SIDS INITIAL ASSESSMENT PROFILE

CAS No.	107-02-8
Chemical Name	Acrolein
Structural Formula	$CH_2 = CH – CHO$

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Acrolein is very reactive and conjugates easily with glutathione or other thiol-containing molecules, with protein sulfhydryl groups and primary and secondary amine groups. As a consequence of its high reactivity the acrolein molecule will bind primarily at the application site. Toxicokinetic data on absorption, distribution, metabolism and excretion for the dermal route are lacking. Assessment of the available acute toxicity data indicates that acrolein is toxic by the oral and dermal route, and very toxic after exposure by inhalation. Acrolein is corrosive and irritating to skin and eyes in laboratory animals and humans. Despite the fact that the study designs and descriptions do not allow clear conclusions on human (no) effect levels for irritating effects after short-term inhalation exposure to acrolein vapours, the risk assessment was based on the LOAEL of 0.14 mg/m^3 from the study of Darley et al. (1960) for subjective symptoms, and the NOAEL of 0.34 mg/m^3 from the study of Weber-Tschopp et al. (1977) for measurable effects (increase in eye blinking rate at 0.59 mg/m^3). Based on the data available acrolein should be considered as sensitising to the skin.

The results of the repeated-dose inhalation studies do not permit establishment of a NOAEL. Intermittent exposure (6-7 hours per day, 5 days per week for a total period of 62 days - 13 weeks) to 0.9 mg/m^3 (0.4 ppm, DCV: 0.16 mg/m^3) acrolein vapour (the lowest concentration examined) resulted in slight, but treatment-related changes in rats, but not in hamsters and rabbits. Continuous exposure (24 hours per day, 7 days per week for 90 days) to 0.5 mg/m^3 (0.22 ppm) acrolein (the lowest concentration examined) resulted in treatment-related effects in guinea pigs, monkeys, and dogs, but not in rats. The effects found at the lowest-observed adverse effect concentrations, consisted of histopathological changes in the epithelium of the respiratory system and changes in respiratory tract function; they were minimal to slight and were found in one animal or a few animals only. Effects at higher concentrations included signs of chronic inflammatory changes, and epithelial metaplasia and hyperplasia of the respiratory tract, and at even higher concentrations increased mortality.

The overall NOAEL for oral toxicity amounted to 0.05 mg/kg bw/day and was found in a 102-week rat study. The discriminating effects for establishing NOAELs in the oral studies comprised decreased survival in rats (NOAEL 0.05 mg/kg bw), decreased survival and decreased body weight gain in mice (NOAEL 2 mg/kg bw), and an increased incidence of vomiting accompanied by a decrease in total serum protein, calcium and albumin at the highest dose level (1.5-2 mg/kg/bw) in dogs (NOAEL 0.5 mg/kg bw). Effects at higher dose levels included severe gastric lesions and increased mortality. Acrolein has been found to impair pulmonary antibacterial defence mechanisms upon inhalation exposure *in vivo* and *in vitro* Acrolein is a mutagen for bacteria and may induce gene mutations and sister chromatid exchanges, but no chromosome aberrations in mammalian cells *in vitro*. The mutagenicity/genotoxicity of acrolein in bacteria and mammalian cells *in vitro* is restricted to a narrow dose range that is near to or overlaps the cytotoxic dose range. Acrolein did not induce dominant lethal mutations in mice or

chromosome aberrations in bone marrow cells of rats. There is evidence that acrolein is not an oral carcinogen. The available data do not allow a conclusion with regard to possible carcinogenicity upon exposure by inhalation. However, none of the available repeated-dose inhalation study meets the generally accepted requirement for adequate carcinogenicity testing. On the basis of the experimental data it cannot be excluded therefore, that respiratory tumours may be induced at non-cytotoxic concentrations. No dermal carcinogenicity studies were available.

Developmental effects in mammals *in vivo* were only seen at dose levels that also resulted in maternal toxicity. The overall NOAEL in the oral teratogenicity studies amounted to 2 mg/kg bw or higher for developmental and 0.75 mg/kg bw per day for maternal effects. Except for a slight reduction in *F1* pup weights at 6 mg/kg bw, no effects on reproduction parameters were found in oral 2-generation rat studies. The overall NOAEL amounted to 3 mg/kg bw for developmental and 1 mg/kg bw per day for parental effects.

Environment

Acrolein may be released into the environment during its production and processing of intermediates. This release, however, is very low compared to emissions from several non-industrial diffuse sources (e.g. formation of acrolein during automobile fuel combustion). Acrolein emissions will occur via water, but predominantly via air.

Acrolein does not contain any hydrolysable groups, but it does react with water in a reversible hydration reaction to 3-hydroxypropanal (HPA). The stability of acrolein in the atmosphere is limited by the rapid gas-phase reactions with the hydroxyl radical and ozone. DT50 is less than one day. Based on the entire data set on biodegradation and the QSAR estimates, acrolein is considered as ready biodegradable. Henry's Law constants indicate that volatilisation of acrolein from surface waters and moisty soil is expected to be high. Acrolein is expected to be moderately to highly mobile in soil. No bioaccumulation is expected.

Both short-term and long-term acrolein toxicity data are available for aquatic organisms. There are also a number of studies with bacteria and protozoans. Short term LC50-values for fish range from 14-250 µg/l. NOEC for fish: 11.4 µg/l. Daphnia magna 48 h EC50 values range from 22 to 93 µg/l. NOEC daphnids: 16.9 µg/l. NOEC algae: 10 µg/l. The $PNEC_{water}$ is set at 0.1 g/l, based on an acute *Xenophus laevis* study (LC50 7 µg/l) using an assessment factor of 100 (instead of 1000) as a several acute and long-term studies were available. There is a limited number of studies in which the phytotoxicity of airborne acrolein is investigated. An indicative $PNEC_{plant-air}$ of 2 g/m^3 is derived.

Exposure

In the EU Acrolein is only used as an intermediate in the chemical industry. The main fraction of the isolated acrolein is reacted via the intermediate product methylmercapto-propionaldehyde (MMP) to the amino acid D,L-methionine, which is used as an animal feed additive. In the EU no consumer exposure was dentfed. Outside the EU (e.g. Egypt, Argentina, Australia, Canada and USA) acrolein is used as an effective broad-band biocide. It is applied in process water circuits, irrigation canals, cooling water towers and water treatment basins. The total EU production volume for 1994 was estimated to be between 20,000 to 100,000 tonnes per annum.

NATURE OF FURTHER WORK RECOMMENDED

There is a need for further information and further consideration of exposure and risk assessment for the environment and human health.

This substance has been agreed in the European Union Risk assessment program under Regulation EEC/793/93. The EU risk assessment concludes that there are need for specific measures to limit the risks for workers. No use of acrolein in consumer products has been identified.

It was considered to examine the potential genotoxic effect (gene mutation) of acrolein at the first site of contact after exposure by inhalation. However, at this moment, a validated test system or a system that giving sufficiently reliable results for the target cells of concern i.e. cells of the respiratory tract, does not exist.