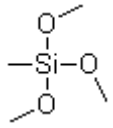
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	1185-55-3
Chemical Name	Trimethoxy(methyl)silane (MTMS)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-Chemical Properties

Reduced Testing rationale

MTMS undergoes rapid hydrolysis in the presence of water; the half life at pD 7 and 25°C is 2.2 hours. Based on the chemical structure of MTMS, this hydrolysis is expected to produce 3 moles of methanol and 1 mole of methylsilanetriol. Silanetriols (at concentrations greater than 500 mg/L) can condense to form highly cross-linked, high molecular weight polymers. Because MTMS is hydrolytically unstable, water solubility, partition coefficient and biodegradation were not measured; modeled values are provided for water solubility and partition coefficient. In aqueous solutions, exposures to MTMS are likely to be transient and observed toxicity is likely due primarily to the hydrolysis products methanol, methylsilanetriol, and condensed silanetriol materials (high molecular weight polymers). Data from the hydrolysis product methanol were presented at SIAM 19. The biodegradation data for methanol are provided; neither methylsilanetriol nor condensed silanetriol materials are expected to be readily biodegradable. A complete data set for the essential endpoints regarding human health is available for MTMS.

The EPISuite program (v 4.0) developed by the U.S. Environmental Protection Agency and Syracuse Research Corporation has not been validated for chemicals that contain silanes in their molecular structure (although some measured data are included in the training data set) ; therefore, there is uncertainty associated with the calculated values and they should be used with caution whenever they are reported.

MTMS is a liquid with a melting point of <-77 °C, a boiling point of 102 °C at 1013 hPa and a measured vapour pressure of 106.8 hPa at 20 °C. The calculated octanol-water partition coefficient (log K_{ow}) is -0.67, and the water solubility is 1 x 10^6 mg/L at 25 °C. The water solubility and log K_{ow} values may not be applicable because the chemical is hydrolytically unstable.

Human Health

No data are available on the toxicokinetics, metabolism or distribution of MTMS. However, under physiological conditions MTMS was hydrolyzed in water, PBS, and PBS plus 10% rat serum with half-lives of 24, 6.7, and 8.6 minutes, respectively producing methanol and silanetriol.

The 6-hr LC_{50} of MTMS as a vapor in rats is > 42 mg/L in a study conducted in accordance with OECD TG 403. Following inhalation exposure, clinical signs included discolored urine, fecal staining, head and muzzle soiling; necropsy showed urinary bladder calculi and kidney foci in both sexes, an enlarged kidney in one male and abscessed prostate glands in two males. The oral LD_{50} of

MTMS in rats is greater than 9500 mg/kg bw in a study conducted in accordance with OECD TG 401. Following oral (gavage) administration, clinical signs included depression, laboured respiration, ataxia, and excessive urination; there were no findings at necropsy. No data are available regarding the acute dermal toxicity of MTMS.

Slight erythema but no edema was observed at the 24 hour observation point when applied to intact skin; no signs of irritation were observed at the 72-hour observation point. Slight conjunctival irritation in 5 animals and moderate conjunctival irritation in one animal was observed but had completely subsided in all six animals by the third day. There was no corneal damage. MTMS was slightly irritating to the rabbit skin and eyes.

No experimental data are available for skin sensitization in animals.

