SIDS INITIAL ASSESSMENT PROFILE

CAS Nos	74-93-1 5188-07-8
Chemical Names	Methanethiol Sodium Methanethiolate
Structural Formulae	$H_3C—SH$ $H_3C——S^-\ \ Na^+$

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

Sodium methanethiolate (CAS No. 5188-07-8) is the sodium salt of methanethiol (CAS No. 74-93-1) and is safer and easier to handle. Upon addition to water, sodium methanethiolate dissociates to the methanethiolate anion and sodium cation. Depending on pH, equilibrium then exists between the methanethiolate anion and methanethiol itself (protonated, neutral form). At environmentally relevant pHs, the substance exists almost entirely in the protonated form, methanethiol. Because the compounds are identical at environmental and biological pH values, toxicity and fate data from either compound can be used to read across to the other compound.

Physical-chemical properties

Methanethiol is a gas and sodium methanethiolate is a solid at room temperature. The melting points of methanethiol and sodium methanethiolate are -123.1 and 40 °C and the boiling points are 5.95 and 69 °C, respectively. The vapor pressure of methanethiol is 1650 hPa at 20 °C. The water solubility of methanethiol is 2.33×10^4 mg/L (20 °C) while sodium methanethiolate completely dissociates in water. The estimated log K_{ow} values for methanethiol and sodium methanethiolate are 0.78 and - 2.33, respectively.

Human Health

In vitro metabolism studies that investigated the fate of methanethiol in blood indicated that it becomes extensively oxidized to formic acid and sulfite or sulfate upon entry into the blood stream.

In rats, the 4-hour inhalation LC_{50} of methanethiol was 675 ppm. The dermal LD_{50} (OECD TG 402) of sodium methanethiolate was > 84.8 mg/kg-bw, the highest dose that could be tested based on corrosivity. At this dose, one female exhibited reversible body weight loss and clinical signs that included hypoactivity and tremors. The oral LD_{50} (OECD TG 401) of sodium methanethiolate in rats was 116 (when diluted in water) and 109 mg/kg body weight (when in methanol). In the oral studies, rats exhibited significant decreases in spontaneous activity and dyspnea, tonic-clonic convulsions, ataxia and coma at the higher doses.

Sodium methanethiolate was corrosive (necrosis and blanching up to grade 4, eschar up to grade 3) to rabbit skin (OECD TG 404). Based on the corrosive properties observed in the primary skin irritation/corrosion studies, no eye irritation studies were performed. Sodium methanethiolate is presumed to be corrosive to the eye. Sodium methanethiolate was not a skin sensitiser in guinea pigs (OECD TG 406).

Repeated-dose toxicity has been investigated in a 3-month inhalation toxicity study with methanethiol and an oral combined repeated-dose/reproductive/developmental toxicity study with sodium methanethiolate. In the 3-month inhalation study with methanethiol, Sprague-Dawley rats (31 males/concentration) were exposed to concentrations of 0, 2, 17 or 57 ppm (0, 0.0039, 0.033 or 0.118 mg/L) for seven hours per day, five days per week. A statistically-significant reduction in body weight at 57 ppm with a statistically-significant dose-related trend among all treated groups was observed. Significant changes in average organ weights (spleen and adrenals) were not considered relevant by the study authors. Average albumin concentration was lower for all exposed groups. Reduced inorganic phosphate and elevated total bilirubin occurred in the 2 and 17 ppm groups and cholesterol was slightly elevated in the 2 ppm group. Blood urea

nitrogen was lower in the 57 ppm group and lactate dehydrogenase was lower in all exposed groups. However, there were no dose-related trends in these parameters or any exposure-related histopathological effects. The authors determined the NOAEC and the LOAEC to be 17 and 57 ppm (0.033 and 0.118 mg/L), respectively.

In the oral repeated-dose toxicity study (OECD TG 422), Sprague-Dawley rats (10/sex) were dosed by gavage with 0 (water), 5, 15 or 45 mg/kg-bw/day sodium methanethiolate for 8 or 9 weeks (males and females, respectively). Treatment-related effects at 45 mg/kg bw/day included low muscle tone, incoordination and excessive salivation; reduction in body weight gain and food consumption for females and/or males; decreased hemoglobin concentration (both sexes) with reduced mean and packed cell volumes, red blood cells and/or mean cell hemoglobin concentrations (females); higher absolute and relative spleens weights with increased incidence and/or severity of extramedullary hematopoiesis and hemosiderosis in the spleen (both sexes) and sinusoidal ectasia (males); higher incidence of extramedullary hematopoiesis in the liver with associated greenish pigment in a few Kupffer's cells (females). The NOAEL and the LOAEL for sodium methanethiolate in rats were considered to be 15 and 45 mg/kg bw/day, respectively.

Sodium methanethiolate was not mutagenic in a bacterial reverse mutation assay (OECD TG 471) *in vitro* either with or without metabolic activation. In a mammalian cell cytogenetic assay (OECD TG 473) using human lymphocytes, sodium methanethiolate did not induce structural chromosome aberrations but did induce polyploidy. Neither methanethiol (via inhalation) nor sodium methanethiolate (oral) resulted in increased chromosomal mutations in the Mammalian Erythrocyte Micronucleus Test (OECD TG 474). Overall, it is concluded that these compounds are not associated with gene mutations in bacteria or chromosomal aberrations *in vivo*. No data are available on the carcinogenicity of methanethiol or sodium methanethiolate.

There were no effects following oral exposure to sodium methanethiolate on reproductive performance, fertility or development in pups in the OECD TG 422 study, described previously. The NOAEL for reproductive performance and developmental toxicity was 45 mg/kg bw/day (the highest dose tested). Based on these screening-level results, sodium methanethiolate or methanethiol is not likely to result in reproductive/developmental toxicity.

