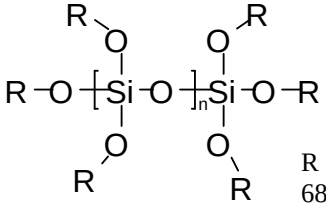
SIDS INITIAL ASSESSMENT PROFILE

Category Name	Ethyl Silicates
CAS No.	78-10-4, 11099-06-2 and 68412-37-3
Chemical Name	Tetraethyl orthosilicate (TEOS), Silicic acid, ethyl ester (PEOS) and Silicic acid (H_4SiO_4), tetraethyl ester, hydrolyzed (PEOS)
Structural Formula	 78-10-4 R = ethyl and n = 0 R = ethyl or hydrogen terminated for 68412-37-3 and 11099-06-2; where n=4 is a representative example for the polymer composition

SUMMARY CONCLUSIONS OF THE SIAR

Category Justification

Tetraethyl orthosilicate (TEOS) and silicic acid, ethyl ester (PEOS) (same as silicic acid (H_4SiO_4), tetraethyl ester, hydrolyzed) hydrolyse on contact with water, and are expected to release either metasilicic acid (CAS No. 10193-36-9) or silicic acid (CAS No. 7699-41-4), respectively, and ethanol (CAS No. 64-17-5). TEOS (CAS No. 78-10-4) may also hydrolyse to form PEOS. Ethanol has previously been assessed in the OECD HPV Programme. Metasilicic acid and silicic acid are expected to react to form oligomers and homopolymers of various chain lengths and degrees of cyclization and branching. These oligomers and homopolymers are represented in this assessment by PEOS and are described by two CAS numbers that are used interchangeably: CAS No. 11099-06-2 and CAS No. 68412-37-3. Based on similarities in chemical structures, physicochemical (hydrolysis) and toxicological properties, and based on the principle that data from the monomer is likely to indicate a higher toxicity than that of the polymerised form, the grouping of TEOS and PEOS, and the use of data for TEOS to supplement data for the human health endpoints for PEOS is appropriate.

Physical-chemical properties

TEOS and PEOS are liquids. TEOS and PEOS have melting points of -82.2°C (measured) and -62.37°C (estimated), boiling points of 166.5°C (measured) and 124.66 °C (estimated) at 1013 hPa and vapor pressures of 2.51 hPa (measured) and 7.25 hPa (estimated) at 20 ºC, respectively. By the chemical reactivity nature of the Si-O-Et bonds, quantitative estimates for water solubility are substituted with qualitative analysis of the hydrolysis products and observations with environmental test data. TEOS and PEOS are expected to be sparingly soluble with TEOS followed by PEOS as being the most sparingly soluble.

Human Health

No data are available on the toxicokinetics, metabolism or distribution of either TEOS or PEOS. However, observation of degenerative/necrotic nephropathy in a repeated dose oral and inhalation studies indicates that TEOS is systemically absorbed. In an OECD TG 403 study, the 4-hr LC_{50} of TEOS was 10.0 mg/L (males) and 16.8 mg/L (females) in Wiskf (SPF71) rats, when exposed nose only to an aerosol atmosphere. Clinical signs of toxicity included mortality, motor behaviour and respiration, palpebral stenosis extending to full lid closure with encrusted blood covered eyelid rims, shivering and tonic cramping. Cyanosis and decreased reflexes occurred in individual animals. Necropsy findings included red and orange lung coloration. The oral LD_{50} of TEOS and PEOS is greater than 2000 mg/kg bw in male and female rats (WISW (SPF Cpb) and Sprague-Dawley), respectively, in studies following OECD TG 401. Clinical signs of toxicity were unremarkable. TEOS was moderately irritating to the skin in rabbits (OECD TG 404). PEOS is not irritating to the skin in rabbits (FIFRA/TSCA test guideline). TEOS was not irritating to the eyes in standard irritation studies (OECD TG 405) in animal tests, but was a moderate/severe eye irritant in an *in vitro* assay and caused eye irritation during a four hour inhalation toxicity study in Wiskf (SPF71) rats. PEOS was a minimal eye irritant in rabbits (FIFRA/TSCA test guideline). Respiratory irritation data were not

available for TEOS or PEOS. However, in an acute inhalation toxicity study with TEOS, signs indicative of respiratory irritation were observed. TEOS and PEOS were not skin sensitising in guinea pigs following either the Buelher test or OECD TG 406.