The repeated dose toxicity of the MTMS has been investigated in two studies. In a repeated dose inhalation toxicity study in rats following OECD TG 413, MTMS was administered via inhalation (whole body) to 10 rats/sex/concentration at ca. 0.14, 0.56, 2.2 and 8.9 mg/L, for 6 hours/day, 5 days/week for 90 days. One 2.2 mg/L/day group male one 8.9 mg/L/day group male died during the study. Increased incidence of abdominal and urogenital soiling was observed in the 2.2 and 8.9 mg/L/day groups. There was an increase in female adrenal weights at 2.2 and 8.9 mg/L/day and an increase in female kidney weights at 8.9 mg/L/day. Findings at necropsy included calculi in the urinary bladder at 2.2 and 8.9 mg/L/day; calculi in urinary bladder of males and females exposed to 8.9 mg/L/day persisted through the 28-day recovery period. Kidney dilation was observed for 8.9 mg/L/day group animals. Histopathological findings were observed in the kidney of male animals exposed to 8.9 mg/L/day, the urinary bladder in males and females at 2.2 and 8.9 mg/L/day, and the prostate in all groups with a slight increase in severity at 8.9 mg/L/day. Based on the increased incidence of grossly observed urinary bladder calculi along with the kidney dilation at the 2.2 mg/L/day exposure level, the No Observable Adverse Effect Level (NOAEL) was 0.56 mg/L (100 ppm) and the LOAEL was 2.2 mg/L/day (400 ppm).

In a combined repeated-dose/reproductive/developmental toxicity screening test (OECD TG 422), the substance was administered via gavage to 10 rats/sex/dose at 0 (corn oil), 50, 250 and 1000 mg/kg bw/day. Males were treated during pre-mating and mating periods. Males and toxicity group females were sacrificed after they had been treated for 28 days. Clinical signs included transient inactivity or salivation following dosing. Statistically significant decreases in body weight gain and food consumption were noted for 1000 mg/kg bw/day group males. Increased liver weight was observed at 250 and 1000 mg/kg bw/day. Liver weights were increased at 250 mg/kg bw/day; males showed significant decrease in thymus weight. Histopathological examination showed changes in the thyroid gland (males and females) and liver (females). Hematological examination indicated an increased prothrombin time (males). At 1000 mg/kg bw/day, increased liver weight, increased platelet concentration, and histopathological changes in the liver, thyroid, adrenal (females only), duodenum and jejunum was observed. Males also had decreased thymus weight, acanthocytosis, increased red blood cell concentration, increased prothrombin time and increased serum alanine amino-transferase activity. Females had an increased incidence of adrenal gland apoptosis and lymphocytic infiltration. The NOAEL for systemic toxicity was 50 mg/kg bw/day with a LOAEL of 250 mg/kg bw/day.

MTMS did not induce gene mutations in *Salmonella typhimurium*/*Escherichia coli* WP2 uvrA *in vitro* (OECD TG 471); however, in TK-locus of mouse lymphoma L5178Y cells (OECD TG 476), it increased the mutation frequency in the presence of metabolic activation. Two *in vitro* chromosomal aberration tests using CHO cells (OECD 473) MTMS induced chromosomal aberrations in the presence of metabolic activation; however, in an *in vivo* micronucleus assay (OECD TG 474) no statistically significant increase in the incidence of micronucleated PCE's over the control value was observed. Based on these results, MTMS showed positive response when tested *in vitro*; however, it

did not cause chromosomal aberrations at the limit dose (2000 mg/kg bw) when tested *in vivo*.

No data are available for the carcinogenicity of MTMS.

The reproductive toxicity of the MTMS has been investigated in a in a reproductive and developmental toxicity screening test in rats [OECD TG 422]. In this study, MTMS was administered via gavage to 10 rats/sex/dose at 0 (corn oil), 50, 250, and 1000 mg/kg bw/day, for at least 28 days (males) and up to PND 4 (females). No adverse effects on reproductive parameters were observed up to the highest dose tested. No adverse effects on development were observed up to the highest dose tested. Based on no adverse effects the NOAEL for reproductive toxicity was considered to be 1000 mg/kg bw/day. Based on no adverse effects the NOAEL for developmental toxicity was considered to be 1000 mg/kg bw/day.

MTMS may present hazard for human health (repeated-dose (kidney and bladder) and genetic toxicity *in vitro*). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD HPV Chemicals Programme.

