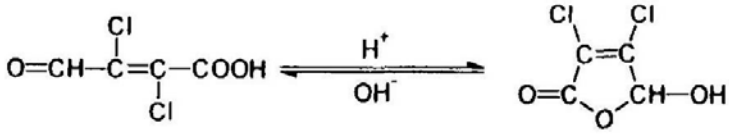
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	87-56-9
Chemical Name	Mucochloric acid
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

There are no reliable experimental data on the toxicokinetic behavior of mucochloric acid (MCA) *in vivo* available. From the results of acute toxicity studies, it is very likely that MCA itself or its metabolites are systemically available after oral exposure. *In vitro*, MCA reacted with N-acetylcysteine, cysteine and glutathione (GSH).

The acute toxicity (LD_{50}) of MCA was between 300 and 400 mg/kg bw in rats after oral exposure and >200 mg/kg bw (highest tested dose) in rabbits after dermal exposure. The LC_{50} after 4-hour inhalation exposure of rats was >5.1 mg/l (highest tested concentration). Clinical signs included atonia and ataxia after oral exposure, preening, dyspnoea and salivation during inhalation, and skin irritation after dermal exposure.
MCA is corrosive to the rabbit skin and eye. A guinea pig sensitization test was negative, but limited experience from occupational exposure in humans indicates a skin sensitizing potential of MCA.

There is limited data on repeated dose toxicity available, indicating that irritant/corrosive effects at the site of first contact are the main effects to be expected after repeated exposure. In pregnant rats, no systemic target organ has been identified after oral exposure from day 6 to 19 p.c. (LOAEL: 30 mg/kg bw/day, based on reduced food consumption and body weight gain together with minor clinical symptoms (ptyalism) and whitish foci in the stomach interpreted as local effects due to the corrosive properties of MCA; NOAEL: 5 mg/kg bw/day). No target organ was identified in mice after dietary exposure to 7 mg/kg bw/day for 18 months (only one dose tested). Because of the limited exposure potential and the availability of reliable, though limited, data on repeat dose toxicity, no further animal testing is warranted.

In vitro, MCA is a direct acting mutagen and clastogen in mammalian and bacterial cells, and forms exocyclic DNA adducts. *In vivo*, mucochloric acid caused a slight, but statistically significant increase in the incidence of total nuclear anomalies (including micronuclei, pyknotic nuclei and karyorrhectic nuclei) in the duodenum of mice after a single oral exposure to 60.8 and 79.4 mg/kg bw. MCA induced micronuclei in one animal out of ten per dose group in the duodenum of mice after single oral doses (38.9, 60.8, and 79.4 mg/kg bw). Based on the available *in vitro* and *in vivo* data, it can be concluded that MCA has a genotoxic potential.

Because of its corrosive properties, and the very limited exposure potential, animal tests with MCA for its effects on fertility were not performed. In an oral developmental study performed in accordance with OECD TG 414 in rats, the NOAEL for maternal toxicity was 5 mg/kg bw/day. The NOAEL for developmental toxicity was 60 mg/kg bw/day, which was the highest dose level applied. There were no signs of developmental toxicity or teratogenicity.
MCA did not induce aberrant crypt foci or intestinal tumors when given in drinking water at dose levels of 0.45 and 0.9 mg/ml over 6 weeks to rats or at dose levels of 0.18 and 0.35 mg/ml over 4 weeks with subsequent 12-weeks recovery to mice, respectively. The available data for MCA are not sufficient to judge its carcinogenicity. Given the

available data for genotoxicity there are, however, concerns with regard to this endpoint.

Environment

The solubility of MCA in water is approximately 27 g/l (pH 2.2) at 20 °C and the vapor pressure is 0.00139 hPa at 25 °C. A Henry's law constant of $8.7*10^{-4}$ $Pa*m^3*mol^{-1}$ can be calculated and the partition coefficient log K_{ow} was measured as 0.697 at 25 °C. The acid-base constant (pKa) is 4.20 at 25 °C.
The distribution modeling (Mackay fugacity model level I), indicates water to be the almost exclusive target compartment. The substance has no considerable potential for bioaccumulation (log K_{ow} = 0.697). It cannot be considered inherently biodegradable according to OECD guidelines, but is partially biodegradable after an appropriate adaptation. From the structure of MCA hydrolysis is not expected. Photodegradation is to be expected under environmental conditions with an estimated half-life of 21.4 h. An estimated K_{oc} value of 1 indicates that mucochloric acid does not tend to adsorb to soil. However, as the structure of the molecule is dependant on pH, the K_{oc} may vary significantly with pH.
Aquatic effects data are available for three trophic levels (fish: LC_{50} (96 h) = 123 mg/l; crustacea: EC_{50} (48 h) = 13 mg/l; algae: E_rC_{50} (72 h) = 65 mg/l, E_bC_{50} (72 h) = 62 mg/l). A $PNEC_{aqua}$ of 13 µg/l was calculated from the available data using an assessment factor of 1000 according to the EU Technical Guidance Document.

Exposure

In the EU there are only two known producers of MCA. The annual production volume in the EU is in the range of 1000 - 5000 tons. There is no information on imported volumes. In Eastern Europe, there is one producer in Slovakia, who produces MCA only for captive use. In China there are two known producers.
MCA was used in the 1970s and 1980s, as a gelatin hardener in the photographic industry and as an intermediate in the pharmaceutical production. Since 1990 MCA has only been used as the starting material for the production of two herbicidal substances: Chloridazon and Norflurazon. Production of MCA and processing to Chloridazon takes place in the EU in closed systems at the same site. For the production of Norflurazon, also in closed systems, MCA is transported under controlled conditions in so-called big bags to a single site in the USA and filled into the reactor via docking the big bags to it. During production, transport and processing of MCA personal protective equipment is used to minimize any workers exposure to the substance. At the production and processing sites in the sponsor country, workplaces are regularly monitored.
MCA is not emitted into the atmosphere; due to its low vapor pressure only traces of MCA are expected in the off-gases, which are held back in the scrubber liquids. There is no emission into the aquatic environment during production and processing of MCA at the sponsor company; any remaining aqueous solution is oxidized or incinerated. Solid wastes, which contain less than 100 ppm of MCA, are disposed of by incineration.
There is no evidence of MCA in the finished products, i.e. herbicide formulations (analytical detection limit: 5 ppm).
Because MCA is only used as an intermediate in closed systems and transported under strictly controlled conditions, there is very limited exposure potential from these sources in the sponsor country, both for humans and the environment.
In certain countries, and independent of its production and processing by the chemical industry, MCA was found in surface waters (µg/l range) resulting from effluents from chlorine bleaching processes and in drinking water (ng/l range) as a chlorination disinfectant byproduct from the reaction of chlorine with humic acids.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health:

The chemical possesses properties indicating a hazard for human health (corrosivity, genotoxicity, potential carcinogenicity), but controls for occupational exposure are in place in OECD countries.

In view of concerns that the chemical may be a genotoxic carcinogen, there is a recommendation for sharing the toxicological and exposure data with regulatory agencies responsible for drinking water, because traces of MCA can occur in drinking water as a disinfection by-product. Based on this, countries may want to consider toxicokinetic/metabolism studies, and, if then indicated, further studies relating to the carcinogenicity endpoint.

Environment:

The chemical possesses properties indicating a hazard for the environment. Based on data presented by the Sponsor country, exposure to the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.