These chemicals possess properties indicating a hazard for human health (lethality from acute inhalation and oral exposures, skin corrosion and repeated-dose toxicity). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD HPV Programme.

Environment

The EPISuite program developed by the U.S. Environmental Protection Agency and Syracuse Research Corporation has not been validated for sodium salts of organic acids; therefore, there is uncertainty associated with the estimated values and they should be used with caution whenever they are reported below.
The estimated Henry's Law constant for methanethiol is 2.84 hPa m^3/mol, suggesting that volatilization from water is expected to be significant.

Sodium methanethiolate will dissociate in water and exist as methanethiolate. At environmental pH, methanethiolate will typically exist as methanethiol (>99.9%), as methanethiol has an acid dissociation constant of 10.7. Hydrolysis of methanethiol does not occur under normal environmental conditions. Because it is a gas and has a high vapor pressure, methanethiol is expected to volatilize in the environment. In the atmosphere, indirect photo-oxidation of methanethiol is predicted to occur. Measurement of reaction with hydroxyl radicals led to half lives ranging from less than 4 to 46 minutes; an estimated half life of 4 hours was obtained using EPISuite. Measurement of the reaction with NO_x resulted in a half life of 2 hours. The half life resulting from indirect photo-oxidation of sodium methanethiolate with hydroxyl radicals is estimated to be 10 days. A test conducted according to OECD TG 301D with sodium methanethiolate resulted in 64% degradation over 21 days, and the 10-day window was met. Based on these results sodium methanethiolate is considered to be readily biodegradable.

The level III fugacity model calculation with equal and continuous distributions of methanethiol to air, water and soil is 9.8% to air, 79% to water, 11% to soil and 0.1% to sediment. A low bioaccumulation potential is expected based on the log partition coefficient (log K_{ow}) of 0.78 for methanethiol (sodium methanethiolate dissociates in water and, at environmentally relevant pH, is present almost entirely as methanethiol). The estimated BCF for methanethiol is 3.16.

The following acute toxicity test results have been determined for aquatic species using sodium methanethiolate as a starting material:

Fish [*Danio rerio*] - (OECD TG 203)	96-h LC_{50} = 1.8 mg/L (measured)
Invertebrates [*Daphnia magna*] - (OECD TG 202)	48-h EC_{50} = 1.32 to 2.46 mg/L (measured)
Algae [*Pseudokirchneriella subcapitata*] - (OECD TG 201)	
	72-h ErC_{50} = 15 mg/L (growth rate) (measured)
	72-h EbC_{50} = 6.3 mg/L (biomass) (measured)

72-h NOEC (biomass) = 0.81 mg/L (measured)
72-h NOEC (growth rate) = 4.11 mg/L (measured)

These chemicals possess properties indicating a hazard for the environment (acute toxicity to fish, invertebrates and algae from 1 to 100 mg/L). However, the chemicals are readily biodegradable and have a limited potential for bioaccumulation. Adequate screening-level data are available to characterize the environmental hazard for the purposes of the OECD HPV Programme.

Exposure

In the United States, companies produced or imported > 450,000 metric tons (> 1 billion pounds) of methanethiol and 450 - 4500 metric tons (1 – 10 million pounds) of sodium methanethiolate in 2002.

During manufacture and use, methanethiol and sodium methanethiolate are primarily handled in closed systems. For example, use of process equipment and venting to a scrubber system are designed to limit release and exposures inside and outside plants that manufacture or use these compounds.

Methanethiol is used exclusively as a chemical intermediate by the submitting companies, with a primary use for the manufacture of methionine for animal nutrition. Other uses for the submitting companies include the use of methanethiol and sodium methanethiolate as intermediates for additives, modifiers and solvents, agricultural intermediates, biocides, health care products and pharmaceuticals. It may be used as an odorant for hazardous/odorless gases, although the submitting companies do not sell in this market. Other minor industrial uses, natural sources and production from fermentation processes may occur.

Methanethiol is also a natural substance found in certain foods, such as some nuts and cheese. Methanethiol is found endogenously in the blood, brain and other tissues of humans. Further, methanethiol is released from decaying organic matter in marshes and is present in the natural gas of certain regions in the United States, in coal tar and in some crude oils. It is also released as a decay product of wood in pulp mills, petroleum refining and sewage treatment plants.

Monitoring in two U.S. plants indicated that exposures over several years exceeded the TLV only once (3 ppm) and were generally less than 0.5 ppm with most exposures less than 0.05 ppm. Over the past several decades, emissions of methanethiol to air from chemical facilities in some locations have been recorded; however, only occasional measurements of low levels of methanethiol in water sources and air have been identified.

Although occupational exposure is possible, it is likely to occur more often as a result of chemical or microbiological reaction in certain settings (e.g., sewage treatment plants) than from production or use of the industrially-manufactured gas. An 8-h TWA-TLV of 0.5 ppm (1 mg/m^3) was adopted for methanethiol by the American Conference of Governmental Industrial Hygienists (ACGIH). Due to the low odor threshold and extremely disagreeable odor even small leaks can be detected and facilities are expected to limit exposure to well below the TLV to avoid odor complaints.

For most uses, consumer exposure is not likely because methanethiol and sodium methanethiolate are used mainly as intermediates and the odor can be detected at low levels. Further, residual levels of methanethiol from its use as an intermediate are unlikely, because of the compound's volatility. For uses where methanethiol may be added specifically to alert individuals to a hazardous/ odorless material, some exposure to the compound may occur. As noted above, the submitting companies do not participate in the gas odorant market.

Environmental exposure through air may be possible as a result of plant emissions, natural sources or as a result of chemical or microbiological reactions described above. However, methanethiol has not been found in groundwater or surface water at hazardous waste sites or in public or private wells.