The repeated-dose toxicity of TEOS has been investigated by the oral route in a seven-day range-finding study and combined repeated-dose/reproductive/developmental toxicity screening study. Daily oral exposures of Sprague-Dawley rats (3/sex/dose) to 0, 200, 600 or 1000 mg/kg bw/day TEOS for seven days resulted in mortality in males (2 out of 3) at the highest dose tested. Clinical findings included significant body weight loss or decreased body weight gain in both sexes. At necropsy, enlargement and abnormal coloration of the kidneys was noted in both sexes in a dose-dependent manner and correlated with high kidney weights. In males, the prostate and seminal vesicles were reduced in size. The dose levels of 600 and 1000 mg/kg-bw/day were considered to exceed the maximum tolerated dose in males. Repeated oral exposure of Sprague-Dawley rats [following OECD TG 422] to 0, 10, 50 or 100 mg/kg bw/day TEOS (10/sex/dose) from the pre-mating period, during mating and until sacrifice (males) or during gestation and lactation until day 4 post-partum (females) (at least four weeks total), induced a transient decrease in body weight gain during lactation at 100 mg/kg bw/day. No change in body weight was noted in males at any dose. In males at 100 and 50 mg/kg-bw/day there was treatment-related degenerative/necrotic nephropathy (9/10 at 100 mg/kg-bw/day; minimal in 4/10 at 50 mg/kg bw/d) and in the females at 100 mg/kg-bw/day there was a slight degenerative/necrotic nephropathy in 3/10 females; there were no findings at 50 or 10 mg/kg-bw/day in females. This was associated with slightly lower plasma levels of sodium, potassium and glucose. Based on the observation of tubular nephropathy and associated clinical chemistry changes, the NOAEL was 10 mg/kg-bw/day and 50 mg/kg-bw/day in male and female rats, respectively. The LOAEL was 50 and 100 mg/kg-bw/day for males and females, respectively. Groups of ten ICR male mice were exposed to TEOS at 50 or 100 ppm for 6 hrs/d, 5d/week for 2 or 4 weeks. Microscopic changes of the nasal mucosa were observed in all exposed mice. Tubulo-interstitial nephritis was observed in mice exposed to 100 ppm (but not 50 ppm) for 2 or 4 weeks. Groups of ten ICR male mice were exposed to TEOS at 200 ppm for 6 hrs/d, 5d/week for 2 or 4 weeks. Decreased body weights of the exposed mice were observed after 2 or 4 weeks exposure; animals in the 2 week (but not 4 week) exposure groups recovered during the two week observation period. Tubulo-interstitial nephritis was observed in mice exposed for 2 or 4 weeks, however clinical chemistry did not confirm renal dysfunction. Infiltration of polymorphonuclear neutrophils into the nasal mucosa was also observed immediately following 2 or 4 week exposure. The NOAEC for systemic renal effects was 50 ppm. The LOAEC for local respiratory effects was 50 ppm.

In bacterial reverse mutation assays with multiple strains of *Salmonella typhimurium*, TEOS and PEOS were negative both with and without metabolic activation (Directive 84/449/EEC, B.14 and Directive 92/69/EEC, B. 14). An *in vitro* chromosomal aberration test using TEOS was negative both with and without metabolic activation (OECD TG 473). Based on these results, TEOS and PEOS are considered to be non-genotoxic *in vitro*.

No data were available regarding the carcinogenicity of TEOS or PEOS.

In the aforementioned screening study [OECD TG 422] with TEOS, no adverse effects on reproduction or development of Sprague-Dawley rats were observed up to the highest dose tested. The NOAEL for reproductive/developmental toxicity for TEOS was 100 mg/kg-bw/day in rats. The NOAEL for maternal toxicity was 50 mg/kg-bw/day. Based on these results, TEOS is considered not likely to be a reproductive or developmental toxicant.

Chemicals in this category possess properties indicating a hazard for human health [skin, eye and respiratory tract irritation (TEOS) and eye irritation (PEOS), and repeated-dose toxicity (kidney and respiratory tract). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD HPV Programme.

Environment

The EPISuite program 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; therefore there is uncertainty associated with the calculated values and they should be used with caution whenever they are reported below.

All chemicals are subject to hydrolysis. The hydrolysis half-life for TEOS is 4.4 hours at pH 7. For PEOS, the hydrolysis is dependent on the solubilities of the individual components. Other hydrolysis products are expected to be metasilicic acid or silicic acid and ethanol. In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 0.4 days for TEOS and 1.1 days for PEOS. A DOC-die away test with TEOS resulted in 98% biodegradation in 28 days. TEOS is readily biodegradable under aerobic conditions. A modified sturm test with PEOS resulted in 47% biodegradation in 28 days. PEOS is not readily biodegradable under aerobic conditions.

