur at significant levels. With regard to the adsorption of MCAA in a soil-water system, organic-water partition coefficients (Koc) of 4 and 3.16 have been calculated using the QSAR for organic acids and non-hydrophobics, respectively. Adsorption to soil is thus not expected to occur.

The available short-term EC50-values and long-term NOEC-values for daphnia and fish in neutralized medium range between 10-1000 mg/l. The short- and long-term results for algae are all < 1 mg/l, except for one EC50-value. The lowest long-term test result is the NOEC of 5.8 µg/l for *Selenastrum subspicatus*. Two NOECs for additional algae species support the lowest obtained NOEC value of 5.8 µg/l. A number of short-term toxicity studies for MCAA with bacteria and protozoa are available. The lowest observed IC50 was 16 mg/l for protozoa. A seedling emergence/growth test with three plant species resulted in a 21 day NOEC of 3.2 mg/kg dwt. A time average NOEC of 0.6 mg/kg dwt (assuming a first order rate degradation during the 21 day experiment) can be estimated based on the neutral soil DT50 value of 66 hours.

Exposure

In the European Union MCAA is produced by three companies at five different locations. Two companies have two production locations each. The total EU production volume of MCAA for 1999 was 145,000 tonnes per annum. According to industry there was no import from outside the EU in 1999. The estimated total export was about 25,000 tonnes per annum. The use volume, i.e. production and import minus export, within the EU was therefore about 120,000 tonnes per annum. Three production companies convert MCAA into the salt SMCA. MCAA is mainly used as a chemical intermediate for the synthesis of other products. Major applications of MCAA are related to the production of: carboxymethylcellulose (CMC), carboxymethyl starch, crop protection chemicals (like 2,4-D and MCPA), plastics, thioglycol acid (TGA), sodium salt of MCAA and other products such as esters and amides. SMCA is mainly used as a chemical intermediate for the production of: amphoteric surfactants (e.g. shampoos and industrial cleaning agents), pigments, dyes (indigo), printing inks, paints, lacquers and varnishes, pharmaceuticals (caffeine, vitamin B6) and CMC.

A number of minor applications of MCAA occur as well: constituent in acidic paint remover or graffiti remover, can coating for food (i.e. as modifier for resins), escharotic agent, wart remover, anti-microbial additive for food and analytical reagent.

MCAA may be released by industry into the environment during its production and processing as intermediate. The emission of MCAA will occur via air and water. However, in view of the low vapor pressure and high water solubility, MCAA is expected to end up mainly in the water compartment. MCAA may also be released by unintentional sources. For instance, MCAA can be formed (indirectly) in the atmosphere from industrial chlorinated chemicals. Besides anthropogenic sources, MCAA is also expected to be formed *de novo* in the environment.

Occupational exposure may occur in industries where MCAA is produced or is used as a raw material or as an intermediate. Routes of exposure are by inhalation and by accidental dermal contact. The presence of MCAA in consumer products was unknown in Denmark (Product Register, June 1997) but known in the US (Product Register, October 1997). MCAA was not available in the inventory of ingredients used in cosmetic products (EC, 1996). Industry does not support applications of MCAA which are not related to the use as intermediate. However, some consumer use has been identified, but this use can be considered mostly as negligible. Possible consumer exposure: MCAA was used as an anti-microbiological additive in food and as a wart remover, use of MCAA as a paint stripper or graffiti remover, and in can coatings for aqueous foodstuffs. The use of antifoliant has been discontinued.

RECOMMENDATION

The chemical is a candidate for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health:

The chemical is a candidate for further work. Hazardous properties have been identified for this substance (acute neurotoxic effects, corrosive to skin and eyes, indications for effects on the heart of the embryo). In an assessment performed in the European Union in the context of the EU Existing Substances Regulation (793/93/EEC), occupational exposure and risks were identified for some scenarios. Other OECD countries may wish to perform an exposure assessment for humans and if necessary a risk assessment.

Note: In the EU the request for a developmental toxicity study depends on the risk reduction strategy. It is noted that effects were observed in developmental toxicity studies at high concentrations/dose levels. This effect at high dose levels and considering that risk reduction measures for corrosivity need to be taken in the EU, it is expected that the exposure will sufficiently be limited. Therefore, developmental toxicity will not lead to a risk for this endpoint.

Environment:

The chemical is a candidate for further work. Hazardous properties have been identified for this substance (aquatic toxicity). In an assessment performed in the European Union in the context of the EU Existing Substances Regulation (793/93/EEC) it was shown that the local PECs in surface water exceed the PNEC for MCAA at two production/processing sites. In one case the conclusion is based on monitoring data. For the other site the PEC/PNEC is >1 for the STP as well. For both sites industry has indicated that the efficiency of the local WWTP will be improved, but up to now no data are available to verify this statement. Other OECD countries may wish to perform an exposure assessment for the environment and if necessary a risk assessment. In addition in an assessment performed in the European Union in the context of the EU Existing Substances Regulation, substantial MCAA levels reported in the literature in various environmental compartments, wet deposition, surface water and soil. These regional/continental background concentrations exceed the corresponding PNEC in some cases, especially in soil. Further research is needed to investigate, quantitatively, the origin of these MCAA levels (natural versus anthropogenic).