FOREWORD INTRODUCTION

TRIMETHOXY[3-(OXIRYNYLMETHOXY)PROPYL]-SILANE

CAS N°: 2530-83-8

SIDS Initial Assessment Report

For

SIAM 19

Berlin, Germany, 19-22 October 2004

1.	**Chemical Name:**	Silane, trimethoxy[3-(oxiranylmethoxy)propyl]-
2.	**CAS Number:**	2530-83-8
3.	**Sponsor Country:**	United States
		Oscar Hernandez Director, Risk Assessment Division (7403M) U.S. Environmental Protection Agency 1200 Pennsylvania Ave, N.W. Washington, DC 20460 Phone: 202-564-7641
4.	**Shared Partnership with:**	Silicones Environmental Health and Safety Council (SEHSC): Clariant LSM (Florida), Inc. Degussa Corporation Dow Corning Corporation GE Silicones Rhodia Inc. Shin-Etsu Silicones of America Wacker Silicones, A Division of Wacker Chemical Corporation
5.	**Roles/Responsibilities of the Partners:**	
•	Name of industry sponsor /consortium	Silicones Environmental Health and Safety Council Contact point: Reo Menning SEHSC 703-904-4322 rmenning@sehsc.com
•	Process used	The SEHSC produced the documents; EPA reviewed the documents and provided additional information where there were data gaps.
6.	**Sponsorship History**	
•	How was the chemical or category brought into the OECD HPV Chemicals Programme ?	Documents were prepared and reviewed by industry prior to submission to sponsor country. Sponsor country conducted reviews of submitted data and offered comments to industry. Industry prepared and resubmitted documents for consideration at SIAM 19.

no testing	(X)
testing	( )

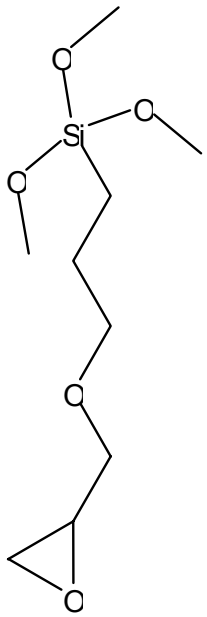
7. Review Process Prior to the SIAM: The U.S. EPA reviewed this case.

8. Quality check process: Literature searches were conducted by the sponsor country to determine if all relevant data have been included in this submission.

9. Date of Submission: 26 July 2004

10. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2530-83-8
Chemical Name	Trimethoxy [3-(oxiranylmethoxy)propyl] silane (TMSPGE)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analogue Rationale

The chemical, trimethoxy[3-(oxiranylmethoxy)propyl]-silane (TMSPGE) rapidly hydrolyzes at environmental pH levels and in acidic conditions. An abiotic hydrolysis study showed that hydrolysis products of the test substance underwent continuous, condensation reactions to produce higher molecular weight cyclic and linear siloxanes; about 73 percent of the area of the chromatogram showed molecular weight peaks greater than 1000 after one hour. Substances with molecular weights of greater than 1000 are generally considered to have a very limited biological availability.

If TMSPGE is slowly released into a water environment such that the concentration of the resulting epoxy-functional silanetriol hydrolysis product is not high enough to result in polymerization, the product will exist largely as a silanetriol monomer. The monomer is known to be water soluble because of the hydroxy groups on the silicon. However, as noted below, water solubility and the partition coefficient of the parent compound cannot be easily measured and only estimates are provided.

Human Health

TMSPGE is subject to rapid hydrolysis, and the observed toxicity is expected to be due primarily to methanol and silanetriols. TMSPGE has been tested for acute toxicity by the oral, dermal, and inhalation routes of exposure. Reported acute oral LD_{50}s in rats range from 7010 to 16900 mg/kg bw and > 5 ml/kg bw to 22.6 ml/kg bw. The dermal LD_{50}s are 6800 mg/kg bw and 4.0 ml/kg bw. The 4-hour inhalation LC_{50} was greater than 2.7 mg/L in one study and greater than 5.3 mg/L in another study. TMSPGE is mildly irritating to the skin and eyes and is not a known skin sensitizer in humans or in animals.

Following inhalation exposures of rats to target aerosol concentrations of 0, 75, 225 and 750 mg/m3 (actual concentrations were 0, 77, 226, 707 mg/m^3 (males) and 0, 73, 226, 734 mg/m^3 (females)), TMSGPE in 9 repeated exposures administered over two weeks, 6 animals in the high dose group died or were sacrificed from three to five days after initiation of the study. These animals had signs of inanition but no acute tissue toxicity. At both the mid and high doses, rats exhibited some clinical signs including a dose-related decrease in body weight. Under the conditions of this study, the No Observed Adverse Effect Concentration is 225 mg/m3. Repeated exposure of rats by gavage to TMSPGE doses of 40, 400 and 1000 mg/kg bw/day for 5 days/week for 4 weeks resulted in no test substance-related organ weights effects or gross or microscopic pathological changes. Under the conditions of this study, the NOAEL for the test substance was found to be 1000 mg/kg bw/day.

TMSPGE did not induce chromosomal damage in mouse bone marrow cells by gavage at doses of 500, 1670 and 5000 mg/kg bw/day, or when administered by intraperitoneal (i.p.) injection at 1600 mg/kg bw/day. However, chromosomal damage was induced in mouse bone marrow cells when administered by i.p. in water at doses of 500, 1000 and 2000 mg/kg bw/day. TMSPGE induced gene mutations in bacteria. TMSPGE induced gene mutations in mouse lymphoma L1578Y TK cells but did not induce forward mutations in CHO cells. TMSPGE induced SCE in vitro. There are no in vivo gene mutation data. TMSPGE was not considered tumorigenic when applied to the clipped skin of mice (25 µl dose of 25% TMSPGE in acetone) three times per week for approximately 78 weeks. Note that there was only one dose level, and this dose was relatively low.

In a one-generation reproduction toxicity study in rats, no reproductive effects were observed at any of the doses tested (250, 500, or 1000 mg/kg bw/day). At 1000 mg/kg bw/day, treatment with TMSPGE resulted in the following signs in parental animals: discomfort after dosing (noted for females from early/mid gestation onwards), decreased body weight gain (males), increased mean relative liver and kidney weights (noted for males and females), and histopathological effects on livers and kidneys (males). Based on these data, a NOAEL for parental animals was established at 500 mg/kg bw/day. A NOAEL for reproductive effects was established at 1000 mg/kg bw/day. Three developmental studies have been conducted using TMSPGE. In a rabbit study, the maternal NOAEL was 200 mg/kg bw/day and the developmental NOAEL was 400 mg/kg bw/day (the highest dose tested). In a rat study, the NOAELs for both maternal and developmental toxicity were also at the highest dose tested (1000 mg/kg bw/day). In another rat study, developmental effects were observed at the maternally-toxic dose of 3000 mg/kg bw/day (again, the highest dose tested).

Environment

The melting point of TMSPGE is < -70°C, the boiling point is 290°C at 1013 hPa, and the vapor pressure is 0.003 hPa at 20°C. Because TMSPGE is hydrolytically unstable, the water solubility was not measured. Estimated values for water solubility (1x 10^{+6} mg/L) and partition coefficient (log K_{ow} = -0.9), may also not be accurate because of the chemical's rapid hydrolysis. From photodegradation modeling, the half-life in the atmosphere due to reaction with photochemically-induced OH radicals is estimated to be 5.8 hours. However, the overall half-life may be even shorter, as concurrent hydrolysis will also occur.

The measured hydrolysis half-life for TMSPGE at 25ºC ranges from 3 minutes to 6.5 hours over the pH range of 5 to 9. At pH 7 and 25 °C, the half-life of the parent compound is 6.5 hours and the conversion of TMSPGE to methanol and 3-glycidoxypropylsilanetriol is expected to reach 99.9% in ≤ 2.8 days. The epoxy group slowly reacts (over a period of months) to form diols in water. The Si-C bond will not undergo hydrolysis. The transient silanol groups will condense with other silanols to yield an epoxy-functional silicone resin (oligomer resin). The measured (and calculated) hydrolysis half-lives demonstrate that TMSPGE is hydrolytically unstable over a range of environmentally relevant pH and temperature conditions.

The EQC Level III model was used to evaluate the fate, transport and distribution of TMSPGE between environmental matrices. Level III Fugacity modeling, using loading rates for air, soil, and water of 1000 kg/h for each media, shows the following percent distribution for TMSPGE: Air = 0.6%; Soil = 92.5%; Water = 6.9 %; Sediment = 0.00 %. However, TMSPGE is unlikely to be found in the environment, as this material is hydrolytically unstable. The environmental fate, transport, and distribution of 3-glycidoxypropylsilanetriol were evaluated to provide a more realistic assessment of TMSPGE. Level III Fugacity modeling, using loading rates for air, soil, and water of 1000 kg/h for each media, shows the following percent distribution for 3-glycidoxypropylsilanetriol: Air = 0.0%; Soil = 60.9%; Water = 39 %; Sediment = 0.1 %. Biodegradation studies suggest that about 37 % of TMSPGE is degraded after 28 days. TMSPGE is not readily biodegradable. Bioaccumulation of the parent compound is not anticipated since the material is hydrolytically unstable. In addition, the silanetriol has a low Log K_{ow} (-2.61, estimated) and is also not expected to bioaccumulate.

A static test using juvenile rainbow trout (*Oncorhynchus mykiss*) resulted in a 96-hour LC50 of 237 mg/L and in a semi-static test, the LC50 was 55 mg/L in carp (*Cyprinus carpio)*. In aquatic invertebrates, the reported 48-hr EC50s for (*Daphnia magna*) were 473 and 710 mg/L. In algae, (*Selenastrum capricornutum*) the 72-hr EC_b50 was 250 mg/L and the 72-hr EC_r50 was 350 mg/L. The 96-hr EC50 for biomass is 260 mg/L. The 72-hour $EC_b50$for *Scenedesmus subspicatus* exposed to TMSPGE was 255 mg/L; the 72-hr EC_r50 was >420 mg/L. In a 21-day daphnia reproduction test, the NOEC was 100 mg/L. Since TMSPGE is subject to hydrolysis, which may occur during preparation of the dosing solutions and/or during testing, the observed toxicity is likely due to the hydrolysis products methanol and silanetriols.

Exposure

Greater than 90% of all uses of TMSPGE are as an intermediate for industrial applications. TMSPGE is used as an additive for adhesion promotion and as a cross-linking agent in adhesives, sealants, encapsulants and coatings and as coupling agents in composites. TMSPGE is generally used at <2% in all of these applications (a level of 1 to 2 % is commonly recommended as a "starting-point" in many applications) and is usually not used at concentrations higher than 6 percent. One sealant product with a higher percentage (10-30 percent) TMSPGE was identified outside the Sponsor Country. In 2002, the annual production volume of TMSPGE in the U.S. was 1702 tonnes.

The physical and chemical properties of TMSPGE minimize the potential for exposure to this substance during its manufacture. In addition, necessary engineering controls during production include proper ventilation, containment, safety equipment and actual hardware designed to minimize exposure through splashing or to the air. More than 50 air samples, collected during production and handling at ambient temperature in production plants, have shown no detectable TMSPGE. The detection limit ranged from 0.05 to 1 ppm, depending upon the volume of air sampled.

