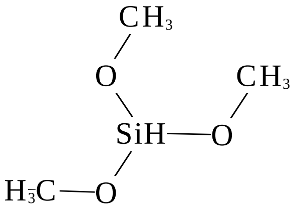
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2487-90-3
Chemical Name	Trimethoxysilane
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Reduced Testing Rationale

Trimethoxysilane undergoes rapid hydrolysis in water; the half life at pH 7 and 2°C is < 0.3 minutes. The hydrolysis product, methanol was measured in this study and based on trimethoxysilane's chemical structure, hydrolysis is expected to produce 3 moles of methanol and 1 mole of silanetriol. Depending on the pH and concentration of the substance, the silanetriols may condense to form oligomers and polymers. Because the material is hydrolytically unstable, water solubility, partition coefficient and biodegradation were not measured. Nonetheless, these endpoints provide valuable information on the behavior of the substance. Modelled values are provided for water solubility and partition coefficient for both trimethoxysilane and silanetriol. In aqueous solutions, exposures to trimethoxysilane are likely to be transient and observed toxicity is likely due primarily to the hydrolysis products methanol, silanetriol, and possible oligomers formed from cross-linking of hydrolysis products. Data from the hydrolysis product methanol (CAS. 67-56-1) were assessed at SIAM. The information on biodegradation potential of methanol is available; both trimethoxysilane and silanetriol are not expected to be readily biodegradable.

No reproductive or developmental toxicity studies have been conducted with trimethoxysilane. Additional testing with this material is not warranted because on a global basis, trimethoxysilane is a site-limited intermediate and is produced and used in closed systems (hard piped). There is no off-site transport and there are no consumer applications of trimethoxysilane. All the trimethoxysilane that is manufactured is consumed on site, in closed systems, in the manufacture of organofunctional silanes that generally contain less than 0.001 %, but may contain up to 0.2% trimethoxysilane. There are no intentional releases to the environment.

Human Health

In rats, exposure to trimethoxysilane by oral gavage resulted in an LD_{50} = 4.47 mL/kg bw (ca. 4291 mg/kg bw). Symptoms of toxicity noted at the two highest dose levels included depression, labored respiration, and ataxia. In an additional rat study, the oral gavage LD_{50} was 2.46 mL/kg bw for males (ca. 2458 mg/kg bw) and 1.56 mL/kg bw in females (ca. 1498 mg/kg bw). Signs of toxicity, observed in some animals, included sluggishness, lacrimation, an unsteady gait, distended abdomens, head and body twitches, piloerection, prostration, moribund appearance, red crust around nose and eyes, diarrhea, unkempt appearance and emaciation. In a third gavage study, the LD_{50} in male rats was 9.33 mL/kg (ca. 9857 mg/kg bw). The animals became sluggish soon after dosing and deaths occurred within the ensuing four-hour period at the highest dose level. The 4-hr inhalation LC_{50} for trimethoxysilane in rats is 60 ppm (ca. 300 mg/m^3). Observations on the day of exposure in the two highest concentration groups (166 or 71 ppm (ca. 830 or 355 mg/m^3)) included involuntary blinking or spasm of eyelids, periocular wetness, mouth and abdominal breathing, decreased motor activity, ataxia, and a slow surface-righting reflex. In the 39 ppm (ca. 195 mg/m3) group, unkempt fur, periocular wetness, abnormal breathing and decreased motor activity were observed. No clinical signs of toxicity were observed in the low concentration group (19 ppm (ca. 95 mg/m^3)). Additional 4-hr studies resulted in inhalation LC_{50}s of 31.25 < LC_{50} < 62.5 ppm (ca. 156 < LC_{50} < 312 mg/m^3) and 53 ppm (ca. 265 mg/m^3; nose only). In the rabbit, one study resulted in dermal LD_{50}s of 7.46 mL/kg bw in males (ca. 7160 mg/kg bw) and 6.73 mL/kg bw in females (ca. 6460 mg/kg bw). Local skin effects in 1 or more animals included erythema, edema, necrosis, ecchymosis, fissuring, ulceration, desquamation, scabs and alopecia. Sluggishness, salivation, prostration, emaciation and a clear or red discharge around nose were among the signs of toxicity observed. Histopathology of the lungs included abscesses, congestion, hemorrhages, edema, alveolar histiocytosis, mononuclear cells and black deposits. In another study, trimethoxysilane was applied to the skin of male rabbits for 24 hours using a covered application; the animals were observed for 14 days. The dermal LD_{50} from this study was 6.30 mL/kg bw (ca. 6050 mg/kg bw). Marked erythema of the skin was observed and gross necropsy findings included congested lungs, mottled livers, and bright mottled kidneys with prominent markings on the surface.

