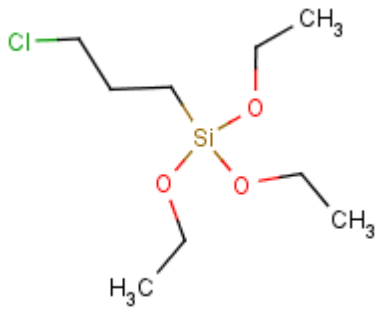
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	5089-70-3
Chemical Name	(3-Chloropropyl)triethoxysilane (**CPTES**)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Justification

The sponsored substance, (3-Chloropropyl)triethoxysilane (**CPTES**) is structurally analogous to (3-chloropropyl)trimethoxysilane (**CPTMO**, CAS No. 2530-87-2). Both **CPTES** and **CPTMO** hydrolyze to form 3 moles of ethanol or methanol, respectively, for each mole of chloropropylsilanetriol. **CPTMO** has previously been assessed in the OECD HPV Programme and the SIDS dossier can be viewed at http://www.chem.unep.ch/irptc/sids/OECDSIDS/2530872.pdf. Similar structures, hydrolysis rates and available toxicological profiles for acute toxicity, irritation and sensitization support the use of **CPTMO** data for the genetic, repeated-dose and reproductive/developmental toxicity endpoints. The hydrolysis half-lives for **CPTES** and **CPTMO** at acidic pH (representative of the mammalian gut) are similarly rapid with half-lives of < 24 minutes (**CPTES**; pH 4) and 14.6 minutes (**CPTMO**; pH 5) at 25°C and therefore significant systemic exposure to unhydrolyzed (**CPTES**/**CPTMO**) parent is unlikely. The analogue approach was not used for ecotoxicity. The hydrolysis product, ethanol (CAS No. 64-17-5), has previously been assessed in the OECD HPV Programme and the SIDS dossier can be viewed at http://www.chem.unep.ch/irptc/sids/OECDSIDS/64175.pdf. **CPTMO** represents a worst case as an analogue for **CPTES**, as methanol is more toxic than ethanol. The contribution of three moles of corresponding alcohol (methanol or ethanol) to the toxicity of the parent silane is expected to be negligible in rodents. However, the possibility of effects in humans that are not expressed in rats cannot be excluded. Methanol exhibits potential hazardous properties for human health (neurological effects, CNS depression, ocular effects, reproductive and developmental effects, and other organ toxicity). Rapid metabolism and excretion is noted depending on the dose. The assessment [of ethanol] is focused on its use as industrial chemical. Ethanol possesses properties that indicate a hazard for human health but these are manifest only at doses associated with consumption of alcoholic beverages.

Physical-Chemical Properties

The EPI Suite 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.

CPTES is a liquid with a measured melting point of less than -20.2 °C, a measured boiling point of 494 °C at

1017.1 hPa and a measured vapour pressure of 0.309 hPa at 25 °C. The measured octanol-water partition coefficient (log K_{ow}) is 3.13 at 21°C, and the measured water solubility is greater than 113 mg/L at room temperature. 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 **CPTES**; however, hydrolysis of this substance is expected to produce 3 moles of ethanol for each mole of chloropropylsilanetriol.

Acute inhalation toxicity data are not available. The dermal LD_{50} of **CPTES** in male and female rats was greater than 2000 mg/kg bw. Erythema was noted at the site of contact. The oral (gavage) LD_{50} of **CPTES** in male and female rats was greater than 5000 mg/kg bw. Clinical signs included urogenital or ventral abdominal staining, soft stool, mucoid feces and piloerection. The dermal LD_{50} in rats of **CPTMO** is greater than 2000 mg/kg bw. Additional dermal LD_{50} values in rabbits include 2.83 mL/kg (male), 3.36 mL/kg (male) and 3.73 mL/kg (female). The oral (gavage) LD_{50} in rats of **CPTMO** is greater than 2000 mg/kg bw. Additional oral LD_{50} values in rats include 6.17 mL/kg (female) and 9.51 mL/kg to 10 g/kg (male).

CPTES is considered non-irritating to slightly to the rabbit skin and rabbit eyes. **CPTES** is not a skin sensitizer. **CPTMO** has been shown to have none to moderate irritation to the skin and eyes. **CPTMO** is not a skin sensitizer when tested under the conditions of OECD TG 406.