Transfer of this material is in closed pipes rather than in open systems to minimize loss of this material (hydrolysis) although some customers do transfer the material in open systems. TMSPGE is transported from the production site as the parent silane to processors/formulators. Although there is no consumer use of the pure substance, it will be found as a minor component (<0.1% as free un-reacted TMSPGE) in caulks. The reactive nature of this material results in the destruction of the parent material in moisture-containing environments, thus limiting public or environmental exposure to the free un-reacted material. TMSPGE will hydrolyze in a spill situation; the rapid hydrolysis means that the parent silane is unlikely to be found in the environment. Once reacted in an application, there is a very low potential for release outside of spills because the glycidoxy- and/or trimethoxysilyl-groups react with the application and no longer exist as free un-reacted TMSPGE.
As noted earlier, TMSPGE hydrolyzes with a half-life of approximately 3 minutes to about 6.5 hours, depending on the aqueous solution temperature, pH and concentration of buffer. Polymerization reduces the potential for exposure to the parent compound and the silanetriol monomer.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

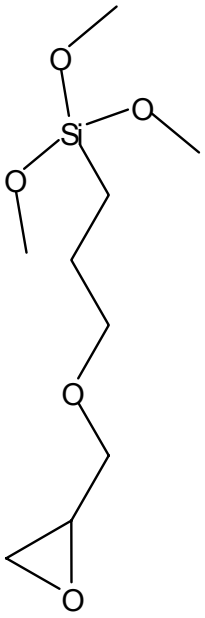
The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for the environment (aquatic toxicity) and a hazard for human health (several positive genetic mutation results *in vitro* and mixed results in several chromosomal aberration studies conducted *in vivo*). Based on exposure data presented by the Sponsor Country (relating to production in one country which accounts for an unknown fraction of the global production and relating to the use pattern in the Sponsor Country as well as Europe and Japan), under normal manufacturing, formulation, industrial and consumer use, this chemical is a low priority for further work. Countries may wish to investigate any exposure scenarios that were not presented by the Sponsor Country.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 2530-83-8
IUPAC Name: Silane, trimethoxy [3-(oxiranylmethoxy)propyl]- (TMSPGE)
Molecular Formula: C9H20O5Si
Structural Formula:



Molecular Weight: 236
Synonyms: Trimethoxy[3-(oxiranylmethoxy)propyl] silane
gamma-Glycidoxypropyltrimethoxysilane
1-(Glycidyloxy)-3-(trimethoxysilyl)propane
A-187
DZ 6040
Glycidoxypropyltrimethoxysilane
Glycidyl 3-(trimethoxysilyl)propyl ether
Glycidyloxypropyltrimethoxysilane
KBM 403
KBM 430
NUCA 187
Silan A-187
Silane A-187
Silane Z-6040
Silane, trimethoxy[3-(oxiranylmethoxy)propyl]-
Silane, [3-(2,3-epoxypropoxy)propyl]trimethoxy-
Silane Y-4087
Silicone A-187
Silicone KBM 403
Silquest A-187 silane
Union Carbide A-187
Y-4087

Z 6040
[3-(2,3-Epoxypropoxy)propyl]trimethoxysilane
[3-(Glycidyloxy)propyl]trimethoxysilane
[[3-(Trimethoxysilyl)propoxy]methyl]oxirane
TMSPGE
Dynasylan GLYMO

1.2 Purity/Impurities/Additives

Purity: 98 to 100 percent
Impurities: Methanol = <0.1 to <0.2 percent

1.3 Physico-Chemical Properties

Table 1: Summary of Physico-chemical Properties

Property	Value	Comment
Physical state		liquid
Melting point	<-70 °C	Crompton Corporation (2001)
Boiling point	262.4 °C at 1013 hPa	Flaningam, O.L. (1979) Other reported values: 262 °C Smith (1985) 290 °C General Electric (2000)
Relative density	1.069 at 25 °C	Crompton Corporation (2001)
Vapor pressure	0.003 hPa at 20 °C	Smith (1985) Other reported values at 20 °C: 0.3 hPa Dow Corning (2001) <1.33 hPa Crompton Corporation (2001)
Water solubility	1 x 10^6 mg/l TMSPGE 7.9 x10^6 mg/l 3-glycidoxypropyl-silanetriol	US EPA (2000) Estimated. The value for TMSPGE may not be applicable because it is hydrolytically unstable.
Partition coefficient n-octanol/water (log value)	-0.92 at 25°C;TMSPGE -2.61 at 25°C; 3-glycidoxypropyl-silanetriol	US EPA (2000) Estimated. The value for TMSPGE may not be applicable because it is hydrolytically unstable.
Henry's law constant	Not available	

2 GENERAL INFORMATION ON EXPOSURE

The information regarding potential exposure described in this chapter was provided by the members of the Silicones Environmental Health and Safety Council (SEHSC, see cover page). Quantitative descriptors of exposure are not available. The information provided is based on an observational database from the last thirty years.

The number of individuals likely to be exposed to TMSPGE is small and the potential levels of TMSPGE to which these individuals may be exposed are expected to be low, as explained below.

Given its chemical and physical properties, manufacturing and processing of TMSPGE generally occurs in enclosed equipment. Thus, the majority of workers who may be potentially exposed to TMSPGE are those who transfer materials from reaction vessels to shipping containers or who are exposed to the material during cleaning operations. More than 50 air samples, collected during production handling at ambient temperature in production plants, have shown no detectable TMSPGE. The detection limit ranged from 0.05 to 1 ppm, depending upon the volume of air sampled (Collins, Silverstein, and Hobbs, 1984).

Necessary engineering controls during production include proper ventilation, containment, safety equipment, and actual hardware designed to minimize exposure through splashing or to TMSGPE as a vapor in the air. Transfer of this material is usually in closed pipes rather than in open systems to minimize loss of this material (via hydrolysis) although some customers do transfer the material in open systems. TMSPGE rapidly hydrolyzes and its saturated vapor concentration at ambient temperatures would not exceed 12 ppm, reducing the potential for inhalation exposure to the parent compound. There may be exposure to one of the hydrolysis products, methanol. The remaining hydrolysis products (hydrolysates of TMSPGE) will have a much lower vapor pressure than the parent compound and thus vapor pressure to these products will remain low. Prior to condensation, the monomer formed through hydrolysis will have a similar molecular weight as the parent material and the vapour pressure is also expected to be similar. The silanols tend to hydrogen bond to the materials in the formulated product, thereby reducing the tendency to volatilize. Once condensation takes place, the molecular weight of the oligomer increases considerably thereby reducing the tendency to volatilize.

TMSPGE is transported from the production site as the parent silane to processors/formulators. After curing, the parent silane is consumed and no longer exists; this greatly reduces potential for consumer or worker exposure to the parent compound although exposure to the hydrolysis products may occur. Due to the rapid hydrolysis of the parent material, available toxicological data on the hydrolysis products is included in this document.

The silane is used as an adhesion promoter in adhesives and sealants (caulks), and is a small component in these products. Although there is no consumer use of the pure substance, it is usually used as a minor component in such adhesives and sealants in the consumer market. In these uses, the silane is reacted through hydrolysis to form methanol and silanetriol and is no longer present as the parent compound. Exposure of the public or the environment to this material is unlikely. Exposure via inhalation following such releases is unlikely based on a low saturated vapor concentration (12 ppm). As TMSPGE hydrolyzes, its saturated vapor concentration at ambient temperatures would not exceed 12 ppm, further reducing the potential for inhalation exposure to the parent compound. There may be vapor exposure to one of the hydrolysis products, methanol. The remaining hydrolysis products (hydrolysates of TMSPGE) will have a much lower vapor pressure than the parent compound and thus vapor exposure to these hydrolysates will be low.

2.1 Production Volumes and Use Pattern

The production volume of TMSPGE was 1702.167 tonnes in 2002 in the United States. This figure was determined based on a survey of manufacturing companies. TMSPGE is produced in North America, Europe and Asia.

Necessary engineering controls during production include proper ventilation, containment, safety equipment and actual hardware designed to minimize exposure through splashing or to TMSPGE in the air. Transfer of this material is usually in closed pipes rather than in open systems to minimize loss of this material (hydrolysis) although some customers do transfer the material in open systems. TMSPGE is transported from the production site as the parent silane to processors/formulators. Generally, TMSPGE is used by the processor/formulator at levels <2 percent, although some uses

may be as high as 30 percent. Once TMSPGE is added to an industrial product, the parent silane is intentionally reacted with the components of the formulation and is generally present as the parent silane at 0.1-0.2 percent until after curing (use). After curing the parent silane is consumed and no longer exists, which greatly reduces the potential for exposure. TMSPGE polymerizes during use. TMSPGE reacts with moisture in the application system (such as coatings, adhesives, composites and filler treatments) causing hydrolysis of the silane, forming methanol and silanols, which polymerize to form higher molecular weight condensates and water. Information on uses was obtained by an informal survey of members of the SEHSC in 2004.

Component in Adhesives and Sealants

TMSPGE is used most frequently in minor proportions (generally <2 percent) as an adhesion promoter, coupling agent, or cross-linker in adhesives, sealants, and encapsulants. Regardless of the particular adhesive or sealant with which it is mixed, TMSPGE is usually never used at concentrations higher than six percent, at least among companies that are members of the Silicones Environmental Health and Safety Council. However, one sealant product with a higher percentage (of 10-30 percent) TMSPGE was identified (Carboline, 2004). A level of one to two percent by weight is commonly recommended as a "starting-point" in many formulations.

Although the precise function of TMSPGE varies based on the sealant or adhesive to which it is added, it usually becomes immobilized during use due to attachment to minerals or polymers in the adhesive or sealant. In silicone sealants, much of the TMSPGE reacts with hydroxyl groups on silanol end-capped silicone polymers, with hydroxyl on the surface of silica reinforcing fillers, or with trace water introduced on mineral filler surfaces. In instances where TMSPGE is used as an additive to improve the adhesion of water-based or latex caulks and sealants, TMSPGE is polymerized and immobilized during the formulation process by reacting with water (hydrolysis) and mineral surfaces that are present in these products.

TMSPGE is sometimes used in solvent-based or 100 percent actives sealants, adhesives, and encapsulants. In these adhesive applications, TMSPGE becomes partially immobilized by reaction with the mineral fillers during the manufacturing process and reacts completely with the organic polymer during the curing process. Thus, when acting as a "coupling agent" or an "adhesion promoter" with any of the above adhesives or sealants, TMSPGE becomes covalently bonded to very high molecular weight polymers and minerals. This bonding to a high molecular weight material greatly reduces potential exposures.

Component of Coatings on Glass Fibers

Another major application for TMSPGE is as a raw material in the manufacture of reinforcing glass fibers. During its use, TMSPGE is deliberately converted to the silanol form by hydrolyzing it in acidified water at concentrations usually below 20 percent by weight and typically between 5 and 10 percent by weight. After the hydrolysis reaction is complete, the aqueous solutions of the corresponding silanol are further diluted with water and possibly other ingredients, such as emulsions of organic polymers, lubricants, surfactants, wetting agent, and other processing aids. These processes result in destruction of the parent silane and result in the formation of hydrolysis products.

During application of these solutions, called sizes or finishes, to the glass fibers, there no longer exists a potential for worker exposure to TMSPGE. After the fibers are dried, the silanols are bonded directly to the glass fibers. This immobilization and chemical reactivity eliminates further end-user exposure to the hydrolysis products. The final end-user takes these fibers and mixes them with organic resins to make composites.

Component of Foundry Additives

Less than 5 percent of the production volume of TMSPGE is consumed as an additive to a foundry resin. In this use, a resin producer blends a phenolic or furan resin (polymer), which contains some water, with a small quantity of TMSPGE, typically between 0.01 and 0.1 percent. As the TMSPGE is blended, it hydrolyzes to silanol and oligomer forms. Moreover, TMSPGE reacts with the resin during curing reactions. Therefore, potential exposure to unreacted TMSPGE is minimal.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

The reactive nature of this material destroys the parent material in any moisture-containing environment, thus limiting environmental exposure to the silane. TMSPGE hydrolyzes rapidly (half-life of approximately 3 minutes to about 6.5 hours, depending on the aqueous solution temperature, pH and concentration of buffer). At a pH of 7 and ambient temperature, the half life is 6.5 hours. Hydrolysis of TMSPGE results in the formation of silanetriols which can then condense to form highly cross-linked, high molecular weight polymers, further reducing the potential for exposure. In the environment, at lower concentrations of the parent compound (and thus lower concentrations of the hydrolysis products), exposure to unpolymerized silanetriols may occur.

2.2.2 Photodegradation

Because the material is hydrolytically unstable and rapidly generates methanol when added to water, photodegradation cannot be measured. Nonetheless, this endpoint provides valuable information on the behavior of the material and is needed to evaluate the transport and distribution (i.e., fugacity) of the TMSPGE between environmental matrices. TMSPGE has an estimated atmospheric half-life (hydroxyl radical oxidation) of 5.8 hours (US EPA, 2004). The overall half-life may be even shorter, as concurrent hydrolysis may also be occurring.

2.2.3 Stability in Water

TMSPGE is a highly reactive chemical and rapidly hydrolyzes to methanol and 3-glycidoxypropyl-silanetriol ($R\text{-}Si(OH)_3$ where $R = -(CH_2)_3OCH_2CHOCH_2$). The consecutive hydrolysis reactions (at pH 5.0, 7.0 and 9.0; at 10, 24.5 and 37.0 deg C) were followed by high performance liquid chromatography (HPLC) with element specific detection for silicon using inductively coupled plasma atomic emission spectroscopy (ICP-AES) using acetate and tris(hydroxymethyl) aminomethane buffers of varying concentrations. The data was modeled by multiple linear regression to determine quantitatively the effect of pH, i.e. hydronium and hydroxide ion concentrations, and buffer concentration on rates of hydrolysis. The calculated half-lives for hydrolysis of TMSPGE at 25ºC as a function of pH are given in Table 2.

Table 2. The Calculated Half-lives (hours) for Hydrolysis of TMSPGE

Temperature	pH		
	5.0	**7.0**	**9.0**
10.0 °C	0.29	18	0.11
24.5 °C	0.15	6.5	0.13
37.0 °C	0.087	3.3	0.053

The measured hydrolysis half-life for TMSPGE at 25ºC ranges from 3 minutes to 6.5 hours over the pH range of 5 to 9 (Kozerski, Ziemelis and Gallavan, 2001). The measured and calculated hydrolysis half-lives demonstrate that TMSPGE is hydrolytically unstable over a range of environmentally relevant pH and temperature conditions. Over the pH range investigated, the intermediate silanol products (the mono- and di-ol) were observed to hydrolyze more rapidly than the original tri-alkoxysilane. Consequently, these breakdown products can be considered transient. The stability of the methanol co-product was not considered, but is probably stable under these conditions. At pH 7 and 25°C, the hydrolytic conversion of TMSPGE to methanol and 3-glycidoxypropyl-silanetriol is expected to reach 99.9 percent in ≤ 2.8 days (Kozerski, Ziemelis, and Gallavan, 2001).

