SIDS INITIAL ASSESSMENT PROFILE

CAS No.	79-20-9
Chemical Name	Methylacetate
Structural Formula	CH_3-C(=O)-O-CH_3

RECOMMENDATIONS

The chemical is currently of low priority for further work (environment and consumer).
Risk reduction measures are recommended for the workers.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Methyl acetate is absorbed via the lungs in animals and humans, absorption via the oral route is demonstrated. After absorption the substance undergoes hydrolysis to methanol and acetic acid. From the available *in vitro* data it may be anticipated that the half-life of methyl acetate in blood ranges between 2 and 4 hours. Immediately after stopping a 6-hours-inhalation exposure to rats (2000 ppm, 6.04 mg/l) blood concentrations below the limit of quantification (< 4.6 mg/l) were determined indicating rapid hydrolysis and high clearance of the substance. Thus, a low systemic availability of methyl acetate can be assumed. The main metabolite methanol is metabolized to formic acid. Formate is introduced into C1-metabolism after activation by reacting with tetrahydrofolate. Humans as well as monkeys are more sensitive to methanol poisoning compared with rats because of a lower tetrahydrofolate content in liver. Therefore, the interspecies differences in the metabolism are considered mainly of concern at dose levels leading to acute toxicity.

Methyl acetate is of low acute toxicity (rats LD50 oral: 6482 mg/kg bw, dermal: > 2000 mg/kg bw, LC50: > 49 mg/l/4h). After oral application and after inhalation animals showed narcotic symptoms, spasms, dyspnea and vomiting. Inhalation of vapors in addition caused irritation of eyes and upper respiratory tract. The narcotic concentrations for mice and cats are 34 mg/l and 56 mg/l, respectively. In humans accidental inhalation of vapors caused severe headache and considerable somnolence.

Methyl acetate causes only weak skin irritation in humans and in rabbits. Eye irritation, however, was strong but reversible within 7 days. Exposure to methyl acetate vapors causes irritation to eyes and respiratory tract of humans. Taking into account the long experience with human exposure, methyl acetate is not supposed to exhibit skin sensitizing properties. No relevant human or animal data are available.

A 28-day inhalation study on rats revealed degeneration/necrosis of the olfactory mucosa (nose) at a methyl acetate concentration of 2000 ppm (6.04 mg/l). In addition, diureses, minimal liver cell dysfunction, adrenal weight increase, and reduces serum cholesterol concentrations are observed. The NOAEC both for local and systemic effects was identified at 350 ppm (1.06 mg/l). No repeated dose studies are available for the oral and dermal route. In a study on cats, inhalation exposure for 5 days to about 20 mg/l methyl acetate resulted in increased hemoglobin and erythrocyte levels, transient leukocytosis, eye irritation and moderate CNS depression.

Methyl acetate showed negative results in a bacterial mutation test and a rat bone marrow micronucleus test. Furthermore, the hydrolysis products methanol and acetic acid do not reveal evidence for a mutagenic potential.

No data are known which give relevant concern on cancerogenicity following methyl acetate exposure, although in methanol studies on rats and mice an increased incidence of lung adenoma/adenomatosis was seen in high dose male rats only.

No data are available on the reproductive toxicity of methyl acetate itself. However, due to the rapid hydrolysis of the compound hazards with respect to reproduction can be assessed on the toxicological properties of the immediate metabolites. No indications of a fetotoxic or teratogenic potential of acetic acid are found, whereas embryo-/fetotoxic and teratogenic effects were demonstrated for methanol in rodents at high, maternally toxic concentrations. A NOEC/fertility for methanol of 1000 ppm (1.3 mg/l) was derived from a 2-generation inhalation study with rats. Assuming an immediate degradation of methyl acetate to methanol at a molar ratio of 1, this value corresponds to a NOAEC/fertility of about 3.0 mg methyl acetate/l. A NOAEC/developmental toxicity for methanol of 1000 ppm (1.3 mg/l) was derived from studies with mice and rats corresponding to a NOAEC/developmental toxicity of about 3.0 mg methyl acetate/l.

Environment

Methylacetate has a water solubility of 250 -295 g/l, a vapor pressure of 217 hPa and a log Kow of 0.18. According to the physico-chemical properties the target compartment for this substance are the atmosphere (69.3 %) and the hydrosphere (30.7 %). Methylacetate is stable in neutral solution. The substance is classified as "readily biodegradable". There is no considerable potential for bio- or geoaccumulation. An atmospheric half-life of 50.4 days was calculated for methylacetate.

The following results from ecotoxicity tests with aquatic species are available:

In a short-term test with fish a 96h LC_{50} of 320 mg/l was found for *Pimephales promelas*. For invertebrates an acute study on *Daphnia magna* had been conducted. A 48 h EC_{50} of 1027 mg/l was found. In a study with *Scenedesmus subspicatus* no effects could be observed after 72 h at a concentration of 120 mg/l. Long-term toxicity tests with fish and invertebrates are not available. With an assessment factor of 1000 a PNEC of 320 µg/l is determined.

Exposure

The production volume of methylacetate in the EU was ca. 30,000 t/a in 1993. Methylacetate is used as intermediate in chemical synthesis for the production of vitamins and crop protection agents. The chemical is also used as a solvent in paints and lacquers, in household chemicals and in adhesives. In Germany, approximately 70 % of the methylacetate is used as solvent, about 10 % is used as intermediate and the remainder 20 % are exported for the production of sweeteners. No information on the use pattern of the substance in the EU is available. However, it is assumed that the use pattern for Germany is also applicable to the EU.

Releases into the hydrosphere and atmosphere are expected from production, processing and use as solvent. Exposure of the terrestrial compartment is expected due to deposition from the atmosphere.

Workers are exposed during production and further processing, use of formulations (paints, adhesives, cleansers) and few other uses (flooring works, use of cosmetics).

NATURE OF FURTHER WORK RECOMMENDED

This substance has been agreed in the European Union Risk Assessment Program under Regulation EEC/793/93 with the following conclusion:

Environment:

There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Human Health:

Consumer: There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Worker: There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

The occupational risk assessment comes to the conclusion that additional risk reduction measures are necessary for inhalation exposure in several scenarios. The relevant toxicological endpoints via inhalation are irritation, repeated dose toxicity (local and systemic effects) and developmental toxicity.