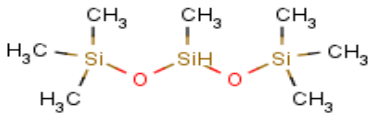
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	1873-88-7
Chemical Name	1,1,1,3,5,5,5-Heptamethyltrisiloxane (HMTS)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Justification

Octamethyltrisiloxane (L3; CAS No. 107-51-7) is used as an analogue to address the potential for chronic aquatic toxicity of 1,1,1,3,5,5,5-heptamethyltrisiloxane (HMTS). L3 has previously been assessed in the OECD HPV programme. Chronic toxicity data are not feasible for HMTS due to hydrolytic instability, low water solubility and high volatility. L3 is an appropriate analogue based on (1) the measured octanol-water partition coefficient (log K_{ow}) of 6.60 at 24.1 °C, (2) the measured water solubility of 0.0345 mg/L at 23 °C, which is within the same order of magnitude as the solubility value for HMTS, and (3) similarities in structure between L3 and HMTS.

Physical-Chemical Properties

HMTS is a liquid with a measured melting point of less than -20.2 °C, a measured boiling point of 140.85 to 142.85°C at 1008.8 to 1027.9 hPa and a measured vapour pressure of 8.47 hPa at 25 °C. The measured octanol-water partition coefficient (log K_{ow}) is 7.84 at 25 °C, and the measured water solubility is 0.02 mg/L at 22.0 °C (pH of 4.0). The water solubility and log K_{ow} values may not be applicable because the substance is hydrolytically unstable.

Human Health

No toxicokinetics data are available for HMTS. Based on reported toxicity following repeated oral exposure (gavage), HMTS is systemically absorbed and then distributed, at least in part, to the liver and kidney.

The oral (gavage) LD_{50} value was >2000 mg/kg bw in female rats [OECD TG 425]. Clinical signs included ruffled fur, sedation, poor coordination, hunched posture and ventral recumbency.

No irritation or sensitization data are available for HMTS.

The repeated-dose toxicity of HMTS has been investigated in one study. In a combined repeated-dose/reproductive/developmental toxicity screening test in rats [OECD TG 422], HMTS was administered via gavage to 10 rats/sex/dose at 0, 50, 200 or 800 mg/kg bw/day during pre-mating, mating (males and females), gestation and lactation day 4 (females). Males were dosed for 5 weeks and females 6-8 weeks. No mortality was seen. There were no treatment-related clinical signs of toxicity. In males, food consumption (800 mg/kg bw) and body weight/body weight gain (at 200 mg/kg bw/day and higher) were statistically significantly reduced. Clinical chemistry changes were limited to males at 800 mg/kg bw/day (cholesterol was increased; total bilirubin was reduced). Absolute and relative weights of liver and kidney were increased in males at 800 mg/kg bw/day. At 200 mg/kg bw/day and higher, absolute and relative liver weight were increased in females. At 800 mg/kg bw/day,

enlarged kidneys were observed in two males and the renal pelvic dilation which occurred in one male correlated with renal tubular lesions observed microscopically. Microscopically, test substance-related lesions were seen in the liver, kidney and thyroid gland. Centrilobular hypertrophy was noted in females at 200 mg/kg bw/day and higher; this was accompanied by extramedullary hematopoiesis in a single female at 800 mg/kg bw/day. The liver cell hypertrophy was considered to be an adaptive response due to metabolism of the test substance. There was increased protoporphyrin within portal bile ducts accompanied by reactive bile duct hyperplasia and perilobular fatty change in 800 mg/kg bw/day males, characteristic features of hepatic protoporphyrin accumulation. In the kidneys, focal or multifocal tubular degeneration/regeneration was increased in all males at 200 mg/kg bw/day and higher, and in some males at 800 mg/kg bw/day; this lesion was associated with tubular simple dilation or hyaline casts. These tubular lesions in males were accompanied by an increase in pelvic dilation, causing macroscopic renal enlargement and pelvic dilation in some males at 800 mg/kg bw/day. Furthermore, the test substance induced an increase in hyaline droplets/granules in males at 200 mg/kg bw/day and higher, and along with increased tubular degeneration/regeneration, may be interpreted as alpha 2u-globulin nephropathy. Diffuse follicular cell hypertrophy (thyroid) and an increase in extramedullary hematopoiesis (spleen) were observed in females at 200 mg/kg bw/day and in all animals at 800 mg/kg bw/day; these were considered adaptive effects. Based on effects at 200 and 800 mg/kg bw/day which included microscopic findings in the kidneys and liver (protein droplet nephropathy and hepatic protoporphyrin accumulation) in males and a statistically significant increase in liver weight in females, the No Observed Adverse Effect Level (NOAEL) for systemic toxicity was 50 mg/kg bw/day.