No test results regarding the hydrolysis of the epoxy ring of TMSGPE is available. However, a published kinetic study of the model compound 1,4-butanediol diglycidyl ether (CAS 2425-79-8) in aqueous solution over the pH range 4.0-6.8 showed the rate of epoxide ring opening by water to be 2-4 orders of magnitude slower than the presently reported rate of methyoxysilyl group hydrolysis. For pH 4, the rate of epoxide ring opening was shown to be similar for the model diglycidyl ether and TMSPGE (Xue et al., 1991; Wade, 1987).

2.2.4 Transport between Environmental Compartments

The EQC Level III model (Mackay, DiGuardo, Paterson, Cowan, 1996) was used to evaluate the fate, transport and distribution of TMSPGE between environmental matrices. Based on Level-III modeling, using loading rates for air, soil, and water of 1000 kg/h for each media, shows the following percent distribution for TMSPGE: Air = 0.6 percent; Soil = 92.5 percent; Water = 6.9 percent; Sediment = 0.00 percent. The environmental fate, transport, and distribution of 3-glycidoxypropylsilanetriol were evaluated to provide a more realistic assessment of TMSPGE. Level III Fugacity modeling, using loading rates for air, soil, and water of 1000 kg/h for each media, shows the following percent distribution for 3-glycidoxypropylsilanetriol: Air = 0.0%; Soil = 60.9%; Water = 39 %; Sediment = 0.1 %.

2.2.5 Biodegradation

Biodegradation studies (Degussa, 1994a) suggest that about 37 percent of the material is degraded after 28 days. TMSPGE is not readily biodegradable. These results reflect the degradation of methanol and not the parent material or the silanetriol hydrolysis product. TMSPGE has a hydrolytic half-life of 6.5 hours at 25 ºC and pH 7.0. Consequently, the biodegradable materials in the test system will be primarily methanol, the silanetriol, and condensed silanetriol materials. Total percent degradation is equal to the combined percent degradation of each material and the overall rate of degradation determined by the material that degrades most rapidly. The observation that 37 percent of the material is degraded after 28 days suggests that most of the degradation was associated with methanol. Methanol is degraded 76 percent in 5 days and 95 percent in 20 days; it is readily biodegradable.

2.2.6 Bioaccumulation

Bioaccumulation is not anticipated since this material is hydrolytically unstable. Rapid hydrolysis of this material produces methanol and silanetriols. The epoxy ring will open to form a diol. It is still attached to the silane molecule. The Si-C bond will not undergo further hydrolysis. The methoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield an epoxy functional silicone resin (oligomer resin).

If the silane is slowly released such that the concentration of the resulting epoxy-functional silanetriol is not high enough to result in polymerization, the silanetriol will exist largely as a monomer. The monomer is known to be water soluble by virtue of the three hydroxy groups on the silicon. The silanetriol has a low Kow (-2.6; estimated) because of these hydroxy groups and so is not expected to bioaccumulate. The water solubility of the silanetriol cannot be measured because of its tendency to condense at concentrations greater than 500 ppm (Merrifield, J. (2003) Personal Communication).; the estimated water solubility is 7.9 x 10^6 mg/l. The equilibrium constant for the condensation of a 3-methacryloxypropylsilanetriol to the dimer is about 480 ppm (Osterholtz and Pohl, 1992). It is possible that TMSPGE would react similarly. The *estimated* water solubility of TMSPGE is 1 x 10^6 mg/L (USEPA, 2004). At higher concentrations, the silanetriol and small condensation products will precipitate out of water due to formation of larger, water insoluble polymeric resins.

2.3 Human Exposure

2.3.1 Occupational Exposure

In production, this material is mostly handled in closed systems. Necessary engineering controls during production include proper ventilation, containment, safety equipment and actual hardware designed to minimize exposure through splashing or to the air. Transfer of this material is in closed pipes (which would preclude reaction with moisture in the atmosphere) rather than in open systems to minimize loss of this material (hydrolysis) although some customers do transfer the material in open systems. The material is shipped via air, road, and marine transport in returnable intermediate bulk containers (IBCs), non-returnable IBCs, steel drums, steel pails and steel cans.

The physical and chemical properties of TMSPGE minimize the potential for exposure to this substance during its manufacture. Because TMSPGE has a low vapor pressure (the saturated vapor concentration at ambient temperatures is approximately 12 ppm), there is little potential for inhalation exposure. More than 50 air samples, collected during production handling at ambient temperature in production plants, have shown no detectable TMSPGE. The detection limit ranged from 0.05 to 1 ppm, depending upon the volume of air sampled (Collins, Silverstein, and Hobbs, 1984). The likelihood of forming aerosols is very low and would occur only if improper handling procedures are used.

TMSPGE is a moisture-reactive material that hydrolyzes rapidly (half-life of approximately 3 minutes to about 6.5 hours, depending on the aqueous solution temperature, pH and concentration of buffer). Hydrolysis of TMSPGE results in the formation of silanetriols which can then condense to form highly cross-linked, high molecular weight polymers when the concentration of the chemical is high enough for the hydrolysis products to come in contact with each other. Any polymerization would further reduce the potential for exposure.

The number of workers that may be exposed to TMSPGE during its manufacture or handling is small. Given its chemical and physical properties, manufacturing and processing of TMSPGE generally occurs in enclosed equipment. Thus, the majority of workers that may be potentially exposed to TMSPGE are those who transfer materials from reaction vessels to shipping containers or who are exposed to the material during cleaning operations. As indicated previously, TMSPGE rapidly hydrolyzes and its saturated vapor concentration at ambient temperatures would not exceed 12 ppm, reducing the potential for inhalation exposure to any parent compound. There may be vapor exposure to one of the hydrolysis products, methanol. The remaining hydrolysis products (hydrolysates of TMSPGE) will have a much lower vapor pressure than the parent compound and thus vapor exposure to these hydrolysates will be low.

A worker may be exposed (when making product formulations in an open system) usually to low levels (generally <2 percent although one product was found with up to 30 percent TMSPGE)) of the silane during formulation and to a much less extent, during its use in the final product. Worker exposure to TMSPGE is low during its use in applications. In many of its applications, TMSPGE is intentionally altered during use by hydrolysis, condensation with surfaces, or oligomerization. The dilution and reactions of TMSPGE reduce its bioavailability and apply with equal validity to all of the end-use applications of this material. The low final percentage in the product (generally 0.1-0.2 percent) reflects the fact that this material is designed to be reactive and to not survive the application processing at the customer level, although there may be some exposure to the reaction products methanol and silanetriols. There are no known production processes that involve aerosolized material. In coatings that are applied by spraying, low levels of free silane may be present (generally <2 percent), although the percentage may be higher in some products. The vapor pressure of this material is low enough that vapor inhalation is not considered a potential route of exposure.

2.3.2 Consumer Exposure

The silane is used as an adhesion promoter in adhesives and sealants (caulks), and is usually a small component in these products. Although there is no consumer use of the pure substance, it will be found as a minor component (<2 percent) in such adhesives and sealants in the consumer market although one product was found with up to 30 percent TMSPGE. Exposure of the public or the environment to this material is not likely.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

No data available.

3.1.2 Acute Toxicity

Numerous acute toxicity studies have been conducted with TMSPGE via the inhalation, dermal and oral route of exposure.

Studies in Animals

Inhalation

In one study, groups of four rats/sex were exposed via inhalation to 0.7, 1.4, and 2.7 mg/l (saturated vapor) of TMSPGE for four hours. No deaths or untoward behavioral reactions were noted. There were no gross abnormalities noted at the necropsy and the LC_{50} for TMSPGE is greater than 2.7 mg/l (DCC, 1963).

In a second study, groups of five rats/sex were exposed via inhalation to 0.8, 1.9, and 5.3 mg/l of TMSPGE for four hours. No deaths occurred at the two lower concentrations (0.8 and 1.9 mg/l). At the highest concentration (5.3 mg/l), three rats died, one male on day 1, one female on day 1 and one female on day 2. Clinical signs included excessive lacrimation, dry and moist rales, nasal discharge, and yellow staining in the anal-genital area. These signs were considered to be dose-related and were not generally observed during the second week following exposure. Discolored lungs and autolytic changes were seen in the three rats that died. There were no gross abnormalities

noted at the necropsy of survivors. The LC_{50} for TMSPGE is greater than 5.3 mg/l (Allied Corporation, 1981).

Dermal

The calculated dermal LD50 in rabbits exposed to doses of 4600, 6800, 10200, and 15400 mg/kg bw TMSPGE for 24 hours is 6800 mg/kg bw (DCC, 1963). The calculated dermal LD50 in male rabbits exposed to doses of 2.5 and 5.0 ml/kg bw TMSPGE for 24 hours is 3.97 ml/kg bw (Mellon Institute, 1962).

Oral

Groups of five rats/sex were exposed once via gavage to 3.9, 5.0, 6.3, 10.0 and 12.6 ml/kg bw of TMSPGE. Piloerection and lethargy were observed within 1 hour of administration, followed by coma and death. All deaths occurred within 48 hours of administration: 1/10, 3/10, 3/10, 7/10 and 8/10 rats died at 3.9, 5.0, 6.3, 10.0 and 12.6 ml/kg bw dose levels, respectively. All survivors were generally asymptomatic after this time. The LD50 for TMSPGE was reported as 7.5 ml/kg bw (DCC, 1976). Additional acute oral studies have been conducted with TMSPGE. Reported LD50 values are greater than 5000 mg/kg bw:

Reported LD_{50}	Reference
>5 ml/kg bw	Degussa, 1978
7010 mg/kg bw	DCC, 1976
8400 mg/kg bw	DCC, 1963
22.6 ml/kg bw	Mellon Institute, 1962
16900 mg/kg bw	Allied Corporation, 1978a

Studies in Humans

No data available.

Other Studies

The low order of acute oral toxicity associated with TMSPGE is likely to be due to the limited bioavailability. A non-GLP study was conducted to examine the fate of TMSPGE following gavage (WIL Research, 2000). Five fasted female Sprague-Dawley rats were dosed with 2000 mg/kg bw TMSPGE mixed with activated charcoal as a tracer. After 20 or 30 minutes the animals were sacrificed, and the stomachs and gastrointestinal tracts examined for presence of test article. The study was also repeated in the absence of the activated charcoal tracer. In all cases, the test article was found in the stomach contents or in the upper gastrointestinal tract, and was observed to have the consistency of thick mucous. In cases where the stomach contents included food, small waxy particles of test article were observed. Both the thick mucous and waxy particle forms of the test article observed in the stomach and upper gastrointestinal tract support the rapid polymerization of TMSPGE under oral (gavage) conditions, as the test article exists as a clear, water-like liquid. In contrast, there was no liquid present in the stomachs of animals gavaged with an equivalent dose of water and sacrificed after 30 minutes.

A non-GLP study conducted in support of this test plan used gel permeation chromatography (GPC) to determine the relative molecular weight distribution of the hydrolysis and condensation products of TMSPGE in an environment meant to mimic the stomach (Sun et al., 2001). The number-

average and weight-average molecular weights of the TMSPGE solution were determined by GPC to be 1102 and 1312, respectively, with 73 percent of the chromatogram area higher than 1000 molecular weight at the1-hour reaction time. At the 4-hour reaction time, the number-average and weight-average molecular weights increased to 1269 and 1524, respectively, with 84 percent of the chromatogram area higher than a molecular weight of 1000.

Conclusion

The test substance has a low order of acute toxicity in rats and/or rabbits by the inhalation, oral or dermal routes of exposure.

Hydrolysis after application on or contact with the skin is very likely to occur. If the concentration of TMSPGE is high enough, the silanetriol hydrolysis product will form high molecular weight polymers that, due to their size, are not capable of penetrating the skin barrier such that systemic bioavailability is minimal. The low order of acute dermal toxicity is consistent with the possibility that high molecular weight polymers have been formed.

The lack of clinical signs of toxicity following acute dosing is likely related to the hydrolysis of TMSPGE and subsequent polymerization of the hydrolysis products with MW greater than 1000, and thus, resulting in limited bioavailability.

3.1.3 Irritation

Numerous irritation studies have been conducted with TMSPGE. Invalid studies are not described here.

Skin Irritation

Studies in Animals

A 0.5 ml sample of TMSPGE was applied to the clipped skin of six rabbits under semi-occlusive cover for 24 hours. All six rabbits developed well-defined erythema at 24 and 48 hours post application, which remained at the 72-hour observation and persisted through 96 hours in all animals. The erythema was not accompanied by edema. The test material was classified as a mild dermal irritant based on a Primary Irritation Index (PII) of 1.94 (DCC, 1982g). A 0.5 ml sample of the test material was applied to areas of both intact and abraded skin of four rabbits under semi-occlusive cover. After 24 hours the patches were removed and the skin reaction were evaluated according to the Draize scale. The test material was found to be a non-irritant under the conditions of the study, with a PII of 0.06 (DCC, 1976). A 0.5 ml sample of the test material was applied to areas of both intact and abraded skin of four rabbits under semi-occlusive cover. After 24 hours the patches were removed and the skin reactions were evaluated according to the Draize scale. The test material was found to be a mild irritant under the conditions of the study, with a PII of 1.8 (DCC, 1963).

