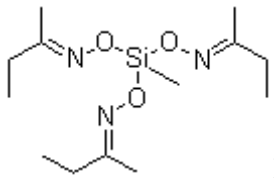
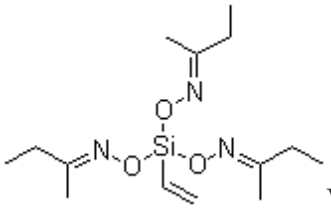
SIDS INITIAL ASSESSMENT PROFILE

Category Name	Oximino Silanes Category
Chemical Names and CAS Nos.	2-Butanone, O,O',O''-(methylsilylidyne)trioxime (MOS) (CAS No. 22984-54-9) 2-Butanone, O,O',O''-(ethenylsilylidyne)trioxime (VOS) (CAS No. 2224-33-1)
Structural Formulas	 MOS  VOS

SUMMARY CONCLUSIONS OF THE SIAR

Category rationale

2-Butanone, O,O',O''-(methylsilylidyne)trioxime (MOS) and 2-Butanone, O,O',O''-(ethenylsilylidyne)trioxime (VOS) are grouped together as a category because the chemical structure of these two substances is essentially identical. They each contain three methylethylketoxime groups with the primary difference being methyl or vinyl in the fourth position on the silicon atom. Both substances hydrolyze rapidly (within minutes) to form three moles of methylethylketoxime (CAS No. 96-29-7; MEKO), and one mole reactive methyl or vinyl substituted silanetriol. The methyl or vinyl silanetriol (at concentrations greater than 500 mg/L) can condense to form substituted silanols or disilanols. In aqueous solutions, exposures to the Oximino silanes are likely to be transient and observed toxicity is likely due primarily to the hydrolysis products MEKO, methyl or vinyl substituted silanetriols, and condensed silanetriol materials (high molecular weight polymers). Physical-chemical properties (vapor pressure, melting point and boiling point) are similar for the two substances, thus supporting the category justification. Data from the hydrolysis product MEKO have been presented at SIAM 17 (sponsored by Japan and US). The mammalian toxicity profile of MEKO is similar to that seen for MOS and VOS; data for other hydrolysis products are not available. All human health SIDS endpoints have been addressed by data for MOS. These data are read across to address data gaps for VOS for repeated-dose and reproductive toxicity endpoints.

Reduced Testing Rationale

The oximino silanes (MOS and VOS) undergo rapid hydrolysis in the presence of water; the half life of MOS at pH 7 and 2°C is less than 1 minute. This hydrolysis of MOS is expected to produce 3 moles of methylethylketoxime (CAS No. 96-29-7; MEKO) and 1 mole of methylsilanetriol. The hydrolysis of VOS could not be determined, but is expected to be more rapid than MOS, and to produce 3 moles of MEKO and 1 mole of vinylsilanetriol. Depending on the pH and concentration of the substance, the reactive methyl or vinyl substituted silanetriols may condense to form oligomers and polymers. Because the materials are hydrolytically unstable, water solubility, partition coefficient and biodegradation were not measured. Nonetheless, these endpoints provide

valuable information on the behaviour of the substance. Therefore, modelled values are provided for water solubility and partition coefficient. The biodegradation data for MEKO are provided in SIAM 17 documents; silanetriols and condensed silanetriol materials are not expected to be readily biodegradable.

The EPISuite program (v4.00) developed by the U.S. Environmental Protection Agency and Syracuse Research Corporation has not been validated for silanes that contain silicone 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 below.

Physical-Chemical Properties

MOS is a clear, colourless liquid with a measured melting point of <-73 °C, a measured boiling point of 250 °C at 997 hPa and a measured vapour pressure of 0.085 Pa at 25 °C. The calculated octanol-water partition coefficient (log K_{ow}) is 9.83, and the calculated water solubility is 0.00006 mg/ at 25 °C. VOS is a clear, colorless liquid with a measured melting point of <-20 °C, decomposes at high temperatures (calculated boiling point of 359 °C) and a measured vapour pressure of 0.025 Pa at 25 °C. The calculated octanol-water partition coefficient (log K_{ow}) is 10.19, and the calculated water solubility is 0. 00003 mg/L at 25 °C.

