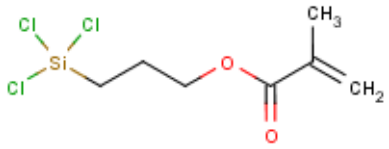
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7351-61-3
Chemical Name	2-Propenoic acid, 2-methyl-, 3-(trichlorosilyl)propyl ester (MPTClS)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Justification

Like all chlorosilanes, 2-Propenoic acid, 2-methyl-, 3-(trichlorosilyl)propyl ester (MPTClS), reacts rapidly when exposed to moisture or polar reagents, producing hydrogen chloride (HCl; CAS No. 7647-01-0) and the corresponding silanol: (γ-methacryloxypropyl)silanetriol (CAS No. 18834-30-5). The hydrolysis half-life of MPTClS is characterized using data for a structurally analogous chlorosilane, trichloro(methyl)silane (C3MS; CAS No 75-79-6). C3MS has previously been assessed in the OECD HPV Programme as a member of the alkyl chlorosilanes category (http://www.oecd/env/hazard/data). For mammalian toxicity and acute aquatic toxicity endpoints, data are provided for a structurally similar analogue, 3-trimethoxysilylpropyl methacrylate (MPTMS, CAS No. 2530-85-0) and for the hydrolysis product HCl, both of which have been previously assessed in the OECD Cooperative Chemicals Assessment Program (http://www.oecd/env/hazard/data). Both MPTClS and MPTMS rapidly hydrolyze to form 1 mole of (γ-methacryloxypropyl)silanetriol (CAS No. 18834-30-5). MPTClS also forms 3 moles of HCl per mole of silanetriol, while MPTMS forms 3 moles of methanol per mole of silanetriol. Although methanol is a hydrolysis product associated with the analogue substance, MPTMS, the primary human health hazard for MPTClS is considered to be exposure to the hydrolysis product, HCl. Similar structures and rapid hydrolysis to the same silanol hydrolysis product support the use of MPTMS data for the mammalian and aquatic toxicity endpoints. The levels of MPTClS required to generate significantly toxic concentrations of silanols would result in severely corrosive HCl concentrations. (γ-Methacryloxypropyl)silanetriol cannot be isolated for testing as it is not stable; in higher concentrations, it will condense to form highly cross-linked, high molecular weight polymers.

Physical-chemical properties

MPTClS is a liquid with an estimated melting point of -53.15 ^{o}C at 1013 hPa and an estimated boiling point of 250.6 ^{o}C at 1013 hPa. The extrapolated vapor pressure value from measured data is 0.017 hPa at 25^{o}C. The calculated water solubility is 98.72 mg/L. The estimated log K_{ow} of MPTClS is 3.43. 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 of MPTClS. However, MPTClS rapidly hydrolyzes on contact with moisture generating 3 moles of HCl for every mole of (γ-methacryloxypropyl)silanetriol. The hydrophilic nature of (γ-methacryloxypropyl)silanetriol will limit its diffusion across membranes and its accumulation in fatty tissues and may lead to some retention in the mucous of the lungs. HCl dissociates; its effects are thought to be a result of pH change.

Experimental data regarding MPTClS for human health toxicological endpoints are not available. Acute toxicity data are available for MPTMS and HCl. The range of 1 hour acute inhalation LC_{50} for MPTClS is 8.41-10.64 mg/L (predicted based on chlorine content). The principal clinical signs are expected to be indicative of respiratory and ocular effects resulting from HCl exposure. Inhalation LC_{50} values for HCl were determined to be 4.2-4.7 mg/L for 1 hour for rats. A 4-hour LC_{50} value for MPTMS (hydrolyzed) was >2.28 mg/L (highest attainable aerosol concentration) for rats [OECD TG 403]. The dermal LD_{50}s [OECD TG 402] of MPTMS in rats and male rabbits were 2000 mg/kg bw and greater than 2090 mg/kg bw, respectively. Clinical signs of exposure included slight erythema and edema in rats; no findings were noted for rabbits. The oral (gavage) LD_{50} [OECD TG 401] of MPTMS in rats has been shown in several studies to be greater than 2000 mg/kg bw. Clinical signs of exposure included wet and/or dried yellow and/or clear material around the mouth, forelimb(s), anogenital area and/or base of tail. There were no findings at necropsy. The acute oral LD_{50} values of HCl were determined to be 238-277 mg/kg bw for female rats. Acute toxicity of MPTClS is expected to be similar to that of HCl.