No data are available for the repeated-dose toxicity of **CPTES**. Repeated-dose toxicity data via the inhalation route are available for the analogue substance, **CPTMO**. In a 90-day inhalation repeated-dose toxicity study [OECD TG 413], rats were exposed to 0, 4, 41, 814 and 1627 mg/m^3 (reported as 0, 0.5, 5, 100 and 200 ppm) **CPTMO** vapor six hours/day, five days/week. [Note that the animals from the 200 ppm group were evaluated only in the micronucleus assay.] Treatment-related histopathologic changes were observed in the urinary bladder in both sexes at 100 ppm (814 mg/m^3), whereas histopathological changes in the kidneys (increased incidence and severity of alpha 2µ-globulin inclusions; hyaline droplet nephropathy) were observed only in males exposed to 100 ppm (814 mg/m^3). Based on these effects the lowest-observed-adverse-effect-concentration (LOAEC) in the rat was established at 100 ppm (814 mg/m^3). The no-observed-adverse-effect-concentration (NOAEC) for male and female rats was reported to be 5 ppm (41 mg/m^3). In a 28-day inhalation repeated-dose toxicity study [OECD TG 412], rats were exposed whole-body to mean concentrations of **CPTMO** at 0, 81, 407, 798 or 1563 mg/m^3 (reported as 0, 10, 50, 100 or 200 ppm) for six hours/day, five days/week. Histopathological changes included effects on adrenal glands (in males at 798 mg/m^3 and in both sexes at 1563 mg/m^3), kidneys (in males at 407, 798 and 1563 mg/m^3), liver (in males at 1563 mg/m^3) and, at 81 mg/m^3 on the urinary bladder of females (also at 407, 798 and 1563 mg/m^3 in both sexes). A NOAEC was not established in this study. In a combined repeated-dose/reproductive/development toxicity screening test [OECD TG 422], male rats were exposed whole body to **CPTMO** concentrations at 0, 41, 203 or 814 mg/m^3 (target concentrations of 0, 5, 25 or 100 ppm) for six hours/day for 28 days and female rats were exposed to the same concentrations throughout the 14-day pre-pairing, pairing and gestation periods until day 19 post coitum. **CPTMO** exposure up to and including the high concentration of 100 ppm (814 mg/m^3) did not result in any signs of general toxicity of the test substance, including effects in the urinary bladder and kidney. Based on these results, the NOAEC in the rat was established at 100 ppm (814 mg/m^3). Although the effect on the urinary bladder and kidney was not observed in all repeated inhalation exposure studies with **CPTMO**, the NOAEC for this effect across all studies is considered to be 5 ppm (41 mg/m^3). The conclusion has been reached that it is plausible the biological variation is often seen among tests and possibly, between testing laboratories; and, the 90-day study should be considered as carrying the most weight as it is the study with the longest duration and provides the most conservative NOAEL. The estimated overall NOAEC for **CPTES** is 100 ppm (814 mg/m^3).

One bacterial reverse mutation test with **CPTES** was positive, and one was negative. **CPTMO** was not considered to be an inducer of micronuclei *in vivo* in two studies, but was mutagenic *in vitro* (positive in all bacterial mutation assays conducted in the presence and absence of metabolic activation, and in an *in vitro* mouse lymphoma mutagenesis assay). The balance of evidence is that ethanol is not genotoxic. Negative results from a number of bacterial mutation assays appear to be reliable. Of the mammalian cell mutation assays a weak mutagenic effect in mouse lymphoma cells occurred only at very high ethanol concentrations. *In vivo* tests for chromosome aberrations in both rats and Chinese hamsters have given negative results [with ethanol]. There is very little evidence to suggest that ethanol is genotoxic in somatic cells and it may have a very limited capacity to induce genetic changes

in vivo but under very specific circumstances and at very high doses achievable in humans only by deliberate oral ingestion [of ethanol]. **CPTES** may be expected to be mutagenic in *in vitro* systems.

No data are available for the carcinogenicity of **CPTES** or the analogue substance, **CPTMO**. Evidence of the carcinogenicity of ethanol is confined to epidemiological studies assessing the impact of alcoholic beverage consumption. These do not indicate any such hazard exists from potential exposure to ethanol in the work place or from the use of ethanol in consumer products.

