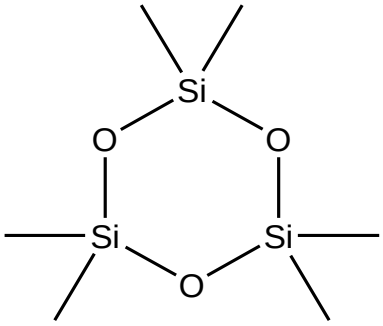
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	541-05-9
Chemical Name	Hexamethylcyclotrisiloxane (D3)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

No data are available on absorption, distribution, metabolism or excretion. The oral LD_{50} of D3 in rats is greater than 15,400 mg/kg bw. Undiluted D3 was not irritating to rabbit's eyes in a study with one rabbit. Repeated dermal application of undiluted D3 in a single rabbit resulted in minimal skin irritation (slight redness). No experimental data are available for skin sensitization.

Two inhalation exposure studies and one repeated-dose oral toxicity study were conducted with D3. The oral study, although not conducted according to an OECD guideline, was designed to investigate whether D3 increases liver weight similar to other oligomeric cyclosiloxanes. Test article-related increases in liver weights were seen in the male rats as low as 100 mg/kg-bw/day and in female rats at dose levels of 400 mg/kg-bw/day and above. In a combined repeated-dose/reproductive/developmental toxicity study conducted according to OECD TG 422, Sprague-Dawley rats were exposed to D3 vapor via inhalation at 100, 500 or 2500 ppm (approximately 0.61, 4.5 or 22.8 mg/L) for up to 29 days for 6 hrs/day, 7 days/week. Decreased body weight gains and food consumption, increased liver weights and incidence of centrilobular hepatocellular hypertrophy (both sexes), increased kidney weights and decreased seminal vesicle weight (with an increased incidence of atrophy) in males were seen at 2500 ppm (22.8 mg/L). Males showed protein droplet nephropathy with markedly increased incidence at 500 and 2500 ppm (4.5 and 22.8 mg/L). Decreased serum glucose was observed at 500 ppm (4.5 mg/L) and above. Serum cholesterol was increased in females at the highest concentration. The LOAEC was considered to be 0.61 mg/L (100 ppm) (the lowest dose tested) based on kidney findings in males and food consumption in both sexes. Sprague-Dawley rats (5/sex/dose at 0.084 and 0.945 mg/L; 10/sex/dose at 9.041 mg/L) were exposed to D3 aerosols via nose-only inhalation for 6 hrs/day, 7 days/week for 4 weeks. Mortality was noted in males and females at 9.041 mg/L. Symptoms prior to death were dyspnea, ataxia, reduced reflexes and piloerection. Hemorrhagic encrustation of the nose was seen at 0.945 mg/L and above. Slight inflammatory changes were seen in the nasal cavity at the highest concentration. Microscopically, aggregation of macrophages and perivascular round cell infiltration was seen in the lungs of high exposure animals. These changes are consistent with respiratory tract irritation. Complete recovery for the local effects was not achieved during the 4-week recovery period. The NOAEC for local effects was considered to be 0.084 mg/L with a LOAEC for systemic effects of 0.61 mg/L. No NOAEC could be identified for systemic effects.

D3 tested negative in bacterial cells (*Salmonella typhimurium* and *Escherichia coli)* and yeast (*Saccharomyces cerevisiae*) and in some mammalian cells *in vitro*. D3 was slightly cytotoxic in the L5178Y Fischer mouse lymphoma cell line at

concentrations of 0.016 and 1 mg/ml in the absence and presence of metabolic activation, respectively. However, D3 gave equivocal or weak positive results in tests for sister chromatid exchange, DNA repair and chromosomal aberrations (L5178Y mouse lymphoma cell line) at a concentration of about 1 mg/ml or higher. D3 tested negative in an *in vivo* cytogenetic assay in CD® rats. In the rat bone marrow cytogenetic assay, male and female rats were injected D3 intraperitoneally up to 1080 mg/kg-bw. Although it cannot be confirmed that D3 reached the bone marrow in the cytogenetic assay, D3 was tested at a high enough level that further attempts to increase the dose to demonstrate that D3 did reach the bone marrow would have resulted in death of the rat. Appropriate positive and negative controls were included and the expected responses were observed. D3 did not increase the frequency of chromosomal aberrations or chromosomal breaks in bone marrow cells.D3 is not expected to be genotoxic *in vitro* or *in vivo*. Carcinogenicity data are not available.

In the combined repeated-dose/reproductive/developmental toxicity screening study described above, D3 vapor caused an adverse effect on fertility following inhalation exposure, with decreased litter size and number of implantation sites at a concentration of 2500 ppm (22.8 mg/L), the highest concentration tested. No external abnormalities were observed in the pups. Mean litter weight was decreased at 22.8 mg/L. The litter weight decreases at the high dose level are probably due to the reduced litter size and not treatment-related manifestation of developmental toxicity. A NOAEC of 500 ppm (4.5 mg/L) and LOAEC of 2500 ppm (22.8 mg/L) for reproductive/developmental toxicity were determined based on the decreased litter size and implantation sites. The maternal NOAEC and LOAEC were 500 ppm (4.5 mg/L) and 2500 ppm (22.8 mg/L) based on the decrease in body weights.