In bacterial reverse mutation assays with multiple strains of *Salmonella typhimurium* and *E. coli* [OECD TG 471] HMTS was negative both with and without metabolic activation. In an *in vitro* cytogenetic assay in Chinese hamster V79 cells [OECD TG 473] HTMS did not induce chromosomal aberrations with or without metabolic activation. Based on these results, HTMS is not considered to be genotoxic *in vitro*.

No data are available for the carcinogenicity of HMTS.

The reproductive and developmental toxicity of HTMS has been investigated in a repeated-dose/reproductive/developmental toxicity screening test [OECD TG 422]. In this study, HTMS was administered via gavage to 10 rats/sex/dose at 0, 50, 200 or 800 mg/kg bw/day during pre-mating, mating (males and females), gestation and lactation day 4 (females). No mortality was seen. There were no test substance-related effects on any fertility parameter; the NOAEL for effects on fertility was 800 mg/kg bw/day, the highest dose tested. A statistically significantly higher postnatal loss and lower pup weight gain were noted at 800 mg/kg bw/day. As described above, maternal toxicity was seen at and above 200 mg/kg bw/day. The NOAELs for maternal and developmental toxicity were considered to be 50 mg/kg-bw/day and 200 mg/kg bw/day (in the presence of maternal toxicity), respectively.

1,1,1,3,5,5,5-Heptamethyltrisiloxane possesses properties indicating a hazard for human health (repeated-dose and developmental toxicity following oral exposure). 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 and water solubility modules, found in the current version of EPI Suite (v4.10), give reasonable estimates for silanes and siloxanes.

HMTS has low water solubility (0.02 mg/L). A hydrolysis study with HMTS was not conducted due to its high volatility and low water solubility. These properties make it very difficult to devise an appropriate experimental setup to test for hydrolysis [OECD TG 111] because losses due to hydrolysis are very hard to distinguish from losses due to volatilization. Significant test substance losses were often found in the extensive pre-experiments, but no hydrolysis product was observed. As a result, a hydrolysis test with HMTS was not performed because no experimental setup, together with an accurate and sensitive analytical method, could be devised. At pH 9 and greater, the hydrolysis of HMTS is expected to be rapid (t½ in minutes to hours; ignoring its low water solubility, basic pH is a catalyst for hydrolysis of HMTS). At pH 7, hydrolysis is expected to be slow (2-3 days) and at pH 4, hydrolysis is expected to occur in hours to days. These estimates are based solely on best professional judgment. HMTS is expected to hydrolyze to 1 mole of hydrogen gas for each mole of 1,1,1,3,5,5,5-heptamethyl-3-trisiloxanol. The trisiloxanol condenses to disiloxane dimers; this condensation of silanols is affected by both concentration and pH (as basicity increases, condensation of silanols increases), and since both change over time

it is not feasible to isolate specific silanols for analysis (the structures continue to evolve until they either reach equilibrium or precipitate out of solution). The Si-O bond may also be susceptible to hydrolysis, resulting in the formation of two moles of trimethylsilanol and one mole of methylhydridyldisilanol. If HMTS is slowly released such that the concentration of the resulting trisiloxanol is not high enough to result in polymerization, the trisiloxanol will exist largely as a monomer. Thus, there is some uncertainty about the environmental fate of the parent substance and potential hydrolysis products. The estimated log Kow and water solubility for the trisiloxanol are 3.39 and 7.53 mg/L at 25 ^{o}C, respectively. In the atmosphere, indirect photo-oxidation by reaction of HMTS with hydroxyl radicals is predicted to occur with an estimated half-life of 10.2 days. The biodegradation of HMTS was determined in the CO_2 headspace test [OECD TG 310]; HMTS was not readily biodegradable (0 % after 28 days).