MPTMS is slightly irritating to the skin and eye of rabbits. HCl is corrosive and highly irritating to the skin, eyes and respiratory tract with no data located for skin sensitization. In a guinea pig maximization test, MPTMS was a weak skin sensitizer. MPTClS is expected to be a skin, eye, and respiratory tract irritant and a skin sensitizer.

Data from an analogous substance, MPTMS, and the hydrolysis product HCl are available to address the repeated-dose toxicity endpoint via inhalation exposure. In three 14-week repeated exposures in rats to an aerosol of MPTMS and its hydrolysis products at nominal concentrations up to 0.1 mg/L, a NOAEC was not established. MPTMS produced histopathological changes in the upper respiratory tract at nominal concentrations greater than or equal to 0.005 mg/L, the major findings being cytoplasmic hyalinization and the formation of laryngeal granulomas. In three 4-week repeated aerosol exposures in rats, there were similar findings; the measured LOAEC was 0.0135 mg/L. By the inhalation route, during repeated-dose toxicity studies, the local effects of irritation of HCl were observed in the groups of 0.015 mg/L and above in the 90-day inhalation study. The NOAEC for systemic toxicity for HCl, excluding the local effects of irritation, has been determined to be 0.030 mg/L for rats and mice based on body weight gain and liver weight changes. As a result of hydrolysis, repeated dose toxicity of MPTClS is expected to be characterized by HCl formation.

Data for genetic toxicity are available for MPTMS and HCl. The analogous substance, MPTMS, did not induce gene mutations in bacterial or mammalian cells *in vitro*, but did induce chromosomal aberrations in mammalian cells *in vitro*. All *in vitro* studies were conducted with and without metabolic activation. MPTMS was negative for sister chromatid exchange *in vitro* and in a mouse micronucleus assay *in vivo*. MPTMS is not considered to be genotoxic *in vivo*. Positive results in the *in vitro* chromosome aberration test with HCl were considered to be the effect of low pH. Based on the available data, MPTClS is not expected to be genotoxic.

No data were available for the carcinogenicity of MPTMS. Carcinogenicity data are available for HCl. No pre-neoplastic or neoplastic nasal lesions were observed in a 128-week inhalation study with male rats at 10 ppm hydrogen chloride gas. No evidence of treatment related carcinogenicity was observed either in other animal studies performed by inhalation, oral or dermal administration. In humans, no association between hydrogen chloride exposure and tumor incidence was observed.

Data for the reproductive/developmental toxicity endpoints for the analogous substance, MPTMS are available. Repeated inhalation of aerosolized and hydrolyzed MPTMS at concentrations up to 0.1 mg/L for 14 weeks showed no adverse histopathological effects on the reproductive organs of rats; the NOAEC was established at 0.1 mg/L. In an oral gavage OECD TG 414 developmental toxicity study in rats at concentrations of 522.5, 2090 and 5225 mg/kg bw/day, maternal and developmental effects were noted at 2090 mg/kg bw/day and higher. Maternal toxicity included staining of fur, uncoordination, reductions in body weight and food consumption, increases in the absolute and relative liver and kidney weights and mortality at 2090 and/or 5225 mg/kg bw/day. Developmental effects were decreased fetal weights, increases in the incidence of soft tissue malformations and delayed ossification at 2090 and/or 5225 mg/kg bw/day. Based on these results, the NOAEL for maternal and developmental toxicity was 522.5 mg/kg bw/day. Developmental effects, consistent with a general profile of developmental delay, were observed only at the mid- and high-dose levels. These doses are quite high – 2-fold and 5-fold higher than the "limit dose" of 1000 mg/kg bw/day as specified in OECD TG 414. No reliable studies have been reported regarding toxicity to reproduction and development in animals after oral, dermal or inhalation exposure to hydrogen chloride/hydrochloric acid. Because protons and chloride ions are normal constituents in the body fluid of animal species, low concentrations of hydrogen chloride gas/mist or solution do not seem to cause adverse effects to animals. In fact, the cells of gastric glands secrete hydrochloric acid into the cavity of the stomach and orally administered sulfuric acid, which results in pH change as well, did not cause developmental toxicity to laboratory animals. These facts indicate that hydrogen chloride/hydrochloric acid is not expected to have developmental toxicity. In addition, no effects on the gonads were observed in a 90-day repeated-dose inhalation study up to 50 ppm. Based on these data,

MPTClS is not expected to show reproductive/developmental toxicity up to the limit dose.