Human Health

Toxicokinetics data for MOS and VOS are not available. However, data indicate that MEKO, the hydrolysis product, is rapidly absorbed from the gastrointestinal tract and skin, and then it is rapidly metabolized and excreted.

The oral LD_{50} values for MOS were 2260 mg/kg bw for male Fischer 344 rats and 2650 mg/kg bw for female Fischer 344 rats. The substance caused reversible narcotic type effects on the nervous system, significant oxidative destruction of red blood cells, and splenic changes indicative of erythrolysis (at all dose levels [295, 980, 1960, and 2950 mg/kg bw]); generalized hepatocyte cytoplasmic vacuolation and lymphoid depletion/necrosis was observed in some animals that died. The oral LD_{50} values for VOS were >2000 mg/kg bw for male Fischer 344 rats and 1920 mg/kg bw for male Crl: CD (SD) IGS BR VAF/Plus rats and 2610 mg/kg bw for female Crl: CD (SD) IGS BR VAF/Plus rats. Clinical signs included absence of/reduced activity, increased lacrimation, chromodacryorrhea, partially closed eye lids bilaterally, irregular respiration rate, red soiling of the muzzle, bilateral forepaws and/or clear/yellow anal/urogenital staining. No information regarding acute inhalation and acute dermal toxicity is available for MOS or VOS.

MOS was slightly irritating to rabbit skin. Erythema and edema were observed. VOS was moderately irritating to rabbit skin. Reversible, superficial necrosis was observed in 2/6 animals. MOS was slightly irritating to moderately irritating to rabbit eyes producing corneal opacity, circumcorneal injection of the iris, conjunctival redness, chemosis, and discharge, which completely subsided by day 7. VOS was severely irritating to rabbit eyes. Corneal opacity, iritis, conjunctival redness, chemosis, and discharge effects persisted for up to 21 days in 2 animals with eyes "unrinsed"; for those rabbits' eyes that had been "rinsed", irritation resolved by day 14. No information is available on the respiratory tract irritation.

No experimental data are available for skin sensitization in animals.

The repeated dose toxicity of the MOS has been investigated in one study. In a combined repeated–dose/reproductive/developmental toxicity screening test (OECD TG 422) 10 Wistar rats/sex/dose were administered MOS via gavage at 0, 10, 50 and 250 mg/kg bw/day for at least 28 days. No mortality, treatment-related clinical signs or effects on food consumption, body weights and body weight gain were seen. In the Functional Observational Battery, a decreased number of rearings and decreased mean grip strength of hindpaws was observed in males at 250 mg/kg bw/day. Decreased mean body temperature was observed in both sexes at 250 mg/kg bw/day and in males at 50 mg/kg bw/day. Hematology measurements were not possible for animals at 250 mg/kg bw/day; at 50 mg/kg bw/day, changes in hematology were noted. Changes in clinical chemistry were observed in animals dosed at 250 mg/kg bw/day. Discolored kidneys (250 mg/kg bw) and enlarged spleen (50 and 250 mg/kg bw/day) were observed at necropsy. Heart (250 mg/kg bw/day), liver (50 (males only) and 250 mg/kg bw/day) and spleen (50 and 250 mg/kg bw) weights were increased. At 50 and/or 250 mg/kg bw/day, microscopic

changes in the liver, spleen, kidneys and bone marrow were observed. Based on hematology, blood chemistry and histopathological findings, the NOAEL for repeated dose oral toxicity was 10 mg/kg bw/day. A similar toxicity profile was observed for MEKO. Similar repeated dose toxicity is expected for VOS.