Trimethoxysilane has been shown to be corrosive to the skin and a moderate to severe eye irritant. Signs of respiratory tract irritation have been observed in workers and following repeated exposure to experimental animals. Trimethoxysilane is not a skin sensitizer.

Several inhalation repeated-dose studies of various durations have been conducted in rats and other mammals with trimethoxysilane. Groups of rats were exposed by inhalation at target concentrations of 10, 25, and 50 ppm (ca. 50, 125 or 250 mg/m^3) trimethoxysilane for seven hours/day for five days; the LC_{50} value was 13 ppm (ca. 65 mg/m^3). Gross clinical observations indicated the respiratory system was the target organ of toxicity. Repeated (9 days) inhalation exposure of rats to trimethoxysilane resulted in lethality at 5 ppm (25 mg/m^3), with death likely due to respiratory tract injury; the NOEC was 0.2 ppm (ca. 1 mg/m^3) and the LOAEC was 1 ppm (ca. 5 mg/m^3). No signs of systemic toxicity were observed and histopathological changes were seen only in the respiratory tract (the site of contact). Repeated inhalation exposure of rats to trimethoxysilane for 28 days at 5 and 10 ppm (ca. 25 or 50 mg/m^3) was lethal, with death probably being a consequence of respiratory tract injury. Based on the body weight, organ weight, clinical pathology, histopathologic observations, and deaths, the NOAEC from this study appeared to be 0.5 ppm (ca. 2.4 mg/m^3). In each of these repeated exposure studies, there were no other organs or tissues noted to have histopathological lesions even at the highest exposure concentration which produced severe effects in the respiratory tract and/or death. Exposure of rats to trimethoxysilane vapor (0.02, 0.1 or 0.5 ppm; ca. 0.1, 0.5 or 2.5 mg/m^3) for 90 days, followed by a 4-week recovery period produced no exposure-related effects in the biologic parameters monitored during this study. The NOEC in this 90-day inhalation study with rats was determined to be at least 0.5 ppm (ca. 2.5 mg/m^3). Groups of mice and hamsters were exposed by inhalation at target concentrations of 10, 25, and 50 ppm (ca. 50, 125 or 250 mg/m^3) trimethoxysilane for seven hours/day for five days; the LC_{50} values were 14 ppm (ca. 70 mg/m^3; mouse) and 72 ppm (ca. 360 mg/m^3; hamster). Gross clinical observations indicated the respiratory system was the target organ of toxicity.

Trimethoxysilane was not mutagenic *in vitro* in bacterial reverse mutation assays. Trimethoxysilane was negative for the induction of structural and numerical chromosome aberrations *in vitro* in the non-activated test system, but was positive in the S9-activated test system. Trimethoxysilane was not considered to be an inducer of micronuclei *in vivo.* The available information suggests that this substance is not likely to be genotoxic.

Exposure to trimethoxysilane up to 0.5 ppm (ca. 2.5 mg/m^3) for 90 days or 5 ppm (ca. 25 mg/m^3) for 9 days did not result in any signs of reproductive organ toxicity in rats. Developmental toxicity studies have not been conducted with trimethoxysilane. As noted above under **Reduced Testing Rationale,** no additional testing is needed because trimethoxysilane is a site-limited intermediate.

Environment

Trimethoxysilane is hydrolytically unstable over a range of environmentally relevant pH and temperature conditions. At pH 7 and 2°C, the half-life is < 0.3 minutes. This hydrolysis is expected to produce 3 moles of methanol and 1 mole of silanetriol. Silanetriols (at concentrations greater than 500 ppm) can condense to form highly cross-linked, high molecular weight polymers, further reducing the potential for exposure. If trimethoxysilane is slowly released such that the concentration of the resulting silanetriol is not high enough to result in polymerization, the silanetriol will exist largely as a monomer. The melting point of trimethoxysilane is -113.6°C and the boiling point is 84.4 °C at 1013 hPa. The vapor pressure is 75.11 hPa at 20ºC. The estimated water solubility of trimethoxysilane is 1,000,000 mg/L; the estimated log K_{ow} is -1.22. The water solubility and log K_{ow} values may not be applicable because the chemical is hydrolytically unstable. The estimated water solubility of silanetriol is also 1,000,000 mg/L; the estimated log K_{ow} is -2.91.