MPTClS possesses properties indicating a hazard for human health (severe skin, eye and respiratory tract irritation, repeated-dose toxicity). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

Not all programs within EPI Suite have been validated for chemicals that contain the element Si, but recent upgrades to the Kow module, found in the current version of EPI Suite (v4.10), may improve estimates for silanes and siloxanes for this endpoint. However, there is still uncertainty associated with the calculated values and they should be used with caution whenever they are reported.

A hydrolysis study was not conducted on MPTClS. Using an analogous substance, trichloro(methyl)silane (CAS No. 75-79-6), MPTClS is expected to hydrolyze to HCl and the corresponding silanol in less than 1 minute at pH 4, 7, and 9 at 1.5ºC. MPTClS in air is not expected to undergo direct photolysis, but may undergo indirect photolysis through hydroxyl radical oxidation. The hydroxyl radical reaction was calculated using a 12-hr day and a hydroxyl radical concentration of 1.5E6 OH molecules/cm^3 in AOPWIN® ver. 1.92. The overall OH rate constant and estimated half-life is 2.26E-11 cm^3/molecule-sec and 5.7 hours, respectively. Any potential for photodegradation might be superseded by hydrolysis of the parent compound depending on the concentration of water vapor in the air. The results of Level III fugacity modeling, using equal loading rates of 1000 kg/h each for air, soil and water show that when MPTClS is released simultaneously to all three compartments it will distribute mainly to air (47.6 %) and soil (47.7 %), with a minor fraction to water (4.77 %) and negligible distribution to sediment (< 0.1 %). Since the parent material is not expected to be released to soil or water based on its uses and handling, a scenario of 100% emission to air is more realistic. When MPTClS is released to air exclusively, 0.2% remains in air (100%). The modeling results show that the environmental fate of MPTClS is controlled by its high reactivity with water in all compartments. Level III fugacity modeling using equal loading rates of 1000 kg/h each for air, soil and water predicts that the hydrolysis product, (γ-methacryloxypropyl)silanetriol, will distribute mainly to soil (82.2%), with a smaller fraction to water (17.6%) and negligible amounts to sediment and air (0.18 and < 0.1%). Based on the more realistic scenario of 100% release to air, the fugacity modeling predicts that (γ-methacryloxypropyl)silanetriol will distribute mainly to soil (94.9%), with a smaller fraction going to water (5.1%) and negligible fractions in air and sediment (<0.1%)[EPI Suite (v4.10)]. Fugacity modeling of HCl is not applicable. The biodegradation of MPTClS was not determined due to rapid hydrolysis; any potential for biodegradation is likely to be of the hydrolysis products. Consequently, the only potentially biodegradable materials in the test system will be silanols, and condensed silanol materials (high molecular weight polymers). No measured data are available for the hydrolysis product (γ-methacryloxypropyl)silanetriol exclusively, as it cannot be isolated. Although extensive biodegradation was observed for MPTMS, this substance hydrolyzes to form methanol as a co-product, which complicates interpretation of the biodegradation studies. HCl is an inorganic compound and biodegradation tests are not applicable.

The bioaccumulation potential of MPTClS was not determined due to rapid hydrolysis. An estimated BCF for MPTClS is 85.41 L/kg wet-wt, indicating MPTClS is not expected to bioaccumulate.