No data are available for the reproductive and developmental toxicity of **CPTES**. The analogue substance, **CPTMO** has been assessed for reproduction and developmental toxicity following inhalation exposure in the combined repeated-dose/reproductive/developmental toxicity screening test [OECD TG 422] in rats, described above. Exposure to **CPTMO** up to and including the highest concentration of 100 ppm (814 mg/m^3) did not result in any signs of systemic, reproductive or developmental toxicity. Based on these results the NOAEC for reproductive and developmental toxicity in the rat was 100 ppm (814 mg/m^3). **CPTES** is not expected to be a reproductive or developmental toxicant. Methanol exhibits potential hazardous properties including reproductive and developmental effects. The assessment of [ethanol] is focused on its use as industrial chemical. Ethanol possesses properties that indicate a hazard for human health but these are manifest only at doses associated with consumption of alcoholic beverages.

(3-Chloropropyl) triethoxysilane may possess properties indicating hazard for human health (based on slight skin and eye irritation and *in vitro* genotoxicity). 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 **CPTES** is 35 hours at 25 °C and pH 7 resulting in the formation of ethanol and chloropropylsilanetriol. In the atmosphere, indirect photo-oxidation by reaction of **CPTES** with hydroxyl radicals is predicted to occur with a half-life of 6.2 hours with an overall OH rate constant of 2.06 x 10^{-11} cm^3/molecule-sec. **CPTES** was biodegraded by 46% in 28 days, indicating the test substance is not readily biodegradable; based on the hydrolysis of this substance, some potential for biodegradation of the hydrolysis product ethanol is likely. In aerobic conditions using adapted wastewater from domestic sewage, degradation of ethanol was 74% after 5 days rising to 95% by day 15 and in similar conditions in synthetic seawater, ethanol was degraded by 45% after 5 days rising to 75% by day 20. Neither chloropropylsilanetriol 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 **CPTES** will distribute mainly to soil (83.3%) compartment with minor distribution to water and sediment compartment (9.1 and 6.8%, respectively) and negligible amount in the air compartment. However, **CPTES** is unlikely to be found in the environment, as this substance is hydrolytically unstable. Henry's Law constant of 12.8 Pa-m3/mole (1.26 x 10^{-4} atm-m3/mole) suggests that volatilization from the water phase for **CPTES** is expected to be moderate.

Bioaccumulation is not anticipated since the parent substance CPTES is hydrolytically unstable. The estimated BCF for CPTES is low (1.73). However, as the model is not validated for compounds containing silane in their structure, a final conclusion cannot be drawn with accuracy for CPTES and its hydrolysis product chloropropylsilanetriol. Ethanol is not likely to bioaccumulate (calculated BCF=3.16).

Due to the hydrolysis of **CPTES**, aquatic organisms are likely exposed to a mixture of the parent and its hydrolysis products, ethanol, chloropropylsilanetriol, and condensed silanetriol materials.

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

Fish [*Brachydanio rerio*] 96 h LC_{50}:	80 mg/L (semi-static; measured)
Invertebrate [*Daphnia magna*] 48 h EC50:	140 mg/L (static; nominal)
Algae [*Scenedesmus subspicatus*] 72 h EC_{50}:	> 819 mg/L (biomass and growth rate) (static; nominal)

(3-Chloropropyl) triethoxysilane possesses properties indicating a hazard for the environment (acute aquatic toxicity values for fish between 1 and 100 mg/L). The substance is not readily biodegradable. Adequate screening-level data are available to characterize the environmental hazard for the purposes of

the OECD HPV Chemicals Programme.

Exposure

CPTES was produced and/or imported in the United States at a volume of 4,540 – < 22,680 tonnes (10 - < 50 million pounds) during 2005. The only use of **CPTES** is as a chemical reactant; it is used as an intermediate for synthesis of organofunctional silane coupling agents. It is used in formulations at 100% or up to 50 mole-% (up to 80 weight %); no parent substance is expected to remain after end use. Uses are the same in the US, Europe and Japan.

At the manufacturing site, **CPTES** is manufactured and consumed in closed systems. Ventilation devices and other related equipment such as closed sampling loops and special measuring and control equipment are used. Personal protective equipment (PPE) includes safety glasses, respirator, gloves (impermeable chemical resistant), fire resistant clothing, safety shoes, and hard hat. Worker exposure to **CPTES** due to non-accidental releases at the facility level is not expected; PPE minimizing the potential for exposure via the dermal and inhalation routes. No environmental exposure is expected.

There are no consumer uses of **CPTES**.