The overall OH rate constant for trimethoxysilane and resulting half-life and rate constant due to indirect photolysis are estimated to be 2.5×10^{-12} cm^3/molecule-sec and 6.4 days, respectively, using a hydroxyl radical concentration of 5.0×10^5 molecule/cm^3. Photodegradation as a mode of removal is unlikely as trimethoxysilane is hydrolytically unstable. It is assumed that reaction with water vapor is the predominant degradation process for trimethoxysilane in air. The products resulting from trimethoxysilane hydrolysis in the atmosphere are expected to further react with hydroxyl radicals. For the hydrolysis product, silanetriol, the half life due to the atmospheric oxidation from indirect photolysis was determined to be 1.6 days; the overall OH rate constant is 10.35×10^{-12} cm^3/molecule-sec.

Level III Fugacity modeling, using loading rates of 1000 kg/h each for air, soil, and water, shows the following percent distribution of trimethoxysilane when it is released simultaneously to all three compartments: Air = 47.6%; Soil = 47.6%; Water = 4.8%; Sediment = 0%. However, because it is hydrolytically unstable, trimethoxysilane is unlikely to be found in the environment. Therefore, Level III Fugacity modeling for the hydrolysis product, silanetriol was conducted using loading rates of 1000 kg/h each for air, soil, and water. The model estimated the following percent distribution, when silanetriol is released simultaneously to all three compartments: Air = 1.07%; Soil = 56.7%, Water = 42.24%; and Sediment = 0.08 %. Modeling suggests trimethoxysilane is not readily biodegradable. Any expected biodegradation is likely reflective of the hydrolysis product, methanol, which is readily biodegradable. Silanetriol and condensed silanetriol materials are inorganic compounds and therefore standard biodegradation tests are not applicable. Bioaccumulation of the parent substance is not anticipated since this material is hydrolytically unstable. The bioaccumulation of silanetriol is also unlikely given its low Log K_{ow} value.

Due to the rapid hydrolysis of trimethoxysilane, observed aquatic toxicity is likely due primarily to the hydrolysis products. The 96-hour LC_{50} and LC_0 of trimethoxysilane in freshwater fish (*Oncorhynchus mykiss*) are >= 100 mg/L. The 48 hour EC_{50} of trimethoxysilane is >100 mg/L for the water flea (*Daphnia magna*) under static conditions. In an algae study with trimethoxysilane, the 72 hr E_bC_{50} values and NOEC for biomass were > 100 mg/L and < 6.3 mg/L, respectively. The 72 hr E_rC_{50} values and NOEC for growth rate were > 100 mg/L and < 6.3 mg/L, respectively.

Exposure

In the Sponsor Country, production volume in 2001 was 1702 tonnes. Trimethoxysilane is not imported in the Sponsor Country; on a global basis this material is a site limited intermediate and is not transported. In production, this material is handled in closed systems (hard piped). Trimethoxysilane is used as a key intermediate in the manufacture of other chemicals (organofunctional silanes). Final industrial products generally contain less than 0.001 %, but may contain up to 0.2% trimethoxysilane. The substance is reacted during use and loses its chemical identity.

There are no intentional releases to the environment. The reactive nature of this material destroys the parent material in water, thus limiting environmental exposure to trimethoxysilane. Due to known and expected reactions, some exposure to methanol, silanetriols, or highly cross-linked, high molecular weight polymers may occur.

Five plants in the Sponsor Country use/manufacture trimethoxysilane. The reactive nature of trimethoxysilane requires handling in closed systems that exclude moisture. Trimethoxysilane is produced in closed reactors that are fed directly to strippers. The stripper separates the lights (solvent) and recycles it back to the reactor; the crude trimethoxysilane is cooled and transferred by hard piping to storage tanks. The crude trimethoxysilane is transferred to a stripper by means of hard piping and then transferred to tanks following condensation. The “heavies” are removed from the bottom of the stripper, and piped directly to a “heavies” storage tank; this tank is hard piped to an incinerator. Trimethoxysilane is transferred by hard piping to a tank where it is intentionally reacted. There is no intentional exposure to trimethoxysilane during production. Trimethoxysilane is not sold in industrial consumer markets and is not shipped from the original point of manufacture.

There are no consumer applications that use trimethoxysilane; the substance is used as a key intermediate in the manufacture of other chemicals (organofunctional silanes). Trimethoxysilane is not sold in consumer markets.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (corrosivity to the skin, moderate to severe eye irritation, respiratory tract irritation and/or death due to respiratory failure in repeated-dose toxicity studies). Due to the rapid hydrolysis to methanol and the corresponding silanetriol and based on exposure data presented by the Sponsor country (closed system site limited intermediate with no transport globally) and relating to use pattern in one country, this chemical is currently of low priority for further work. These properties should nevertheless be noted by chemical safety professionals and users. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment: The chemical is currently of low priority for further work based on its low hazard profile.