A level III fugacity model calculation (Epiwin v 3.20) with equal and continuous distributions to air, water and soil

compartments suggests that TEOS will distribute mainly to soil (74.1 51%,), with lesser amounts to air (17.6 %) and water (8.3 %) and negligible amounts to sediment (0.0 %); PEOS will distribute more evenly between water and soil (46.4 and 51%, respectively), with lesser amounts distributed to air (2.5%) and sediment (<1%). The bioaccumulation potential is considered to be low based on the chemical reactivity for these chemicals. Because TEOS and PEOS react to form different substances through hydrolysis, the BCF for the ethyl esters cannot be predicted, but is expected to below if hydrolysis products predominate.

An LC_0 of 245 mg/L (measured) was determined in a 96-hr study with TEOS and *Brachydanio rerio.* An LC_0 of 119 mg/L (measured) was determined in a 96-hr study with PEOS and *Brachydanio rerio.* The 48-hr EC_{50} of TEOS under flow-through conditions was > 75 mg/L (expressed as measured concentrations) for the water flea (*Daphnia magna*). The 48- hr EC_{50} of PEOS was > 193 mg/L (measured) for the water flea (*Daphnia magna*). There were no effects observed in these studies. The 72-hr ErC_{50} and EbC_{50} values for TEOS and *Pseudokirchneriella subcapitata* were >100 mg/L (expressed as nominal concentrations due to rapid hydrolysis of the substance). The 72-hr NOEC for growth rate or biomass was determined to be 100 mg/L. *Scenedesmus subspicatus* was exposed to TEOS and PEOS for 72 hrs; on the basis of cell growth, the 72-hr E_bC_{50} was 889.2 and >207 mg/L, respectively; on the basis of growth rate, the 0-72 hr E_bC_{50} was >1039.3 and >207 mg/L, respectively. The NOEC was 115.5 and 115 mg/L for TEOS and PEOS, respectively.

The chemicals in this category have a low hazard profile for the environment. Adequate screening-level data are available to characterize the hazard for the environment for the purposes of the OECD HPV Programme.

Exposure

The 2005 production volumes in tonnes by region for TEOS and PEOS are:

Region	TEOS	PEOS
North America	ca. 380.4	< 0.45 (produced) < 453.6 (imported)
Europe	ca. 2948.4	ca. 7810.9
Japan	ca. 399.2	ca. 562.5

Traditional application areas for ethyl silicates are:

- Binders for zinc-rich paints in heavy-duty corrosion protection
- Binders for precision castings and refractory materials
- Formation of SiO2 layers on silicon chips
- Modification of organic polymers in the chemical industry
- Binders for stone consolidation
- Marine and protective coatings
- Clear coupling agent for textile coatings.

Ethyl silicates are increasingly used in sol-gel processes for the manufacture of modern materials: via hydrolysis and condensation processes, liquids (called "sols") are converted into solids (called "gels"). By using alkoxysilanes or organofunctional silanes it is possible to produce submicron or spherical silica powders, thin-film coatings, fibers, porous (aerogels) or dense materials. These materials are used in many sectors, e.g. for chromatography, for the surface coating of glass and pigments, in the ceramics industry, for the production of catalysts and for polymer modification. In paints, industrial customers generally make a hydrolysate of PEOS before adding it to the formulation; at this point in the process the parent substance has already been changed. Use levels of the PEOS hydrolysate in paints range from 10-20%. TEOS is also used as a raw material in semiconductor manufacture. TEOS and PEOS are shipped by road and marine routes in drums and cans.

There are no intentional releases to the environment during manufacturing and any exposure to the parent compounds would be limited due to hydrolysis of both chemicals. TEOS is manufactured in both open and closed systems where engineering controls are routinely used. TEOS and PEOS are stored on-site in drums and cans. The Occupational Safety and Health Administration (OSHA) in the Sponsor country has set a permissible exposure limit (PEL), for an 8-hour time weighted average period, of 100 ppm (850 mg/m^3). In addition, OSHA has issued guidance on minimizing exposure to ethyl silicates that discusses appropriate engineering controls. Occupational exposure via the inhalation and dermal routes is possible but would be controlled by use of these engineering controls and adherence to the PEL.

TEOS is used in consumer sealants and in some mold-making products with indirect food contact at levels < 6%.

PEOS is used in consumer sealants and adhesives at levels < 0.1%. The consumer sealants and adhesives contain unreacted PEOS by design, as the products are developed so that upon use (as soon as the product is exposed to air/moisture), PEOS will crosslink as the sealant cures, releasing ethanol. Thus, the sponsored substances are reacted during use and are not expected to be present in the final sealant or adhesive product.