Studies in Humans

A range-finding primary irritation patch test was conducted with the test article to determine its ability to irritate the skin of human volunteer subjects using an occlusive primary irritation patch test. Under the conditions employed in the study (0.2 ml; 48-hour exposure period), the test article caused definite irritation when applied undiluted and at concentrations of 75 percent, 50 percent and 25 percent in methanol. The irritation was not clinically significant at concentrations of 1 percent and 10 percent in methanol (TKL Research, 2001).

Eye Irritation

Studies in Animals

In a rabbit study, 0.1 ml of undiluted TMSPGE was administered topically to the eyes of 9 animals. Twenty seconds after instillation, the treated eyes of 3 of the 9 rabbits were washed for 1 minute with tap water. Eyes were examined up to 21 days after exposure. A second group of 9 rabbits was treated similarly with a 5 percent solution of the test material diluted in water. The eyes of the second group of rabbits were examined up to 7 days after exposure. In unwashed eyes treated with undiluted test material, blinking and tearing were observed in all eyes within minutes after instillation. Pannus of the cornea developed in 2 of the 6 animals. Corneal opacities, covering a minimal area of the cornea, persisted for 21 days in the animals that developed pannus. Conjunctival redness was also observed in several test eyes. In the washed eyes, treated with undiluted test material and washed 20 seconds later, minimal signs of irritation were reported. No irritation was observed in the washed and unwashed eyes of rabbits exposed to 5 percent of the test material in water. The test material was considered to be an eye irritant according to the Federal Hazardous Substances Act (DCC, 1982f).

In a second study, 0.1 ml of undiluted TMSPGE was administered topically to the eyes of 6 rabbits. The test material elicited only very mild eye irritation in those animals in which the treated eyes remained unwashed. This irritation was confined to slight erythema and edema of the conjunctiva, which did not persist beyond 48 hours after instillation. At no time was the cornea or iris of any animal affected (DCC, 1976). In a third study, 0.1 ml of undiluted TMSPGE was instilled into the right eye of five test rabbits. The left eye of each animal served as a control. At 1, 24, 48, 72 96 hours and 7 days following instillation, the cornea, iris and palpebral conjunctiva were examined individually and graded for irritation and injury. No irritation was observed after 1 hour. The material was considered minimally irritating (DCC, 1963).

Respiratory Tract Irritation

No data available.

Conclusion

TMSPGE is a mild skin and eye irritant in animals, and caused skin irritation in humans when applied undiluted or as a dilution in methanol.

3.1.4 Sensitisation

Studies in Animals

Skin

The dermal sensitization potential of TMSPGE was evaluated in a Buehler test in guinea pigs (DCC, 1982e). A range-finding study was performed to determine the highest concentration which produced mild irritation (for induction) and the highest non-irritating concentration (for challenge). Undiluted TMSPGE was selected for both induction and challenge phases. Positive, negative, and irritation controls were incorporated into the study. Evaluation of the dermal responses was made at 24 and 48 hours after administration of each challenge dose. Dose levels for induction and challenge were 0.2 ml of 100 percent TMSPGE. Under the conditions of this study, the test material was not a sensitizer in guinea pigs. The dermal sensitization potential of TMSPGE in peanut oil was evaluated in a Maximization test in guinea pigs (DCC, 1984). No evidence of skin irritation or skin sensitization was observed in any of the animals following challenge phase. Under the conditions of these studies, the test material was not a skin sensitizer. In a Buhler test, 20

guinea pigs were induced with 100 percent TMSPGE on days 0, 7 and 14 and subsequently challenged with 100 percent test substance on day 28. A control group of 10 animals was induced and challenged with corn oil. There was no skin irritation observed in either test or control animals in the challenge phase, and TMSPGE was not considered a sensitizer (Huls, 1993).

Studies in Humans

Skin

One hundred eleven subjects between the ages of 20 and 75 years, with a mean age of 47.9, were enrolled in a human patch repeated insult test (TKL Research, 2001). The majority of subjects were Caucasian women. One hundred subjects completed the study, six were lost to follow-up, one voluntarily withdrew, and four reported non-test article-related adverse events. No dermal reactions were noted during induction or challenge with TMSPGE. Based on the conditions employed in this study and the elicited individual dermatological response grades, there was no evidence of sensitization to the test article.

Conclusion

TMSPGE is not a skin sensitizer in humans or in animals.

3.1.5 Repeated-Dose Toxicity

Studies in Animals

Inhalation

Rats were exposed for a total of nine times for 6 hours per day over a two-week period (i.e., 5 exposures during week 1 and 4 exposures during week 2) to target aerosol concentrations of 0, 75, 225 and 750 mg/m^3 TMSPGE (DCC, 1982d). Actual concentrations were 0, 77, 226, 707 mg/m^3 (males) and 0, 73, 226, 734 mg/m^3 (females). No deaths occurred in the controls or in animals treated with 75 or 225 mg/m^3 test material. However, six rats at the high exposure level (5 males and one female) either died or were sacrificed in a moribund state from three to five days after initiation of the study. Microscopic examinations were performed for both dead and surviving animals in all groups. The animals had no evidence of acute tissue toxicity but appeared to have succumbed to inanition. The mid and high exposure level groups exhibited signs of nasal discharge and dry and moist rales and bodyweight depressions following a dose-response pattern. The body weight decrease was noted only at 750 mg/m^3. Males lost about 13% and females lost 2.6% in the first week. In the second week, however, no body weight loss was observed in the females, but males lost 3.7% bw. Microscopic examination of the tissues revealed no histopathological effects or localized (respiratory tract) effect of the test material. Under the conditions of this study, the No Observed Adverse Effect Concentration is 225 mg/m^3.

Rats were exposed five days per week for three weeks followed by four days of exposure during the fourth week for a total of 19 exposures over a 4-week period to a 2 percent TMSPGE-hydrolysate solution (mean concentration of 119 mg/m^3; determined over 4 measurements per day) (BRRC, 1991). No mortality or exposure-related clinical signs were observed during the study. Decreases in absolute body weight (11%) and/or body weight gain (29%) were observed for the TMSPGE-hydrolysate treated animals at the end of the study. Microscopic exam was performed for all animals. Repeated exposure of rats to 119 mg/m^3 of aerosol generated from a 2 percent TMSPGE-hydrolysate solution did not produce any evidence of laryngeal granuloma formation.

Dermal

There were no valid repeated-dose studies conducted with TMSPGE via the dermal route.

Oral

Rats were exposed by gavage to TMSPGE for 5 consecutive days per week for 4 weeks to dose levels of 40, 400 and 1000 mg/kg bw/day (DCC, 1981a). There were no test substance-related mortalities. One male dosed with 40 mg/kg bw/day and two 1000 mg/kg bw/day males died during the course of the study. However, necropsy of these rats revealed test substance to be present in the lungs and thus the deaths were associated with dosing trauma. There were no test substance-related effects on clinical condition, behavior, body weight, body weight changes or food consumption, nor were there any test substance-related effects on hematological, blood biochemical or urinalysis parameters; some statistical differences from control values were present in these data, but all values for the treated groups were within normal ranges. No test substance-related organ weights effects or gross or microscopic pathological changes were observed.

Under the conditions of this study, the No Observed Adverse Effect Level (NOAEL) for the test substance was found to be 1000 mg/kg bw/day when administered orally five days per week for four weeks to male and female rats.

Studies in Humans

No data available.

Conclusion

TMSPGE was administered in 9 repeated inhalation exposures over two weeks of rats to target vapor concentrations of 0, 75, 225 and 750 mg/m^3. Six rats at the high exposure level (5 males and one female) either died or were sacrificed in a moribund state from three to five days after initiation of the study after succumbing to inanition. The mid and high exposure level groups exhibited signs of nasal discharge and dry and moist rales and bodyweight depressions following a dose-response pattern. Repeated exposure of rats to 119 mg/m^3 of aerosol generated from TMSPGE-hydrolysate for 5 days /week for three weeks did not produce any evidence of laryngeal granuloma formation.

Repeated exposure of rats to TMSPGE by gavage to dose levels of 40, 400 and 1000 mg/kg bw/day for 5 days/week for 4 weeks resulted in no test substance-related organ weights effects or gross or microscopic pathological changes. Under the conditions of this study, the NOAEL for the test substance was found to be 1000 mg/kg bw/day.

3.1.6 Genetic Toxicity (Gene Mutations and Chromosomal Aberrations)

Numerous bacterial and mammalian cell mutagenicity studies have been conducted with TMSPGE. Invalid studies as well as studies that are not relevant to the two major genetic toxicity endpoints considered under SIDS are not described here.

In vitro Studies

Gene Mutations. The weight of evidence indicates that TMSPGE is mutagenic in several strains of *Salmonella* bacteria (TA100, TA97, TA98, TA1535 and/or TA 1538) in the presence and absence of metabolic activation (DCC, 1977; Litton Bionetics, 1977, 1983a; DCC, 1977, 1979; Allied Corporation, 1978b; Degussa-Huls, 1988). Although some study details were not available, TMSPGE induced mutations in mouse lymphoma L1578Y TK cells, both with and without metabolic activation (Litton Bionetics, 1983b). In another test, TMSPGE did not induce forward mutations in Chinese hamster ovary (CHO) cells (Allied Corporation, 1979), although the highest concentration tested was below the limit concentration suggested by OECD TG 476. The test substance was evaluated for its ability to induce sister chromatid exchanges (SCE) in Chinese hamster ovary (CHO) cells (Allied Corporation, 1982). The test material produced increases in SCE

in a dose-related manner in CHO cells at the 0.04, 0.06, 0.08 and 0.10 concentrations. Although the actual numbers of SCE were low (less than a two-fold increase over untreated controls), the concentrations of the test material were also low (higher concentrations were cytotoxic) and the increases were statistically significant (as well as dose-responsive). Therefore, it was concluded that TMSPGE was a moderate in vitro inducer of SCE. In a second study, peripheral lymphocytes were exposed for one hour to TMSPGE at concentrations of 0.05, 0.1, and 0.2 mg/ml (Allied Corporation, 1999). Statistically significant increases in SCE frequencies were present at the 0.10 and 0.20 mg/ml concentrations.

In vivo Studies

Chromosomal Aberrations. Ten mice per group were administered 500, 1670 and 5000 mg/kg bw TMSPGE (undiluted) by gavage (DCC, 1982a). A negative control group and a positive control group were also included. TMSPGE did not induce chromosome damage in the bone marrow cells at doses as high as 5000 mg/kg bw. In a second micronucleus study, 10 mice per group were administered 500, 1000 and 2000 mg/kg bw TMSPGE by intraperitoneal (i.p.) administration in distilled water (BioReliance, 1999). TMSPGE is a highly reactive chemical and is subject to rapid hydrolysis; the animals were likely not exposed to the parent silane alone. A negative control group and a positive control group were also included. TMSPGE induced chromosome damage in the bone marrow cells of mice following i.p. administration of the test substance at all three dose levels tested. In a third study, 10 mice per group were administered 1600 mg/kg bw TMSPGE i.p. as a suspension in corn oil (Degussa, 1994b). A negative control group and a positive control group were also included. Two of 20 animals died following dosing with 1600 mg/kg bw, thereby indicating that this dose is very close to the MTD. Although there was a statistically significant increase of the micronucleus frequency in males only at the 24-hour sacrifice time point only, this was determined to be due to a low incidence in the concurrent control group. The increase observed approximated the historic control level for this strain of mouse in this laboratory. The report authors concluded that the small increase was not biologically significant.

Conclusion

TMSPGE did not induce chromosomal damage in mouse bone marrow cells by gavage at doses as high as 5000 mg/kg bw/day. However, by i.p. administration, it induced chromosomal damage in mouse bone marrow cells when administered in water. TMSPGE induced gene mutations in bacteria. TMSPGE induced gene mutations in mouse lymphoma L1578Y TK cells but did not induce forward mutations in CHO cells. TMSPGE induced SCEs in vitro. There are no in vivo gene mutation data.

