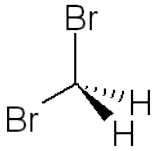
SIDS INITIAL ASSESSMENT PROFILE

CAS No(s).	74-95-3
Chemical Name(s)	DIBROMOMETHANE (DBM)
Structural Formula(s)	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-chemical Properties

Dibromomethane is a clear, colourless liquid with a sweetish odour and a measured boiling point of 94±1°C and a measured vapour pressure of 4700 Pa at 25°C. The measured octanol-water partition coefficient (log K_{ow}) is 1.68, and the measured water solubility is 9000 mg/L at 20°C.

Human Health

Toxicokinetics

A standard toxicokinetic study is not available. Dibromomethane appears to be absorbed after oral and inhalation exposure in rats and rabbits (concluded based on repeated dose toxicity section) and after dermal exposure.

Dibromomethane was metabolized *in vitro* to carbon monoxide and inorganic bromide by microsomal enzymes of the liver, lungs, and kidney, but not of the brain or spleen. The oxidation appears to be catalysed by a cytochrome P-450 dependent system. During dermal exposure, the metabolism of dibromomethane was saturable as indicated by the nonlinear increase in plasma bromide ion concentration. Intraperitoneal administration of 522 mg/kg dibromomethane to male rats resulted in a peak of carboxyhemoglobin level of 14% of the hemoglobin concentration at 4 hours treatment. By 10 hours after treatment, the carboxyhemoglobin level was approaching the pre-treatment level. Repeated daily exposure did not result in accumulation of carboxyhemoglobin. The only information regarding the excretion of dibromomethane is that the metabolite carbon monoxide is excreted in the exhaled air.

Acute Toxicity

In a 4-hour inhalation study CD albino rats were exposed to 21.4 - 22.3 mg/L dibromomethane. Immediately after exposure excessive fluid excretion was observed, accompanied by impaired spontaneous motor activity as exhibited by slow breathing, uncoordinated and atactic walk, continuous tremor, and excessive preening. All these effects wore off within about 3 hours when most of the exposed animals were found in deep sleep**.** No mortalities occurred and no toxicologically relevant changes were noted on autopsy at 18 and 20 days post treatment. An LC_{50} was > 22.3 mg/L.

A rat oral LD_{50} > 1000 mg/kg bw was derived from a 14 day range-finding reproduction/developmental toxicity test with six animals. Clinical signs were bodyweight loss and a decline in the clinical condition.

No reliable acute dermal toxicity information is available.

Skin and Eye Irritation

Dibromomethane was moderately to severely irritating to the skin and moderately irritating to the eye in rabbits in two reliable studies.

Skin Sensitisation

Dibromomethane was not a skin sensitiser in a Local lymph node assay performed in mice.

Repeated Dose Toxicity

The repeated dose toxicity of dibromomethane has been investigated via the inhalation route. No reliable data for oral repeated dose toxicity were available. Based on substance volatility, exposure through the inhalation route can be consider as a major route of exposure.

Oral Route

No reliable repeated dose toxicity study for the oral route is available.

In a reproductive and developmental toxicity screening test, rats (10 animals/sex/dose) received 0, 50, 150, 500 mg/kg bw/day of dibromomethane via gavage for 40 days. No treatment related deaths were observed in either sex. There were no significant treatment-related clinical signs of toxicity. At 500 mg/kg bw/day, lower bodyweight gain and lower food conversion efficiency was observed in females during gestation. However, this study has the following limitations: there were only histopathological examinations and organ weight determinations for reproductive organs, and no clinical chemistry or haemathology was conducted. The NOAEL for repeated dose oral toxicity can be considered to be 150 mg/kg bw/day.

Supporting information on repeated dose oral toxicity of dibromomethane was derived from a preliminary 14-day oral repeated dose range-finding study for a reproduction/developmental toxicity screening test. There was no information on food consumption, haematology, clinical biochemistry, organ weight changes, macroscopical/histopathological findings. Treatment related effects (clinical signs and decreased body weight gain) were observed mainly in males at dose level 1000 mg/kg bw/day (highest dose tested). The NOAEL for repeated dose oral toxicity can be considered to be 500 mg/kg bw/day.

Inhalation Route

Repeated exposure of rats and rabbits to 1000 mg/L dibromomethane for 73 days caused effects on coordination, weight gain and histopathological changes in the lungs, liver and kidneys in rats. Rabbits were less affected, but their blood bromide was elevated and degeneration of liver and kidney occurred. Repeated exposure of rats and rabbits at lower dose of 200 mg/L dibromomethane resulted in much less effect, but evidence of stress was still present and histopathological changes were found in livers and kidneys of rats and rabbits. Based on these effects, the LOAEC for rats can be set to 200 mg/L (1422 mg/m^3).