Environment

The hydrolysis half-life for MTMS is 2.2 hours at 25 °C and pD7. In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 4.1 days. The biodegradation of MTMS was not determined; based on the rapid hydrolysis of this material, any potential for biodegradation is likely to be of the hydrolysis products. Consequently, the only biodegradable materials in the test system will be methanol, silanetriol, and condensed silanetriol materials (high molecular weight polymers). Methanol is readily biodegradable (75 – 82 % and 95% removal in standard ready tests after 5 and 20 days respectively). Neither methylsilanetriol nor condensed silanetriol materials are expected to be readily biodegradable.

A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that MTMS will distribute mainly to the water (46.5%) and soil (41.2%) compartments with minor distribution to the air compartment (12.2%) and negligible amount in the sediment compartment. However, MTMS is unlikely to be found in the environment, as this material is hydrolytically unstable. Henry's Law constant of 8.67 x 10^{-5} atm-m^3/mole (8.8 Pa-m^3/mole) suggests that volatilization from the water phase for MTMS is not expected to be high.

MTMS reacts to form methanol and silanetriol through hydrolysis. The BCF for MTMS and silanetriol cannot be accurately predicted, but are expected to be low. Methanol has a low estimated bioaccumulation potential (BCF= 3.2). Furthermore, due to these properties, current estimation models are not capable of calculating physicochemical or environmental fate values with a known degree of accuracy. No information on the environmental fate of methyl silanetriol was found. However, based on studies on related monomeric silanols, it is expected that the adsorption of methyl silanetriol onto surfaces and condensation to disiloxanes in dilute aqueous solution may be important properties of this chemical. Methyl silanetriol is expected to partition primarily to water, soil and sediment due to its high water solubility and potential to bind to mineral surfaces. In water and air, methyl silanetriol may degrade photolytically. Slow biodegradation in water and soil might also occur.

Due to the rapid hydrolysis of MTMS, aquatic organisms are likely exposed to the parent material and its hydrolysis products, methanol, silanetriol, and condensed silanetriol materials.

The following acute and chronic toxicity test results have been determined for aquatic species:

Fish [*Oncorhynchus mykiss*]	96 h LC_{50} > 110 mg/L (flow-through; measured)
Invertebrate [*Daphnia magna*]	48 h EC_{50} > 122 mg/L (flow-through; measured)
Algae [*Pseudokirchneriella subcapitata*]	72 h ErC_{50} > 120 mg/L (growth rate method)

(static; nominal)
72 h EbC_{50} > 120 mg/L (area under growth curve method)
72 h NOEC = 120 mg/L

MTMS does not present hazard for the environment based on its low hazard profile. Adequate screening-level data are available to characterize the environmental hazard for the purposes of the OECD HPV Chemicals Programme.

Exposure

MTMS is commercially produced with an annual production volume of approximately 1769 tonnes in 2005 in the United States of America. Worldwide production volume was estimated to be approximately 3140 tonnes/year in 2005. MTMS is used in formulations at <5-100% as a coupling agent in thermoplastics and thermosetting resins, crosslinker in silicone sealants, polymeric filler treatment, water repellent component, adhesives, as a key ingredient in silicone hardcoats for plastics or manufacturing intermediate.

No monitoring data for effluents, surface water in occupational settings are available from the production and processing sites in the United States. During manufacturing, occupational exposure through dermal and inhalation routes is possible, although worker exposures due to non-accidental releases are expected to be low, and are expected to occur only during packaging and sampling. These exposures are minimized by use of personal protective equipment (PPE) and engineering controls. PPE includes impermeable chemical resistant gloves, goggles, fire resistant clothing, safety shoes, hard hat, and respirators. Engineering controls include ventilation devices and related equipment, closed sampling loops, and vacuum systems. At the industrial customer level, MTMS is used in open and/or closed systems; however, engineering controls and PPE are recommended to minimize exposures.

Consumer exposure may occur through oral, dermal or inhalation routes. At the consumer level, MTMS is used in silicone sealants at concentrations less than 10%. Dermal and inhalation exposures are possible during application. Once cured, silicone sealants are expected to contain essentially no MTMS, because it is reacted during use and loses its chemical identity. Therefore, environmental exposure is also expected to be low.