3.1.7 Carcinogenicity

In vivo Studies

Dermal

C3H male mice (40/group), approximately 51 to 76 days of age, received either the test chemical (25 µl dose of 25 percent TMSPGE in acetone) or a control material (25 µl dose of 0.1 percent methylcholanthrene in acetone or acetone alone) three times per week to the clipped skin of the back of each mouse. The mice were observed daily for mortality and were carefully examined for lesions of the skin once per month. A necropsy was performed on all dead mice and on moribund mice, which were sacrificed. A necropsy consisted of a careful examination of the skin and body cavities. All observations were recorded. The dorsal skin and any suspect internal tumors from all non-autolyzed mice were fixed in 10 percent neutral buffered formalin. Tissues fixed in formalin were carefully trimmed, embedded, sectioned and stained with hematoxylin and eosin for

examination by a pathologist. All neoplastic and non-neoplastic lesions discovered during the histopathologic examination were recorded and tabulated. No epidermal or subcutaneous tumors were observed in the TMSPGE group. Eight animals had hyperkeratosis (compared to the acetone controls) suggesting a possible irritating effect on the epidermis. No epidermal tumors were observed in the group treated with acetone although two mice had subcutaneous sarcomas outside the treatment area (one subcutaneous fibrosarcoma of the left foreleg and one subcutaneous lymphosarcoma over the left hip). One mouse had epidermal hyperplasia. The positive control (MC) group had 39 animals with skin tumors including 33 with confirmed squamous cell carcinomas, two mice with papillomas; four mice had gross carcinomas that were not confirmed histologically because of cannabilism. These results confirm the sensitivity of the animals to a known skin carcinogen. TMSPGE was not considered tumorigenic when applied to the skin of C3H mice under the conditions of this study (BRRC, 1982). Note that there was only one dose level, and this dose was relatively low.

Conclusion

There is no evidence from the available data to suggest TMSPGE is tumorigenic.

3.1.8 Toxicity for Reproduction

A one-generation reproductive toxicity study was conducted with TMSPGE. In addition, two rat and one rabbit developmental studies have been conducted on TMSPGE. These studies confirm that TMSPGE exhibited no adverse effects on fertility or the developing unborn.

Effects on Fertility

A one-generation reproductive toxicity study was conducted with TMSPGE (Becker, Flade, and Weber, 2004). This study was designed to investigate the effects of continuous administration of TMSPGE to the rat on reproductive performance, such as gonadal function, estrous cycle, mating behavior, conception, parturition, lactation and weaning. TMSPGE was administered orally, by gavage, once daily to males for a 70-day pre-pairing period, during the pairing period and until the last litter had reached day 7 post partum. Females received the test item during a 14-day pre-pairing period, and also during the pairing, gestation and lactation periods. The following dose levels were applied: Group 1 - 0 mg/kg bw/day (vehicle control); Group 2 - 250 mg/kg bw/d; Group 3 - 500 mg/kg bw/d; and Group 4 - 1000 mg/kg bw/d. A standard dose volume of 2 ml/kg body weight with a daily adjustment to the actual body weight was used. Control animals were dosed with the vehicle alone (dried corn oil). The test material was shown to be stable in the selected vehicle. All males survived until scheduled necropsy and no clinical signs that were attributable to treatment with the test item were noted. All females survived until scheduled necropsy. At 1000 mg/kg bw/d, starting during early/mid gestation, all females displayed signs of discomfort after dosing (pushing head through bedding). This behavior was noted as long as the females were dosed (i.e., one day prior to scheduled necropsy). Mean food consumption of males and females was not affected by treatment with the test substance. At 1000 mg/kg bw/d, mean body weight gain of males during the prepairing period was slightly decreased, resulting in a slightly lower mean body weight at the end of the prepairing period (375 g compared with 409 g in the vehicle control). Although statistical significance was only reached on single days, this reduction was considered to be test item related. During the pairing and after pairing period, lower absolute body weights at 1000 mg/kg bw/d persisted, while body weight gain was similar to that of the vehicle control. Body weight development of females was not affected by treatment with the test item.

For both generations, the fertility rate was high resulting in at least 23 litters per group for evaluation of reproduction data. At all dosages, there were no treatment related effects on mean or median precoital time, fertility indices, mean duration of gestation and number of implantations,

post-implantation loss, pup survival or litter size from birth through to weaning. No test-item related findings or clinical signs were noted at first litter check on day 0 post partum or during the lactation period. Pup weights at birth and during lactation were unaffected by treatment with the test item No treatment-related effects on sex ratios were noted.

No test-item related findings were noted at macroscopic examination of parental males or females. At 1000 mg/kg bw/d, statistically significant increased mean relative liver and kidney weights were noted for males and females. In the liver of males, the severity of glycogen deposition was slightly increased at 1000 mg/kg bw/d. This finding was considered in relation with the nutritional state of the animals and of no adverse character. In the kidneys of males, the severity of tubular change was slightly increased at 1000 mg/kg bw/d. The findings in the kidney are not considered to be of much toxicological significance. No test-item related findings were noted at macroscopic examination of pups.

In a one-generation reproduction toxicity study, no reproductive effects were observed at the highest dose tested, 1000 mg/kg bw/d. At 1000 mg/kg bw/d, treatment with TMSPGE resulted in signs of discomfort after dosing (noted for parental females from early /mid gestation onwards), decreased body weight gain of males, and increased absolute and relative liver and kidney weights in parental males and females. Histopathology revealed effects on livers and kidneys of males. Based on these data a NOAEL for parental animals was established at 500 mg/kg bw/d. A NOAEL for reproductive effects was established at 1000 mg/kg bw/d.

Developmental Toxicity

Sprague-Dawley rats were exposed by oral gavage to TMSPGE during the primary period of organogenesis, i.e., gestation days 6-15, at dose-levels of 50, 500 and 1000 mg/kg bw/day (DCC, 1982). There were no test substance-related mortalities. One rat (subsequently replaced) in the 50 mg/kg bw/day group died as the result of dosing trauma. There were no test substance-related effects on clinical condition, behavior, body weight, body weight gain or food consumption. No effects on liver or gravid uterine weight were observed. No effects on the number of implantation sites or corpora lutea per dam were observed. The incidence of pregnancy was not affected by treatment with the test substance; all rats were confirmed to be pregnant at the gestation day 20 laparohysterectomies. No adverse effects on the number of live fetuses per litter, mean litter size, sex ratio, fetal body weight or crown-rump length were observed. The incidence of fetal resorptions was not altered by test substance administration. No external, visceral or skeletal alterations were observed among test substance-treated rats at an incidence that was statistically different from the control group. When considered collectively, the incidence of total major malformations observed in the external, soft tissue or skeletal examinations was not significantly different among the treated groups as compared to the control group. No major malformations were observed among litters of rats in any dose group. The sporadic variations and malformations seen occurred at an incidence comparable to a historical control incidence for Sprague-Dawley rats reported in the literature. Under the conditions of this study, the NOAEL of the test substance for embryotoxicity, developmental toxicity and maternal toxicity was found to be 1000 mg/kg bw/day when administered orally on gestation days 6-15 to rats.

In a second study, Fisher 344 rats were exposed by oral gavage during the primary period of organogenesis, i.e., gestation days 6-15, at dose-levels of 500, 1500 and 3000 mg kg/day (BRRC, 1990). There were no treatment-related maternal deaths. No dams aborted. One female each at 0 and 500 mg/kg bw/day delivered early and was removed from study. 17-23 litters were examined in each dose group. There were no statistically significant differences among groups for maternal gestational body weights. Gestational weight gain was significantly reduced at 3000 mg/kg bw/day for gestation day 6-12 and 6-15 (the treatment period), and food consumption was significantly reduced at 3000 mg/kg bw/day for gestation day 9-12. Treatment-related (but not statistically

significant) clinical signs, observed only at 3000 mg/kg bw/day, included hypoactivity, audible respiration and unkempt appearance (one to two dams each). At the gestation day 21 sacrifice there were no effects of treatment on maternal body weight or gestational weight gain (absolute or corrected), on gravid uterine weight or on liver weight (absolute and relative). Gestational parameters, including number of ovarian corpora lutea, total, viable and nonviable implantations per litter, and sex ratio were unaffected by treatment. Fetal body weights per litter (all fetuses, males or females) were equivalent across dose groups. There was no significant increase in the incidence of malformations (individual, pooled external, visceral, skeletal or total) in any treatment group relative to controls. There were no treatment-related differences among groups for individual external variations, for pooled external, visceral or skeletal variations or for total variations. One skeletal variation, unossified anterior arch of the atlas, exhibited a significantly increased incidence at 3000 mg/kg bw/day, indicating minimal fetotoxicity. Otherwise, there were no indications of variations. Under the conditions of this study, dosing rats with the test substance by gavage during organogenesis resulted in evidence of maternal toxicity at 3000 mg/kg bw/day and evidence of developmental delay at 3000 mg/kg bw/day. No teratogenicity was observed at any dosage employed, including that which produced maternal toxicity. The NOAEL (No Observed Adverse Effect Level) of the test substance for embryotoxicity, developmental toxicity and maternal toxicity was found to be 1500 mg/kg bw/day when administered orally on gestation days 6-15 to rats.

In a study with New Zealand White rabbits, the animals were exposed by oral gavage during the primary period of organogenesis, i.e., gestation days 6-18, at dose-levels of 50, 200 and 400 mg kg/day (BRRC, 1993). The pregnancy rate was equivalent for all groups. One of 19 pregnant does at 400 mg/kg bw/day exhibited characteristic signs of gasping, labored and audible respiration, and was found dead on the morning of scheduled sacrifice, gestation day 29. No additional signs of maternal toxicity were observed in the 400 mg/kg bw/day group. There was no evidence of maternal toxicity at 200 or 50 mg/kg bw/day. Fetal examination indicated no evidence of embryotoxicity or malformations in any of the treatment groups. There were no effects on mean fetal body weight and no treatment-related differences in the incidences of external, visceral or skeletal variations. Under the conditions of this study, dosing rabbits with the test substance by gavage during organogenesis resulted in 5.3 percent maternal mortality at 400 mg/kg bw/day. No developmental toxicity was observed in this study. The NOEL (No Observed Adverse Effect Level) of the test substance for maternal effects was 200 mg/kg bw/day. The NOAEL for developmental toxicity was at least 400 mg/kg bw/day.

Conclusion

In a one-generation reproduction toxicity study, no reproductive effects were observed at the highest dose tested, 1000 mg/kg bw/d. At 1000 mg/kg bw/d, treatment with TMSPGE resulted in signs of discomfort after dosing (noted for parental females from early /mid gestation onwards), decreased body weight gain of males, and increased absolute and relative liver and kidney weights in parental males and females. Histopathology revealed effects on livers and kidneys of males. Based on these data a NOAEL for parental animals was established at 500 mg/kg bw/d. A NOAEL for reproductive effects was established at 1000 mg/kg bw/d.

In another study in rats, TMSPGE exhibited no adverse effects on the maternal animals or the developing unborn. The no observed adverse effects level in this developmental study was 1500 mg/kg bw/day. For developmental toxicity in rabbits, the no observed adverse effects level was 400 mg/kg bw/day when administered by gavage.

3.2 Initial Assessment for Human Health

TMSPGE is sensitive to rapid hydrolysis, which may occur during testing, such that observed toxicity is likely due primarily to methanol and silanetriols. Abiotic hydrolysis studies show that

hydrolysis products from the test substance undergo continuous, condensation reactions to produce higher molecular weight cyclic and linear siloxanes (the number-average and weight-average molecular weights were determined to be 1102 and 1312, respectively, with 73 percent of the chromatogram represented by a MW range higher than 1000 at one hour). Thus, the polymerization products are in a molecular weight range large enough to be generally considered to have a very limited biological availability.

TMSPGE has been tested for acute toxicity by the oral, dermal, and inhalation routes of exposure. Reported acute oral LD_{50} in rats include a range from >5 ml/kg to 22.6 ml/kg and 7010 mg/kg bw to 16900 mg/kg bw. The dermal LD_{50} is 3.97 ml/kg and the 4-hour inhalation LC_{50} is greater than 2.7 mg/l. TMSPGE is mildly irritating to the skin and eyes. TMSPGE is not a known skin sensitizer in humans or in animals.

TMSPGE was administered in 9 repeated inhalation exposures over two weeks of rats to target vapor concentrations of 0, 75, 225 and 750 mg/m^3. Six rats at the high exposure level (5 males and one female) either died or were sacrificed in a moribund state from three to five days after initiation of the study after succumbing to inanition. The mid and high exposure level groups exhibited signs of nasal discharge and dry and moist rales and bodyweight depressions following a dose-response pattern. Repeated exposure of rats to 119 mg/m^3 of aerosol generated from TMSPGE-hydrolysate for 5 days /week for three weeks did not produce any evidence of laryngeal granuloma formation.

Repeated exposure of rats to TMSPGE by gavage to dose levels of 40, 400 and 1000 mg/kg bw/day for 5 days/week for 4 weeks resulted in no test substance-related organ weights effects or gross or microscopic pathological changes. Under the conditions of this study, the NOAEL for the test substance was found to be 1000 mg/kg bw/day.

TMSPGE did not induce chromosomal damage in mouse bone marrow cells by gavage or inhalation at doses as high as 5000 mg/kg bw/day; or by i.p. when administered in a non-aqueous vehicle. However, TMSPGE induced chromosomal damage in mouse bone marrow cells by i.p., when administered in water. TMSPGE induced gene mutations in mouse lymphoma L1578Y TK cells but did not induce forward mutations in CHO cells. TMSPGE induced SCE in vitro. There are no *in vivo* gene mutation data. There is no evidence to indicate that TMSPGE is tumorigenic based on the results of a dermal study.