Repeated inhalation exposure of rats and dogs to 25 - 150 mg/L dibromomethane for 90 days showed no significant exposure related effects on gross pathology, histopathologic examination, and urinalysis. There were slight increases in liver weight in female rats at 75 and 150 mg/L and dose–related increases in percent saturation of carboxyhemoglobin at > 25 mg/L in both sexes of rats and at 150 mg/L in dogs. The NOAEL for rats was determined to be 25 mg/L and the LOAEL was set to 75 mg/L. The NOAEL for dogs was determined to be 75 mg/L and the LOAEL was set to 150 mg/L.

Genetic Toxicity

Dibromomethane was found to be mutagenic with and without mammalian metabolic activation in three (limited) Ames tests. In an *in vitro* mammalian chromosome aberration test conducted in human lymphocytes dibromomethane was found positive. Therefore, it is concluded that dibromomethane is mutagenic *in vitro.*

Dibromomethane was reported not mutagenic in a *Drosophila melanogaster* sex-linked recessive lethal study. There are no *in vivo* mammalian genotoxic studies available. Therefore, it is concluded that the *in vivo* potential of dibromomethane has not been adequately investigated.

Carcinogenicity

No data are available for the carcinogenicity of dibromomethane from standard carcinogenicity studies. In a 90-day repeated dose inhalation toxicity study in rats with 2 years post exposure observation period, gross pathological examination revealed no indication of any increased incidence of nontumours or tumour-like lesions at any exposure level.

Fertility/developmental toxicity

The reproductive toxicity of dibromomethane was well investigated in a reproductive and developmental toxicity screening test in rats. In this study, dibromomethane was administered via gavage to 10 animals/sex/dose at 0, 50, 150, 500 mg/kg bw/day, for 40 days. No death were observed in either sex. There were no significant treatment-related clinical signs of toxicity. At 500 mg/kg bw/day, lower bodyweight gain and lower food conversion efficiency was observed in females during gestation. At 50 or 150 mg/kg bw/day, mating performance, fertility and gestation length were unaffected by treatment. However, treatment at 500 mg/kg bw/day was associated with an effect on mating performance (increased pre-coital interval) and a reduction in litter size at birth. Treatment at 500 mg/kg bw/day did not adversely affect fertility with 8/10 females achieving pregnancy.

Necropsy did not indicate any effect of the test material on adult animals. The NOAEL for reproductive and developmental toxicity was considered to be 150 mg/kg bw/day.

Dibromomethane possesses properties indicating a hazard for human health (skin and eye irritation, *in vitro* mutagenicity and reproductive toxicity (fertility and developmental toxicity)). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

Environmental fate properties

The hydrolysis half-life for this compound is 143 days.

In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 105.9 days. No ready biodegradation guideline studies are available. BIOWIN estimation predict that the substance is not readily biodegradable. However, a non-guideline study shows a half life value of 2 days based on 14C labelled CO_2 evolution from natural salt water and fresh water sediments. This suggest that dibromomethane is degradable in the environment and will not be persistent.

A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that dibromomethane will distribute to the air (33.9 %), water (35.9%) and soil (30.1%) and negligible distribution to the sediments compartment (0.098%). If released only to the air compartment, dibromomethane stays in the air compartment (96%) with negligible amounts in other compartments. A Henry's law constant of 83.3 $Pa.m^3$/mole at 25 °C suggests that volatilization of chemical dibromomethane from the water phase is expected to be high. A log K_{oc} of 1.475 was estimated based on the log K_{ow} and indicates a low potential for accumulation in soil.

The bioaccumulation potential is predicted to be low based on a BCF value of 5.963 estimated with BCFWIN.

Aquatic Toxicity

The following acute toxicity test results have been determined for aquatic species, e.g.:

Fish [*Rainbow Trout*]	96 h LC_{50} = 45 mg/L (nominal) Semi static
Invertebrate [*Daphnia magna*]	48 h EC_{50} = 66 mg/L (nominal) Semi static
Algae [*Pseudokirchneriella subcapitata*]	96 h E_rC_{50} = 150 mg/L (growth rate method) (measured)

Algae [*Pseudokirchneriella subcapitata*] 96 h E_bC_{50} = 95 mg/L (area under growth curve method)

The fish and daphnia tests were conducted in sealed vessels to prevent volatilization, and analytically monitoring was performed in all three ecotoxicity tests.

Dibromomethane possesses properties indicating a hazard for the environment (acute aquatic toxicity values between 10 and 100 mg/L). The chemical is considered biodegradable and has a low bioaccumulation potential. Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

Dibromomethane is commercially produced with an annual estimated production volume of several thousands of tonnes in Israel (sponsor country), and a similar amount in USA. Some production might be available in China. Dibromomethane is mainly produced by reaction of methylene chloride with hydrogen bromide. Dibromomethane is used as an intermediate in the production of organic intermediates, fine chemicals and as an organic solvent.

No monitoring data for effluents/drinking water/surface water/in occupational settings/etc are available.