Gene mutation data are not available for MOS. MOS did not induce chromosomal aberration in Chinese hamster ovary cells *in vitro* with and without metabolic activation. In a bacterial reverse mutation assay with multiple strains of *Salmonella typhimurium* /*E.coli*, VOS was negative both with and without metabolic activation. In an *in vitro* chromosomal aberration test using OECD 473 and CHO cells, VOS induced chromosomal aberrations. In an *in vivo* micronucleus assay, VOS was negative when administered as a single intraperitoneal injection up to the maximum tolerated dose. Based on these results, VOS is considered to be non genotoxic *in vivo*. MOS and VOS are not expected to be genotoxic *in vivo*.

No data are available for the carcinogenicity of MOS and VOS.

The reproductive and developmental toxicity of the MOS has been investigated in a combined repeated-dose/reproductive/developmental toxicity screening test in rats [OECD 422]. In this study, MOS was administered via gavage to 10 animals/sex/dose at 0, 10, 50 and 250 mg/kg bw/day. Dosing occurred in all groups for at least 28 days. Groups of ten female Wistar rats were dosed for 14 days prior to pairing, through the pairing and gestation periods until the F1 generation reached day 4 post partum. No death was observed in either sex. No adverse effects on reproductive parameters were observed up to the highest dose tested. No test substance-related effects were observed in any of the developmental parameters evaluated. Based on hematology, blood chemistry and histopathological findings, the NOAEL for repeated dose oral toxicity was considered to be 10 mg/kg bw/day. Based on no adverse effects on reproductive parameters NOAEL for reproductive/developmental toxicity was 250 mg/kg bw/day (the highest dose tested). A similar toxicity profile was observed for MEKO. MOS did not cause any reproductive or developmental toxicity; VOS is expected to have a similar profile.

The oximino silanes may present hazard for human health (repeated- dose toxicity; eye and skin irritation). 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 MOS is <1 minute at pH 7 and 2^{o}C. Determination of the hydrolysis rate of VOS was not possible. VOS is expected to rapidly hydrolyze (less than 1 minute at pH 7 and 2 ºC); substitution of vinyl for methyl may actually increase the rate of hydrolysis of VOS relative to MOS. Hydrolysis of the oximino silanes is expected to produce 3 moles of MEKO and 1 mole of reactive methyl or vinyl substituted silanetriols. Silanetriols (at concentrations greater than 500 mg/L) can condense to form highly cross-linked, high molecular weight polymers, further reducing the potential for exposure. If the oximino silanes are slowly released such that the concentration of the resulting silanetriol is not high enough to result in polymerization, the silanetriol will exist largely as a monomer. In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 27.9 and 4.2 hours, for MOS and VOS, respectively. Based on the rapid hydrolysis of these materials, any potential for biodegradation is likely to be of the hydrolysis products. The hydrolysis products silanetriol and condensed silanetriol materials are not expected to be readily biodegradable. Biodegradation endpoint for MEKO has been addressed at SIAM 17 where it was found to be inherently biodegradable in one test, and not inherently biodegradable in the second test. Level III fugacity model with equal and continuous distributions to air, water and soil compartments suggests that MOS and VOS will distribute mainly to the soil (80 %) and water (18%) compartments with minor distribution to the air compartment (ca. 1%) and negligible amount in the sediment compartment. However, the oximino silanes are unlikely to be found in the environment, as these materials are hydrolytically unstable. A Henry's law constant for MOS and VOS of 500 Pa m^3/mole at 25 °C suggests that volatilization of these chemicals from the water phase is expected to be high.

MOS and VOS react to form MEKO and reactive methyl or vinyl substituted silanetriol through hydrolysis. The BCF for the oximino silanes and the methyl or vinyl substituted silanetriol cannot be accurately predicted, but are expected to be low. The measured BCFs for MEKO in fish generally range from 0.5 to less than 2.5, indicating low or no bioaccumulation potential.

Due to the rapid hydrolysis of the oximino silanes, aquatic organisms are likely exposed to the parent and its hydrolysis products, MEKO, methyl and vinyl substituted silanetriols, and condensed silanetriol materials.