In a one-generation reproduction toxicity study, no reproductive effects were observed at the highest dose tested, 1000 mg/kg bw/d. At 1000 mg/kg bw/d, treatment with TMSPGE resulted in signs of discomfort after dosing (noted for parental females from early/mid gestation onwards), decreased body weight gain of males, and increased absolute and relative liver and kidney weights in parental males and females. Histopathology revealed effects on livers and kidneys of males. Based on these data a NOAEL for parental animals was established at 500 mg/kg bw/d. A NOAEL for reproductive effects was established at 1000 mg/kg bw/d.

Three developmental studies have been conducted using TMSPGE. In a rabbit study, the maternal NOAEL was 200 mg/kg bw/day and the developmental NOAEL was 400 mg/kg bw/day (the highest dose tested). In one rat study, the NOAELs for both maternal and developmental toxicity were also at the highest dose tested (1000 mg/kg bw/day). In another rat study, one skeletal variation (unossified anterior arch of the atlas) was observed at the maternally-toxic dose of 3000 mg/kg bw/day (again, the highest dose tested).

Any toxicological effects originating from the parent silane are greatly reduced as a result of the intentional coupling process during use. That is, after curing, the parent silane is consumed and no longer exists; this greatly reduces potential for consumer or worker exposure to the parent compound although exposure to the hydrolysis products may occur.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

TMSPGE is sensitive to hydrolysis, which may occur during preparation of the dosing solutions Rapid hydrolysis of this material produces methanol and silanetriols. The epoxy ring will open to form a diol. It is still attached to the silane molecule. The Si-C bond will not undergo further hydrolysis. The methoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield an epoxy functional silicone resin (oligomer resin).

If the silane is slowly released such that the concentration of the resulting epoxy-functional silanetriol is not high enough to result in polymerization, the silanetriol will exist largely as a monomer. The monomer is known to be water soluble by virtue of the three hydroxy groups on the silicon. It is expected that this silanetriol will have a low Kow (-2.61, estimated) because of these hydroxy groups and so is not expected to bioaccumulate. The water solubility of the silanetriol cannot be measured because of the tendency to condense at concentrations greater than 500 ppm (Merrifield, J. (2003) Personal Communication).

The estimated water solubility of the silanetriol is 7.88×10^6 mg/l. It is known, however, that the silanetriol and small condensation products will only precipitate out of water due to formation of larger, water insoluble polymeric resins.

Acute Toxicity Test Results

The 96-hour LC50 for juvenile rainbow trout (*Oncorhynchus mykiss*) exposed to TMSPGE under static conditions was 237 mg/l (NOEC 180 mg/l) (Annelin and Cerro, 1978). Similar results were obtained with bluegill sunfish (*Lepomis macrochirus*), (LC50 = 276 mg/l) (Annelin and Cerro, 1978). In a semi-static test, the 96-hour LC50 for *Cyprinus carpio* was 55 mg/l (Infracor Degussa Group, 1996). The test material was stirred for about 18 hour in water and filtered; the resulting "aged" solution served as the stock solution. For the interpretation of the results, it should to be taken into account that TMSPGE is sensitive to hydrolysis during the preparation of the stock solution and during the exposure time, and exposure was primarily to the hydrolysis products.

Table 3. Summary of Acute Aquatic Toxicity Test Results (Fish)

Species	Endpoint	Value	Reference
Oncorhynchus mykiss	96-hour LC50	237 mg/l	Annelin and Cerro, 1978
Oncorhynchus mykiss	96-hour NOEC	180 mg/l	Annelin and Cerro, 1978
Lepomis macrochirus	96-hour LC50	276 mg/l	Annelin and Cerro, 1978
Cyprinus carpio	96-hour LC50	55 mg/l	Infracor Degussa Group, 1996

The 48-hour EC50 for *Daphnia magna* exposed to TMSPGE was 710 mg/l (NOEC 250 mg/l) (Machado, 2002). In a second study, the 48-hour EC50 for *Daphnia magna* exposed to TMSPGE was 473 mg/l (NOEC 299 mg/l) (Infracor Degussa Group, 1993a). The test material was stirred for about 18 hour in water and filtered; the resulting "aged" solution served as the stock solution. For the interpretation of the results, it should to be taken into account that TMSPGE is sensitive to hydrolysis during the preparation of the stock solution and during the exposure time, and exposure was primarily to the hydrolysis products. TMSPGE was considered practically non-toxic (48-hour EC50 = 324 mg/l) to *Simocephalus vetulus* (Family Daphnidae) (Annelin and Cerro, 1978).

Table 4. Summary of Acute Aquatic Toxicity Test Results (Daphnia)

Species	Endpoint	Value	Reference
Daphnia magna	48-hour EC50	710 mg/l	Machado, 2002
Daphnia magna	48-hour NOEC	250 mg/l	Machado, 2002
Daphnia magna	48-hour EC50	473 mg/l	Infracor Degussa Group, 1993a
Daphnia magna	48-hour NOEC	299 mg/l	Infracor Degussa Group, 1993a
Simocephalus vetulus	48-hour EC50	324 mg/l	Annelin and Cerro, 1978

In algae, the most sensitive endpoint identified was 72-hour biomass. The 72-hour EC_b50 for *Selenastrum capricornutum* exposed to TMSPGE was 250 mg/l (nominal concentration). Analytical monitoring of the test substance concentration was not conducted. The calculated 96-hour EC50 (cell density) was 260 mg/l. The NOEC was 130 mg/L for cell density, biomass and growth rate (Hoberg, 2002). The 72-hour EC_b50 for *Scenedesmus subspicatus* exposed to TMSPGE was 255 mg/l (Infracor Degussa Group, 1993b) (analytically determined concentrations). The 72-hour EC50 (cell density) was greater than 420 mg/l. The NOEC was 53 mg/l for biomass. The test material was stirred for about 18 hour in water and filtered; the resulting "aged" solution served as the stock solution. For the interpretation of the results, it should to be taken into account that TMSPGE is sensitive to hydrolysis during the preparation of the stock solution and during the exposure time, and exposure was primarily to the hydrolysis products. A 7-day study with *Anabaena flos-aquae* (blue-green algae) indicated a low level of toxicity based on final yield (NOEC = <50 mg/l, LOEC = 50 mg/l, and EC50 = 268 mg/l) and growth inhibition (NOEC = <50 mg/l, LOEC = 50 mg/l, and EC50 = 119 mg/l) (nominal concentrations). The test substance and hydrolytic degradation products are considered of low toxicity to *Anabaena flos-aquae* (Annelin and Cerro, 1978).

Table 5. Summary of Acute Aquatic Toxicity Test Results (Algae)

Species	Endpoint	Value	Reference
Selenastrum capricornutum	72-hour EC_b50	250 mg/l	Hoberg, 2002
Selenastrum capricornutum	72-hour EC_r50	350 mg/l	Hoberg, 2002
Selenastrum capricornutum	96-hour EC50	260 mg/l	Hoberg, 2002
Selenastrum capricornutum	72-hour NOEC	130 mg/l	Hoberg, 2002
Scenedesmus subspicatus	72-hour EC_b50	255 mg/l	Infracor Degussa Group, 1993b
Scenedesmus subspicatus	72-hour EC_r50	>420 mg/l	Infracor Degussa Group, 1993b
Scenedesmus subspicatus	72-hour NOEC	53 mg/l	Infracor Degussa Group, 1993b
Anabaena flos-aquae	*7-day* EC50 (yield)	268 mg/l	Annelin and Cerro, 1978
Anabaena flos-aquae	*7-day* EC50 (growth)	119 mg/l	Annelin and Cerro, 1978
Anabaena flos-aquae	*7-day* NOEC	< 50 mg/l	Annelin and Cerro, 1978
Anabaena flos-aquae	*7-day* LOEC	50 mg/l	Annelin and Cerro, 1978

Chronic Toxicity Test Results

In a 21-day Daphnia reproduction test, the NOEC was greater than or equal to 100 mg/l; the LOEC was greater than 100 mg/l (Infracor Degussa Group, 1993c). The test material was stirred for about 18 hour in water and filtered; the resulting "aged" solution served as the stock solution. For the

interpretation of the results, it should to be taken into account that TMSPGE is sensitive to hydrolysis during the preparation of the stock solution and during the exposure time, and exposure was primarily to the hydrolysis products.

Toxicity to Microorganisms

Bacterial suspensions were exposed to TMSPGE at concentrations of 0, 500, 1000, 1500 and 2000 µl/l, and incubated for approximately 5 hours. Comparison of the amounts of oxygen consumed in the reference and test preparations was used to determine the influence on oxygen consumption by the test substance. The EC10 was 1400 µl/l (= 1520 mg/l; related to the density of 1.07 g/m³) (Huls, 1993a).

4.2 Terrestrial Effects

No data available.

4.3 Other Environmental Effects

No data available.

4.4 Initial Assessment for the Environment

The melting point is <-70 °C, the boiling point is 290°C at 1013 hPa, and the vapor pressure is 0.003 hPa at 20°C. The estimated water solubility of TMSPGE is 1 x 10^6 mg/l at 25°C and the estimated log K_{ow} is -0.9. These values may not be applicable because the chemical is hydrolytically unstable. Photodegradation modeling indicates the half-life in the atmosphere due to the reaction with photochemically induced OH radicals is estimated to be approximately 5.8 hours. However, the overall half-life may be even shorter, as concurrent hydrolysis may also be occurring.

TMSPGE is hydrolytically unstable ($t_{1/2}$ < 1 day) over a range of environmentally relevant pH and temperature. The half-life at pH 5, 7 and 9 was determined at 10, 24.5 and 37°C.

Table 6. The Calculated Half-lives (hours) for Hydrolysis of TMSPGE

Temperature	pH		
	5.0	**7.0**	**9.0**
10.0 °C	0.29	18	0.11
24.5 °C	0.15	6.5	0.13
37.0 °C	0.087	3.3	0.053

Rapid hydrolysis of this material produces methanol and silanetriols. The epoxy ring will open to form a diol. It is still attached to the silane molecule. The Si-C bond will not undergo further hydrolysis. The methoxy groups will be hydrolyzed. Over the pH range investigated, the intermediate silanol products (the mono- and di-ol) were observed to hydrolyze more rapidly than the original tri-alkoxysilane. Consequently, these breakdown products can be considered transient. The stability of the methanol co-product was not considered, but is probably stable under these conditions. The transient silanol groups will condense with other silanols to yield an epoxy functional silicone resin (oligomer resin).

The EQC Level III model was used to evaluate the fate, transport and distribution of TMSPGE between environmental matrices. Based on Level-III modeling, using loading rates for air, soil, and

water of 1000 kg/h for each media, shows the following percent distribution for TMSPGE: Air = 0.6 percent; Soil = 92.5 percent; Water = 6.9 percent; Sediment = 0.00 percent. However, TMSPGE is unlikely to be found in the environment, as this material is hydrolytically unstable. The environmental fate, transport, and distribution of 3-glycidoxypropylsilanetriol were evaluated to provide a more realistic assessment of TMSPGE. Results from the simulation suggest that > 99% of the total steady-state mass of 3-glycidoxypropylsilanetriol will reside in the water and soil compartments, and will not be found in air or sediment. It is expected that 65-85% of the 3-glycidoxypropylsilanetriol produced by the steady-state hydrolysis of 3-glycidoxy-propyltrimethoxysilane will degrade in about 20-35 days. TMSPGE is not readily biodegradable. Note that hydrolysis of this material occurs rapidly, such that the observed biodegradation is mainly of the hydrolysis products (methanol and silanetriols). Bioaccumulation of TMSPGE is not anticipated since this material is hydrolytically unstable.

TMSPGE is a moisture-reactive material that hydrolyzes rapidly (half-life of approximately 3 minutes to about 6.5 hours, depending on the aqueous solution temperature, pH and concentration of bufferHydrolysis of TMSPGE results in the formation of silanetriols which can then condense to form highly cross-linked, high molecular weight polymers, further reducing the potential for exposure.

