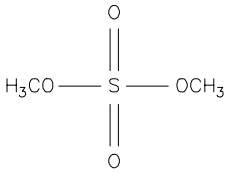
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	77-78-1
Chemical Name	Dimethyl sulphate
Structural Formula	

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Dimethylsulphate (DMS) is a methylating agent, which is found to react with nucleic acids. No data on interference with other nucleophilic macromolecules, e.g. proteins, are available.

Data on dermal absorption are limited and insufficient to draw conclusions. DMS can be absorbed via respiratory and oral routes. For oral absorption this is concluded from toxicodynamic data. Rapid respiratory absorption is observed in rats exposed to dose levels up to 50.3 mg/m^3. At higher dose levels uptake was decreased, probably due to a decreased minute volume. No information is provided on the metabolism of DMS in animals following oral administration. The information on metabolism after inhalatory or dermal exposure is limited. DMS may be hydrolysed to methanol, sulphuric acid, and methyl sulphate, and may be metabolised to a lesser extent to formaldehyde and formate. The toxicokinetic studies do not allow derivation of quantitative figures on absorption that can be used in risk characterisation.

The available acute toxicity data indicate that DMS is toxic after oral administration, and very toxic after exposure by inhalation.

DMS is corrosive to the skin and should be considered to cause risk of serious damage to eyes in laboratory animals. Irritation of the respiratory tract was observed in a poorly reported inhalation experiment with rats.

Local effects of DMS after dermal and respiratory exposure were also seen in humans.

Based on the results of the local lymph node assay, it is concluded that DMS has sensitising properties.
The repeated-dose inhalation studies do not permit the establishment of a NOAEL. No oral and dermal repeated dose toxicity studies are available.

DMS is a potent direct-acting genotoxicant in bacteria and mammalian cells *in vitro*, it is positive in tests for primary DNA damage, gene mutations, and chromosome aberrations *in vitro*. DMS appears genotoxic in various *in vivo* tests in Drosophila, i.e., in tests for somatic mutations and recombination, for sex-linked recessive lethals, and for sex chromosome loss. From the results of the tests with mammals it is concluded that DMS may have clastogenic activity in somatic cells *in vivo*, but there are no indications for the induction of gene mutations *in vivo*. No tests are available to assess the genotoxicity of DMS in germ cells in mammals.

Given the results of the mutagenicity studies, it is assumed that the carcinogenicity of DMS is based on a genotoxic mode of action. Evidence on human carcinogenicity is inadequate. The conclusion of IARC is that DMS produces mainly local tumours in rats following inhalation or subcutaneous injection and that there is sufficient evidence to classify DMS as an animal carcinogen (2A). This conclusion is in agreement with the conclusion of the sponsor country. The sponsor country could not verify IARC's statement on tumours of the nervous system after prenatal exposure of laboratory animals. The study design of the carcinogenicity study of Schlögel does not fulfil the requirements of OECD 451. However, the results of this study can be used to give a indication of the carcinogenic potency of DMS.

The toxicological database of DMS has gaps with respect to systemic toxicity after repeated exposure, and with respect to effects on reproduction. There are no data available on toxicological parameters such as haematology and clinical chemistry. Furthermore, no data are available on fertility effects of DMS.

It is concluded that DMS did only induce slight developmental toxicity after inhalation at maternal toxic concentrations.

Environment

DMS may enter the environment during its production and industrial use (processing), and in emissions from power plants that are burning sulphur-containing coal/fuel. DMS has an estimated atmospheric half-life of 84 days for the reaction with photochemically produced hydroxyl radicals, hydrolysis quickly in water (DT50 < 1day), is readily biodegradable, has a relatively low Henry constant of 0.39 $Pa.m^3/mol$ indicating that the compound shows no tendency to evaporate from water and has a relatively low log Kow of 0.16. From the log Kow a log K_{oc} of 1.38 is calculated indicating that DMS has a low adsorption potential and thus a high mobility/leaching potential. No bioaccumulation of DMS is expected.

Short-term aquatic toxicity data are available for fish, daphnia and algae. Since DMS is known to hydrolyse quickly into monomethylsulphate and methanol the observed toxicity concerns the toxicity of DMS and its hydrolysis products. The PNEC for the aquatic compartment is extrapolated from the lowest short-term toxicity result, i.e. 14 mg/l for the goldfish, using an extrapolation factor of 1000. This results in a PNEC of 14 µg/l. No ecotoxicity data are available for the terrestrial and atmospheric compartment.

Exposure

In the EU, DMS is mainly used as a chemical intermediate. Its major applications are as a methylating agent of many organic chemicals (e.g. amines, carbon acids, thiols and phenols) both in industry and laboratories. The total EU production volume for 1994 was estimated to be between 20,000 and 30,000 tpa. Production and processing in large quantities occur in closed systems in the EU. At these sites no release waste water occurs and emission to air is theoretically assumed to be zero. No use of Dimethyl sulphate in consumer products has been identified.

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.

A detailed risk assessment for this substance has been agreed under the European Union Risk Assessment Program under Regulation EEC/793/93. The risk assessment concludes that there are need for specific measures to limit the risks for workers. Dimethyl sulphate has not been tested for reproductive toxicity, because it is considered to be a non-threshold carcinogen.