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

Fish [rainbow trout; *Oncorhynchus mykiss*];	96 h LC50 >120 mg/L (nominal)
Invertebrate [*Daphnia magna*]	48 h LC50 >120 mg/L (nominal)
Algae [*Pseudokirchneriella subcapitata*]	72 h ErC50 = 94 mg/L (growth rate, nominal)
	72 h E_bC50 = 50 mg/L (biomass) (nominal)

The oximino silanes may present a hazard for the environment (acute aquatic toxicity values between 1 and 100 mg/L for MOS and toxicity to aquatic plants). Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD HPV Chemicals Programme.

Exposure

MOS is commercially produced with an annual production volume of approximately 1361 – 2268 tonnes in the Sponsor Country (2005). VOS is commercially produced with an annual production volume of ca. 227 – 907 tonnes in the Sponsor Country (2005). MOS and VOS are not produced in Europe; VOS is commercially produced with an annual production volume of <227 tonnes in Japan (2005). The oximino silanes are used as cross-linking agents in room temperature vulcanizing silicone adhesive sealants. The oximino silanes are used at <10% in formulations.

No monitoring data in occupational settings are available from the production and processing sites in the Sponsor Country. The oximino silanes are produced and used in closed systems [hard-piped].Necessary engineering controls during production of silicone adhesive/sealants include proper ventilation, containment, safety equipment and actual hardware designed to minimize exposure, through splashing, or exposure to the air. Transfer of this material is in closed pipes or containers rather than in open systems to minimize loss (hydrolysis) although some customers may transfer the material using open systems.

A worker may be exposed during compounding (mixing) of sealant or adhesive to low levels of these silanes. There is no known production process that involves aerosolized material or sprayed material. The vapour pressure of MOS and VOS is low enough that vapour inhalation is not considered a potential route of exposure under normal operating conditions.

Exposure to both MOS and VOS due to non-accidental releases includes cleaning of the mixing vessel and potential routes of exposure are dermal and inhalation. Manufacturers MSDSs recommend general personal protective equipment (PPE) which includes impermeable chemical resistant gloves, goggles, and safety shoes, during the cleaning process. If liquid contact is possible a full face shield is recommended. Recommended engineering controls include flow meters; vacuum; temperature controls; mechanical ventilation devices or a respirator and related equipment. The use of MOS and VOS in the consumer market is limited to use as a cross linker in sealants and adhesives. The substances are used at generally <10% in these formulations and they react with silanol polymers in the formulation during compounding (mixing) and then further react during exposure to atmospheric moisture. After curing, the parent silane is consumed into the polymer matrix and no longer exists, greatly reducing the potential for consumer exposure.

In an experiment conducted to evaluate the potential for exposure to the hydrolysis product, MEKO produced during the curing reaction of adhesive/sealant compositions the maximum concentrations of MEKO in air at the peak of caulk off gassing were the highest (of about 0.011 mg/L or 3 ppm) in the experiment with the lower air exchange rate and hard, non-porous wall surfaces. The lowest concentrations 0.0018 to 0.0027 mg/L (0.5 – 0.75 ppm) were observed with the higher air exchange rate or porous wall surfaces. The manufacturers of MEKO currently recommend an Industrial Hygiene Guideline for inhalation exposure to MEKO. These limits are: 3 ppm (8 hours Time Weighted Average or 8 hours per day, 40 hours a week during normal lifetime exposure) and 10 ppm (15 minutes Short Term Exposure Limit).

MOS and VOS are used in consumer products at <10%. Therefore, the consumer may be exposed while applying the products. However, the substances are reacted during use, losing their chemical identity. Therefore, the final

products generally are expected to contain essentially no MOS or VOS.

No monitoring data for effluents or surface waters are available. However, there are no intentional releases to the environment. Further, the reactive nature of these materials destroys the parent material in water, thus limiting environmental exposure.