Environment

The EPISuite program developed by the U.S. Environmental Protection Agency and Syracuse Research Corporation has not been validated for chemicals that contain siloxanes in their molecular structure; therefore, there is uncertainty associated with the calculated values and they should be used with caution whenever they are reported below; the estimated values reported here are assigned a reliability code of 4.

D3 is a solid material at room temperature with a melting point of 64°C, a boiling point of 135.1°C at 1013 hPa, and an extrapolated vapor pressure of 11.56 hPa at 25°C. The water solubility of D3 is 1.6 mg/L at 25°C. The measured log K_{ow} is 3.85 and the modeled EPISuite log K_{ow} is 4.47. Rapid hydrolysis of D3 makes measurement of the D3 water solubility and octanol/water partition coefficient problematic and the values may not be accurate.

D3 is hydrolytically unstable over a range of environmentally relevant pH and temperature conditions. At pH 4, 7, and 9 (25 °C), the half-lives were 2, 23 and 0.4 minutes respectively. D3 initially hydrolyzes to hexamethyltrisiloxanediol followed by final hydrolysis to dimethylsilanediol (DMSD). In the atmosphere, indirect photooxidation by reaction with hydroxyl radicals is predicted to occur with a half life of 21 days. D3 is hydrolytically unstable therefore reaction with water vapor is likely the predominant degradation process for D3 in air. D3 is not readily biodegradable; an OECD TG 310 study resulted in 0.06% biodegradation after 28 days.
Level III fugacity modeling, using loading rates of 1000 kg/h each to air, soil and water shows the following percent distribution: air = 60.5%; soil = 34.5%; water = 4.9%; sediment = 0%.

In a 14-day study using rainbow trout, a BCF value of 100 ± 49 for D3 was calculated based upon parent D3 analysis in water and fish. Some morbidity and one case of mortality were observed among the ten fish. The impact of the diminished health of the fish on the reported BCF is unknown. This study utilized closed (except for an overflow) flow-through test vessels. It is expected that fish were exposed to the hydrolysis products in addition to D3.

Dimethylsilanediol is the final hydrolysis product of D3, but is not usually isolated because of its tendency to condense and form higher molecular weight oligomers. Dimethylsilanediol can be kept in a stable state only under special acid- and base-free conditions. Thus, most measured physicochemical properties of DMSD are not available; only measured water solubility of $1x\ 10^6$ mg/L at 25ºC. Furthermore, due to these properties, current estimation models are not capable of calculating physicochemical or environmental fate values with any degree of accuracy. Thus, modeled data are not provided for DMSD because estimated physicochemical properties coupled with uncertainty associated with the modeling of this chemical class, could result in an assessment of an unrealistic scenario.

The adsorption of DMSD onto surfaces and its tendency to polymerize itself are important properties of this chemical. In the environment, DMSD is expected to be found in water and air and to be adsorbed by soil and sediment, but is still subject to hydrolysis. Unbound DMSD in air, water, and soil is expected to degrade photolytically to silica and carbon dioxide. DMSD has been shown to biodegrade to methylsilanetriol, carbon dioxide, and silica.

Due to rapid hydrolysis, aquatic toxicity tests invariably expose test organisms to a mixture of D3 and very soluble hydrolysis products. No mortalities were observed in a 96-h flow-through rainbow trout study with 10 renewals per day of the test solution when fish were exposed at the limit of water solubility (1.6 mg/L). Similarly no effects were seen in a 48-h, flow-though *Daphnia magna* study when daphnids were exposed at the limit of water solubility. In a 72-h algal (*Pseudokirchneriella subcapitata)* study, closed-bottle with zero headspace, the EC_{50} of D3 was >1.6 mg/L (nominal) for biomass and growth rate.

Exposure

D3 is used solely as an industrial intermediate in the Sponsor country. It is sold to industrial customers for the manufacture of other chemicals (siloxanes). The substance is reacted during use and loses its chemical identity. The use pattern is the same in the USA, Europe and Japan. In 2001, the North America production volume of D3 was 207 tonnes (455,000 lbs), European production volume was 3221 tonnes (7,100,000 lbs.) and in Japan the production volume was 236 tonnes (520,000 lbs).
There are no intentional releases to the environment. Throughout the world, D3 is produced in closed reactors and transferred by hard piping to storage tanks to exclude moisture until it is intentionally reacted. D3 may be stored at the manufacturing site in tanks or trailers. This method of manufacture of D_3 minimizes the potential that workers will be exposed to the compound. D_3 may be sampled by chemical operators for analysis and both the chemical operators and analytical technicians have the potential for dermal and inhalation exposure to D3 during the sampling.

Consumer exposure directly to D3 is not expected since it is not used in consumer products. However, D3 is an impurity in siloxane polymers and other cyclosiloxanes used in consumer products.

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 (repeated-dose toxicity and effects on fertility). Based on exposure data presented by the Sponsor country, (closed system, site limited intermediate) and relating to use pattern in three world areas (North America, Europe and Japan) 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 because of its low hazard profile.