Aquatic toxicity data are not available for MPTClS; the substance undergoes rapid hydrolysis, which occurs during testing; exposure to the parent chlorosilane is likely to be transient and observed toxicity is likely due its hydrolysis products, HCl and the corresponding silanol hydrolysis product. Aquatic toxicity data are available for MPTMS; based on the hydrolysis half-life of 4 hours of MPTMS, for the duration of aquatic toxicity tests, the organisms were likely exposed to both MPTMS and the hydrolysis products, methanol and (γ-methacryloxypropyl)silanetriol. MPTMS hydrolyzes to form the same silanol as the sponsored substance, MPTClS. The fish studies on MPTMS were conducted as semi-static studies, the *Daphnia* studies were conducted under static conditions. The degree of toxicity caused by HCl is also highly dependent on the buffer capacity of the receiving water. Aquatic toxicity endpoints for MPTClS are also fulfilled through the use of data from the hydrolysis product, HCl.

Fish

MPTMS [*Brachydanio rerio*] 96 h LC_{50} >100 mg/L (OECD TG 203; semi-static, measured as total Si)
HCl [*Oncorhynchus mykiss*] 96 h LC_{50} = 4.92 mg/L (pH 4.3; OECD TG 203; semi-static, nominal)

Aquatic Invertebrate

MPTMS [*Daphnia magna*] 48 h EC_{50} > 100 mg/L (OECD TG 202; static, measured as total Si)

48 h EC_{50} > 876 mg/L (Directive 92/69/EEC, C.3; static, measured as TOC)
HCl [*Daphnia magna*] 48 h LC_{50} = 0.492 mg/L (pH 5.3 ; OECD TG 202, nominal)

Algae

MPTMS [*Scenedesmus subspicatus*] 72 hr ErC_{50} , E_bC_{50} > 100 mg/L (OECD TG 201; measured as total Si)
[*Scenedesmus subspicatus*] 72 hr ErC_{50} , E_bC_{50} > 536 (Directive 92/69/EEC, C.3, measured as DOC)
HCl [*Selenastrum capricornutum]* 72 hr EC_{50} = 0.492 mg/L (pH 5.3) (OECD TG 201; nominal)

Hydrogen Chloride (HCl)

The hazard of hydrochloric acid for the environment is caused by the proton (pH effect). For this reason the effect of hydrogen chloride on the organisms depends on the buffer capacity of the aquatic ecosystem. Also the variation in acute toxicity for aquatic organisms can be explained for a significant extent by the variation in buffer capacity of the test medium. For example, LC_{50} values of acute fish toxicity tests varied from 4.92 to 282 mg/L. The toxicity values to *Selenastrum capricornutum* 72h-EC_{50} is 0.780 mg/L at pH 5.1 for biomass, 0.492 mg/L at pH 5.3 for growth rate and the 72h-NOEC is 0.097 mg/L at pH 6.0 for biomass and growth rate. The 48h-EC_{50} for *Daphnia magna* is 0.492 mg/L at pH 5.3 based on immobilization.

MPTClS possesses properties indicating a hazard for the environment (acute toxicity to fish between 1 and 100 mg/L, acute toxicity to aquatic invertebrates and toxicity to algae, <1 mg/L). Toxic effects are expected primarily from the hydrolysis products (in particular hydrogen chloride, and depend on the buffering capacity of a particular aquatic environment. Therefore, the stated effect levels pertain to unbuffered systems and can be viewed as conservative). MPTClS is not expected to be readily biodegradable. Adequate screening-level data are available to characterize the hazard for the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

The 2010 production volume in the United States (sponsor country) ranged from 45 to 2628 tonnes. Production was not reported in Europe or Japan. 100% of MPTClS is used as an intermediate for silicone oligomers and polymers. MPTClS is reacted during use and loses its chemical identity.

There is no intentional release of MPTClS to the environment.

MPTClS is produced and processed in closed systems. Due to the dynamic and exothermic nature of the processes incorporating chlorosilanes, many engineering controls are in place to prevent occupational exposure such as water scrubber devices and related equipment including ventilation; and closed sampling loops. Employees involved in chlorosilane production and application are required to use personal protective equipment (PPE) such as safety glasses or goggles, steel-tipped shoes, flame-resistant clothing, hard hat, chemical resistant gloves; respirator mask. Potential routes of occupational exposure during routine operations (such as sampling operations, equipment maintenance and waste disposal) at the manufacturing site include inhalation and dermal exposure.

There are no consumer uses of MPTClS.