A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments estimated that HMTS will distribute mainly to water (66%) compartment with lesser distribution to air (26.7%) and soil or sediment compartments (5.71 and 1.52%, respectively). The estimated Henry's Law constant of 3.07 x10^4 Pa-m^3/mole (Bond Estimate) suggests that volatilization from the water phase for HMTS is expected to be high. Note that the Henry's Law constant based on calculated vapour pressure and water solubility is 9.4 x 10^6 Pa-m3/mole; this is the value used for distribution modelling.

The estimated BCF value for HMTS is 5157 L/kg wet-wt indicating a potential for bioaccumulation; the log BAF (Arnot-Gobas upper trophic) was estimated to be 6.41 for HMTS and the BAF was 2.56E+006 L/kg wet-wt. The BCF of the immediate hydrolysis product (1,1,1,3,5,5,5-heptamethyl-3-trisiloxanol) is 630 L/kg wet-wt.

The following acute toxicity test results with a single, nominal concentration of 0.2 mg/L HMTS have been determined for aquatic species:

Fish [*Brachydanio rerio*]	96 h EC_{50} > 0.108 mg/L(OECD TG 203; semi-static; measured)
Invertebrate [*Daphnia magna*]	48 h EC_{50} > 0.030 mg/L(OECD TG 202; semi-static; measured)
Algae [*Pseudokirchneriella subcapitata*]	72-h E_yC_{50}, E_bC_{50} > 0.019 mg/L (OECD TG 201; measured)

Aquatic toxicity tests were conducted in closed systems to avoid loss of the substance through volatilization. Fish and Daphnid studies also included 24 hour substance renewals.

The following chronic toxicity test results are from the analogous substance, CASRN 107-51-7 Octamethyltrisiloxane (L3):

Chronic	
Invertebrate [*Daphnia magna*]	
21-day EC_{50} (mortality/immobility and reproduction)	> 0.015 mg/L (flow-through)*
21-day NOEC (for survival, reproduction and growth)	= 0.015 mg/L*
21-day LOEC (for survival, reproduction and growth)	> 0.015 mg/L*
Sediment	
Invertebrate [*Lumbriculus variegatus*]	
28-day EC50 (survival/reproduction/growth)	> 17 mg/Kg*
28-day NOEC (survival/reproduction)	= 1.1 mg/Kg
28-day LOEC (survival/reproduction)	= 1.6 mg/Kg
28-day NOEC (growth)	= 17 mg/Kg*
28-day LOEC (growth)	> 17 mg/Kg*
Invertebrate [*Chironomus riparius*]	
28-day LC50 (mortality)	= 166 mg/Kg
28-day NOEC (development time/emergence ratio)	= 84 mg/Kg
28-day LOEC (development time/emergence ratio)	= 210 mg/Kg
28-day NOEC (development rate)	= 84 mg/Kg
28-day LOEC (development rate)	= 39mg/Kg

*These results reflect the highest measured concentration tested and the functional limit of solubility under the conditions of administration (no effects at saturation).

HMTS possesses properties indicating a low hazard profile to the aquatic pelagic environment (at the limit of water solubility), the substance hydrolyzes, has potential to bioaccumulate and is not readily

biodegradable. Adequate screening-level data are available to characterize the environmental hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

In the United States (sponsor country), production volume in 2005 was approximately 1043 tonnes. HMTS is produced in North America, Europe (<227 tonnes) and Japan (< 227 tonnes). Uses are the same in the US, Europe and Japan. The substance is used only as an intermediate for manufacturing other surfactants.

There is no intentional release of HMTS to the environment.

The substance is manufactured in closed systems. Open systems may be used for sampling only. Use of engineering controls at the manufacturing site includes general ventilation, closed sample loops, kettle house ventilation and local vent drops, Bailey Controls process system with process interlocks, metered feed and transfer systems, and grounded equipment. Personal protective equipment includes chemical-resistant gloves, glasses/goggles, chemical and fire resistant clothing, hard hat, steel-toed shoes, and respirator. Potential routes of exposure during routine operations (such as sampling operations) at the manufacturing site include dermal and inhalation.

HMTS is not used in consumer products.