Since TMSPGE is sensitive to hydrolysis, which may occur during preparation of the dosing solutions and/or during the testing, the observed toxicity is likely due to the hydrolysis products methanol and silanetriols. The 96-hour LC50 for juvenile rainbow trout (static) exposed to TMSPGE was 237 mg/l (NOEC 180 mg/l). In a semi-static test with carp, the 96-hour LC50 was 55 mg/l (NOEC 30 mg/l). Similar results were obtained with bluegill sunfish, (LC50 = 276 mg/l). The 48-hour EC50 for *Daphnia magna* exposed to TMSPGE were 710 mg/L (NOEC 250 mg/l) and 473 mg/l (NOEC 299 mg/l). In a second study the test substance is considered practically non-toxic (48-hour EC50 = 324 mg/l) to a second aquatic invertebrate (*Simocephalus vetulus*). In a 21-day daphnia reproduction test, the NOEC was greater than or equal to 100 mg/l. In algae, the most sensitive endpoint identified was 72-hour biomass. The 72-hour EC_b50 for *Selenastrum capricornutum* exposed to TMSPGE was 250 mg/l. The 96-hour EC50 (cell density) was 260 mg/l. The NOEC was 130 mg/L for cell density, biomass and growth rate. The 72-hour EC_b50 for *Scenedesmus subspicatus* exposed to TMSPGE was 255 mg/l. The 72-hour EC50 (cell density) was greater than 420 mg/l. The NOEC was 53 mg/l for biomass. A 7-day study with blue-green algae indicated a low level of toxicity based on final yield (NOEC = 0 mg/l, LOEC = 50 mg/l, and EC50 = 268 mg/l) and growth inhibition (NOEC = 0 mg/l, LOEC = 50 mg/l, and EC50 = 119 mg/l). The test substance and hydrolytic degradation products are considered of low toxicity to *Anabaena flos-aquae.*

The EC10 for bacterial suspensions exposed to TMSPGE for about 5 hours was 1400 µl/l.

5 RECOMMENDATIONS

TMSPGE is currently a low priority for further work. The chemical possesses properties indicating a hazard for the environment (aquatic toxicity) and a hazard for human health (several positive genetic mutation results in vitro and positive results in one chromosomal aberration study conducted in vivo). Based on data presented by the Sponsor country, exposure to humans and the environment is anticipated to be low under normal manufacturing and use conditions, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

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S I D S

Dossier

Existing Chemical	:	ID: 2530-83-8
CAS No.	:	2530-83-8
EINECS Name	:	[3-(2,3-epoxypropoxy)propyl]trimethoxysilane
EC No.	:	219-784-2
Molecular Formula	:	C9H20O5Si

Producer related part

Company	:	Epona Associates, LLC
Creation date	:	17.06.2003

Substance related part

Company	:	Epona Associates, LLC
Creation date	:	17.06.2003
Status	:	
Memo	:	SEHSC
Printing date	:	15.09.2005
Revision date	:	
Date of last update	:	15.09.2005
Number of pages	:	155
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name :
Smiles Code : CO[Si](CCCOCC1CO1)(OC)OC
Molecular formula : C9H20O5Si
Molecular weight : 236
Petrol class :

18.06.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance
Substance type : organic
Physical status : liquid
Purity : > 98 - 100 % v/v
Colour : clear, pale
Odour : ester

09.12.2004 (20)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1-(Glycidyloxy)-3-(trimethoxysilyl)propane

13.06.2003

A-187

13.06.2003

Dynasylan GLYMO

29.03.2004

DZ 6040

13.06.2003

gamma-Glycidoxypropyltrimethoxysilane

24.03.2004

Glycidoxypropyltrimethoxysilane

13.06.2003

Glycidyl 3-(trimethoxysilyl)propyl ether

13.06.2003

Glycidyloxypropyltrimethoxysilane

13.06.2003

KBM 403

13.06.2003

KBM 430

13.06.2003

NUCA 187

13.06.2003

Silan A-187

24.03.2004

Silane A-187

24.03.2004

Silane Y-4087

24.03.2004

Silane Z 6040

13.06.2003

Silane, trimethoxy[3-(oxiranylmethoxy)propyl]-

13.06.2003

Silane, [3-(2,3-epoxypropoxy)propyl]trimethoxy-

13.06.2003

Silicone A-187

24.03.2004

Silicone KBM 403

13.06.2003

Silquest A-187 silane

24.03.2004

TMSPGE

24.03.2004

Union Carbide A-187

24.03.2004

Y-4087

24.03.2004

Z 6040

13.06.2003

[.gamma.-(Glycidyloxy)propyl]trimethoxysilane

13.06.2003

[3-(2,3-Epoxypropoxy)propyl]trimethoxysilane

13.06.2003

[3-(Glycidyloxy)propyl]trimethoxysilane

13.06.2003

[[3-(Trimethoxysilyl)propoxy]methyl]oxirane

13.06.2003

1.3 IMPURITIES

Purity	:	typical for marketed substance
CAS-No	:	67-56-1
EC-No	:	
EINECS-Name	:	Methanol
Molecular formula	:	
Value	:	< .1 - .2 % v/v

26.06.2003

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : = 1702.167 - tonnes in 2002

Remark : The production volume provided reflects the Sponsor countries production and use (2002). TMSPGE is produced in North America, Europe and Asia.

Source : SEHSC
14.07.2004

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : other

Remark :

	Metric Tons	Percent
Use resulting in inclusion into or onto matrix	1574.549	92.5
Nondispersive use	127.618	7.5
Total	1702.167	

Source : SEHSC
Flag : confidential
18.06.2003

Type of use : use
Category :

Remark : Component in Adhesives and Sealants
TMSPGE is used most frequently in minor proportions (generally <2%) as an adhesion promoter, coupling agent, or cross-linker in adhesives, sealants, and encapsulants. Regardless of the particular adhesive or sealant with which it is mixed, TMSPGE is essentially never used at concentrations higher than ten percent. A level of one to two percent by weight is commonly recommended as a "starting-point" in many formulations.

Although the precise function of TMSPGE varies based on the sealant or adhesive to which it is added, it usually becomes immobilized during use due to attachment to minerals or polymers in the adhesive or sealant. In silicone sealants, much of the TMSPGE reacts with hydroxyl groups on silanol end-capped silicone polymers, with hydroxyl on the surface of silica reinforcing fillers, or with trace water introduced on mineral filler surfaces. In instances where TMSPGE is used as an additive to improve the adhesion of

water-based or latex caulks and sealants, TMSPGE is polymerized and immobilized during the formulation process by reacting with water (hydrolysis) and mineral surfaces that are present in these products.

TMSPGE is sometimes used in solvent-based or 100% actives sealants, adhesives, and encapsulants. In these adhesive applications, TMSPGE becomes partially immobilized by reaction with the mineral fillers during the manufacturing process and reacts completely with the organic polymer during the curing process. Thus, when acting as a "coupling agent" or an "adhesion promoter" with any of the above adhesives or sealants, TMSPGE becomes covalently bonded to very high molecular weight polymers and minerals. This bonding to a high molecular weight material greatly reduces potential exposures.

Component of Coatings on Glass Fibers
Another major application for TMSPGE is as a raw material in the manufacture of reinforcing glass fibers. During its use, TMSPGE is deliberately converted to the silanol form by hydrolyzing it in acidified water at concentrations usually below 20% by weight and typically between 5 and 10% by weight. After the hydrolysis reaction is complete, the aqueous solutions of the corresponding silanol are further diluted with water and possibly other ingredients, such as emulsions of organic polymers, lubricants, surfactants, wetting agent, and other processing aids. These processes result in destruction of the parent silane and result in the formation of hydrolysis products.

During application of these solutions, called sizes or finishes, to the glass fibers, there no longer exists a potential for worker exposure TMSPGE. After the fibers are dried, the silanols are bonded directly to the glass fibers. This immobilization and chemical reactivity eliminates further end-user exposure to the hydrolysis products. The final end-user takes these fibers and mixes them with organic resins to make composites.

Component of Foundry Additives
Less than 5% of the production volume of TMSPGE is consumed as an additive to a foundry resin. In this use, a resin producer blends a phenolic or furan resin (polymer), which contains some water, with a small quantity of TMSPGE, typically between 0.01 and 0.1 %. As the TMSPGE is blended, it hydrolyzes to silanol and oligomer forms. Moreover, TMSPGE reacts with the resin during curing reactions. Therefore, potential exposure to unreacted TMSPGE is minimal.

09.12.2004

1.7.1 DETAILED USE PATTERN

Industry category	:	15/0 other
Use category	:	55/0 other
Extra details on use category	:	No extra details necessary No extra details necessary

Emission scenario document : not available
Product type/subgroup :
Tonnage for Application :
Year :
Fraction of tonnage for application :
Fraction of chemical in formulation :
Production : :
Formulation : :
Processing : :
Private use :
Recovery :

Remark : Industry Category:

Industry Category	Metric Tons	%
Chemical industry: chemicals used in synthesis;	749.337	44.02
Polymers industry;	578.780	34.00
Textile processing industry;	168.515	9.90
Paints, lacquers and varnishes industry;	205.535	12.07
Total	1702.167	99.99

Use Category:

Use Category:	Metric Tons	%
Adhesive, binding agents;	1565.508	91.97
Intermediates;	121.237	7.12
Surface-active agents;	15.422	0.91
Total	1702.167	100.00

General information on exposure:
The number of individuals likely to be exposed to TMSPGE is small and the potential levels of TMSPGE to which these individuals may be exposed are expected to be low, as explained below.

Given its chemical and physical properties, manufacturing and processing of TMSPGE generally occurs in enclosed equipment. Thus, the majority of workers who may be potentially exposed to TMSPGE are those who transfer materials from reaction vessels to shipping containers or who are exposed to the material during cleaning operations. More than 50 air samples, collected during production handling at ambient temperature in production plants, have shown no detectable TMSPGE. The detection limit ranged from 0.05 to 1 ppm, depending upon the volume of air sampled (Collins, Silverstein, and Hobbs, 1984).

Necessary engineering controls during production include proper ventilation, containment, safety equipment, and actual hardware designed to minimize exposure through splashing or to TMSGPE as a vapor in the air. Transfer of this material is usually in closed pipes rather than in open systems to minimize loss of this material (via hydrolysis) although some customers do transfer the material in open systems. TMSPGE rapidly hydrolyzes and its saturated vapor

concentration at ambient temperatures would not exceed 12 ppm, reducing the potential for inhalation exposure to the parent compound. There may be exposure to one of the hydrolysis products, methanol. The remaining hydrolysis products (hydrolysates of TMSPGE) will have a much lower vapor pressure than the parent compound and thus vapor pressure to these products will remain low.

The silane is used as an adhesion promoter in adhesives and sealants (caulks), and is a small component in these products. Although there is no consumer use of the pure substance, it is usually used as a minor component in such adhesives and sealants in the consumer market. In these uses, the silane is reacted through hydrolysis to form methanol and silanetriol and is no longer present as the parent compound. Exposure of the public or the environment to this material is possible mainly from accidental releases and would likely be of a short duration. Exposure via inhalation following such releases is unlikely based on a low saturated vapor concentration (12 ppm). As TMSPGE hydrolyzes, its saturated vapor concentration at ambient temperatures would not exceed 12 ppm, further reducing the potential for inhalation exposure to the parent compound. There may be vapor exposure to one of the hydrolysis products, methanol. The remaining hydrolysis products (hydrolysates of TMSPGE) will have a much lower vapor pressure than the parent compound and thus vapor exposure to these hydrolysates will be low.

Production Volumes and Use Pattern:
TMSPGE is used most frequently in minor proportions (generally <2 percent) as an adhesion promoter, coupling agent, or cross-linker in adhesives, sealants, and encapsulants. Regardless of the particular adhesive or sealant with which it is mixed, TMSPGE is usually never used at concentrations higher than six percent, at least among companies that are members of the Silicones Environmental Health and Safety Council. However, one sealant product with a higher percentage (of 10-30 percent) TMSPGE was identified (Carboline, 2004). A level of one to two percent by weight is commonly recommended as a "starting-point" in many formulations.

Although the precise function of TMSPGE varies based on the sealant or adhesive to which it is added, it usually becomes immobilized during use due to attachment to minerals or polymers in the adhesive or sealant. In silicone sealants, much of the TMSPGE reacts with hydroxyl groups on silanol end-capped silicone polymers, with hydroxyl on the surface of silica reinforcing fillers, or with trace water introduced on mineral filler surfaces. In instances where TMSPGE is used as an additive to improve the adhesion of water-based or latex caulks and sealants, TMSPGE is polymerized and immobilized during the formulation process by reacting with water (hydrolysis) and mineral surfaces that are present in these products.

TMSPGE is sometimes used in solvent-based or 100 percent actives sealants, adhesives, and encapsulants. In these adhesive applications, TMSPGE becomes partially immobilized

by reaction with the mineral fillers during the manufacturing process and reacts completely with the organic polymer during the curing process. Thus, when acting as a "coupling agent" or an "adhesion promoter" with any of the above adhesives or sealants, TMSPGE becomes covalently bonded to very high molecular weight polymers and minerals. This bonding to a high molecular weight material greatly reduces potential exposures.

Component of Coatings on Glass Fibers:
Another major application for TMSPGE is as a raw material in the manufacture of reinforcing glass fibers. During its use, TMSPGE is deliberately converted to the silanol form by hydrolyzing it in acidified water at concentrations usually below 20 percent by weight and typically between 5 and 10 percent by weight. After the hydrolysis reaction is complete, the aqueous solutions of the corresponding silanol are further diluted with water and possibly other ingredients, such as emulsions of organic polymers, lubricants, surfactants, wetting agent, and other processing aids. These processes result in destruction of the parent silane and result in the formation of hydrolysis products.

During application of these solutions, called sizes or finishes, to the glass fibers, there no longer exists a potential for worker exposure to TMSPGE. After the fibers are dried, the silanols are bonded directly to the glass fibers. This immobilization and chemical reactivity eliminates further end-user exposure to the hydrolysis products. The final end-user takes these fibers and mixes them with organic resins to make composites.

Component of Foundry Additives:
Less than 5 percent of the production volume of TMSPGE is consumed as an additive to a foundry resin. In this use, a resin producer blends a phenolic or furan resin (polymer), which contains some water, with a small quantity of TMSPGE, typically between 0.01 and 0.1 percent. As the TMSPGE is blended, it hydrolyzes to silanol and oligomer forms. Moreover, TMSPGE reacts with the resin during curing reactions. Therefore, potential exposure to unreacted TMSPGE is minimal.

Source **:** SEHSC
09.12.2004

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Source of exposure : Human: exposure by production
Exposure to the : Substance

Remark : The number of workers that may be exposed to TMSPGE during its manufacture or handling is small. Given its chemical and physical properties, manufacturing and processing of TMSPGE occurs in enclosed equipment. Thus, the only workers who may be potentially exposed to TMSPGE are those who transfer materials from reaction vessels to shipping containers or who are exposed to the material during cleaning operations. Necessary engineering controls during production 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 rather than in open systems to minimize loss of this material (hydrolysis) although some customers do transfer the material in open systems. TMSPGE rapidly hydrolyzes and its saturated vapor concentration at ambient temperatures falls to below 12 ppm, reducing the potential for inhalation exposure.
Transport is a source of potential exposure through accidental releases. The material is shipped via air, road, and marine in returnable intermediate bulk containers (IBCs), steel drums, steel pails and steel cans and non-returnable IBCs.

09.12.2004

Source of exposure : Human: exposure of the consumer/bystander
Exposure to the : Substance

Remark : TMSPGE is transported from the production site as the parent silane to processors/formulators. After curing the parent silane is consumed and no longer exists; this greatly reduces potential for consumer or worker exposure.
The silane is used as an adhesion promoter in adhesives and

sealants (caulks), and is a small component in these products. Although there is no consumer use of the pure substance, it will be used as a minor component in such adhesives and sealants in the consumer market. In these uses, the silane is reacted through hydrolysis and is no longer present. Exposure of the public or the environment to this material is possible only from accidental releases and would be of a short duration. Exposure via inhalation following such releases is unlikely based on a low saturated vapor concentration (12 ppm). As TMSPGE hydrolyzes, its saturated vapor concentration at ambient temperatures falls to below 12 ppm, further reducing the potential for inhalation exposure to any residual TMSPGE.

09.12.2004

Source of exposure : other: General
Exposure to the : Substance

Remark : Generally, TMSPGE is used by the processor/formulator at levels <2%, although some uses are as high as 6%. Once TMSPGE is added to an industrial product, the parent silane is intentionally reacted with the components of the formulation and is generally present as the parent silane at 0.1-0.2% until after curing (use). After curing the parent silane is consumed and no longer exists, which greatly reduces the potential for exposure. TMSPGE polymerizes during use.

22.03.2004

Source of exposure : other: Environment: General
Exposure to the : Substance

Remark : The reactive nature of this material destroys the parent material in any moisture-containing environment, thus limiting environmental exposure to the silane. The parent material is hydrolyzed in a spill situation; the rapid hydrolysis means that the parent silane is unlikely to be found in the environment.
TMSPGE is a moisture-reactive material that hydrolyzes rapidly (half-life of < 3 seconds to about 6.5 hours, depending on the aqueous solution temperature, pH and concentration of buffer). In the unlikely event of an accidental spill, TMSPGE could enter the environment through evaporation (limited by the very low saturated vapor concentration) or through direct contamination of surface soil and surface waters. TMSPGE will react with the humidity in the air, moisture in the soil, or directly with the water of streams, lakes, and rivers. The rate of hydrolysis will depend upon the nature of the spill. If TMSPGE is in contact with large amounts of liquid water (either surface water or cleaning solutions) hydrolysis will occur very rapidly (minutes or hours). However, if TMSPGE is only in contact with low humidity air, hydrolysis can take considerably longer. Hydrolysis of TMSPGE results in highly cross-linked, high molecular weight polymers, further reducing the potential for exposure.

09.12.2004

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	< -70 °C
Sublimation	:	
Method	:	other
Year	:	1991
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The purity of the test substance was not identified in this study. However, the purity of this material is generally greater than 98%, and can be considered at least 98% pure during the conduct of this test.
Result	:	Melting Point <-70°C at standard temperature and pressure
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

14.07.2004 (20)

2.2 BOILING POINT

Value	:	= 262.4 °C at 1013 hPa
Decomposition	:	
Method	:	other: ebulliometer
Year	:	1979
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Normal boiling point of 262 +/- 3 C was estimated by extrapolating lower-temperature vapor pressure data in a log(P) vs 1/T plot. Re-analysis of this data in 2002 resulted in a vapor pressure fit that predicts NBP = 262.4 C.
Result	:	Data Ranges: 115 - 201 C, 4- 140 mmHg The vapor pressure of (MeO)3SI(CH2)3OCH2CH O>CH2 (I.E. Z-6040) was determined. The presence of impurities (detected by GLC) caused the pressure to vary during the measurements. This resulted in larger deviations between measured data and data obtained from the Antoine Interpolation Equation.
Test substance	:	Purity = 97.7%
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

14.07.2004 (47)

Value	:	= 262 °C at 1013 hPa
Decomposition	:	no
Method	:	other
Year	:	1985
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Calculated
Result	:	Coefficients for the Halm-Stiel equation were derived from regression of the following measured vapor pressure data:

T (°C)	P (mm Hg)	P (Pa)	Reference
116	4	507	Flaningam 1979
125	5	667	Koetzsch and Vahlensieck 1973
132	10	1280	Flaningam 1979
135	4	533	Plueddemann and Stark 1967
153	23	3066	Flaningam 1979
175	55	7371	Flaningam 1979
200	100	13330	Street 1964
201	140	18595	Flaningam 1979

Test condition : The best-fitting Halm-Stiel vapor pressure equation was used to extrapolate boiling point from vapor pressures measured at temperatures ranging from 100-201°C.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

Purity of the test substance was measured by gas chromatography and reported as 98%.

Conclusion : Although the Halm-Stiel equation is valid for interpolations, serious error may result from extrapolations outside the limits of measured data. Hence, significant error may be associated with the reported boiling point for the test substance (CAS No. 2530-83-8). Nonetheless, the result is comparable to values obtained from the literature and other studies.

Reliability : (2) valid with restrictions
Review of the study report and raw data indicate that the results are scientifically defensible and adequate for assessing the boiling point of the test substance (CAS No. 2530-83-8). The study is considered to be reliable with the following restrictions:
- study was not conducted under GLP
- methods used to generate vapor pressure/temperature data were not documented

17.03.2004 (46) (55) (65) (67) (69)

Value : = 290 °C at 1013 hPa
Decomposition :
Method : other: measured
Year : 1997
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : The purity of the test substance was not identified in this study. However, the purity of this material is generally greater than 98%, and can be considered at least 98% pure during the conduct of this test.

Reliability : (2) valid with restrictions
14.07.2004 (68)

2.3 DENSITY

Type : relative density
Value : = 1.069 at 25 °C
Method :
Year : 2001
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions

17.03.2004 (20)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .003 hPa at 20 °C
Decomposition : no
Method :
Year : 1985
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Measured vapor pressure and temperature data

T (°C)	P (mm Hg)	P (Pa)	Reference
116	4	507	Flaningam 1979
125	5	667	Koetzsch and Vahlensieck 1973
132	10	1280	Flaningam1979
135	4	533	Plueddemann and Stark 1967
153	23	3066	Flaningam 1979
175	55	7371	Flaningam 1979
200	100	13330	Street 1964
201	140	18595	Flaningam 1979

The extrapolated vapor pressure of the test substance at 20°C was 0.3 Pa, based on both the Halm-Stiel equation and the Antoine equation.

Source : Dow Corning Corporation
Test condition : The Halm-Stiel and Antoine equations were used to extrapolate vapor pressure at 20°C from vapor pressures measured at elevated temperatures ranging from 100-201°C.
Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

Purity of the test substance was measured by gas chromatography and reported as 98%.

Conclusion Although the Halm-Stiel and Antoine equations are valid for interpolations, serious error may result from extrapolations outside the limits of measured data. Hence, significant error may be associated with the estimated vapor pressure of the test substance (CAS No. 2530-83-8) at 20°C. Nonetheless, measured vapor pressures obtained at elevated temperatures are comparable to values obtained from other studies.

Reliability : (2) valid with restrictions
Review of the study report and raw data indicate that the results are scientifically defensible and adequate for assessing the vapor pressure of the test substance (CAS No. 2530-83-8). The study is considered to be reliable with the following restrictions:
· study was not conducted under GLP
· methods used to generate vapor pressure/temperature data were not documented
· vapor pressure at 20°C is extrapolated from vapor pressures measured at elevated temperatures ranging from 100-201°C.

Flag : Critical study for SIDS endpoint

17.03.2004 (46) (55) (65) (67) (69)

Value : = .3 hPa at 20 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
17.03.2004 (25)

Value : < 1.33 hPa at 20 °C
Decomposition :
Method :
Year : 2001
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
17.03.2004 (20)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = -.9 at 25 °C
pH value :
Method : other (calculated)
Year : 2000
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : KOWWIN® (version 1.66)
Remark : Because the material is hydrolytically unstable and rapidly generates methanol when added to water, endpoints such as octanol/water partition coefficient can not be measured. Nonetheless, these endpoints provide valuable information on the behavior of the material and are needed to evaluate the transport and distribution (i.e., fugacity) of TMSPGE between environmental matrices. Therefore, octanol/water partition coefficient was estimated using KOWWIN® (version 1.66).
Result : Output from the models predict that TMSPGE has a log Kow of -0.9
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
09.12.2004 (74)

Partition coefficient : octanol-water
Log pow : -2.6 at 25 °C
pH value :
Method : other (calculated)
Year : 2004
GLP : no
Test substance : other TS

Method : This estimate was obtained using the structure activity relationship models provided in EPISuite Version 3.10.

Remark	:	3 Glycidoxypropyl-trimethoxysilane is hydrolytically unstable and will hydrolyze upon contact with water or water vapor. As such, 3 glycidoxypropyl-trimethoxysilane is not likely to exist in the environment but will hydrolyze to methanol and 3 glycidoxypropyl-silanetriol.
Test substance	:	3 glycidoxypropyl-silanetriol
Reliability	:	(2) valid with restrictions

09.12.2004 (74)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 1000 g/l at 20 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	very soluble (> 10000 mg/L)
Stable	:	no
Deg. product	:	
Method	:	other: WSKOWWIN® (version 1.40)
Year	:	2000
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Because the material is hydrolytically unstable and rapidly generates methanol when added to water, endpoints such as water solubility can not be measured. Nonetheless, these endpoints provide valuable information on the behavior of the material and are needed to evaluate the transport and distribution (i.e., fugacity) of TMSPGE between environmental matrices. Therefore, water solubility was estimated using WSKOWWIN® (version 1.40)
Result	:	Output from the models predict that TMSPGE has a water solubility of 1.0 x 10 6 mg/L Water Solubility Estimate from Log Kow (WSKOW v1.41): Water Solubility at 25 deg C (mg/L): 1e+006 log Kow used: -0.92 (estimated) melt pt used: -70.00 deg C
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

09.12.2004 (74)

Solubility in	:	Water
Value	:	7900 g/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Method	:	This estimate was obtained using the structure activity relationship models provided in EPISuite Version 3.10.
Remark	:	3 Glycidoxypropyl-trimethoxysilane is hydrolytically unstable and will hydrolyze upon contact with water or water

vapor. As such, 3 glycidoxypropyl-trimethoxysilane is not likely to exist in the environment but will hydrolyze to methanol and 3 glycidoxypropyl-silanetriol.

Result : Water solubility of 3 glycidoxypropyl-silanetriol is 7.9x10(6) mg/L

Reliability : (2) valid with restrictions

09.12.2004 (74)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = 110 °C
Type : closed cup
Method : other: Pensky-Martens closed cup ASTM D93
Year : 2001
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions

17.03.2004 (20)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 5.8 hour(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated)
Year	:	1999
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	APOWIN® (version 1.90)
Result	:	Output from the models predict that TMSPGE has an atmospheric half-life (hydroxyl radical oxidation) of 5.8 hours.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

13.07.2004 (74)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	= 6.5 hour(s) at 24.5 °C
t1/2 pH9	:	= .1 hour(s) at 24.5 °C
Deg. product	:	
Method	:	OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year	:	2000
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	OECD 111 and OPPTS 835.2110/835.2130
Remark	:	According to the definition put forth in the test guidelines, the test material was found to be hydrolytically unstable (t1/2<1 year) over a range of environmentally relevant pH and temperature conditions. At 24.5 °C, conversion to the final silanetriol was predicted to reach 99.9% in = 2.8 days. The results given in this summary for the hydrolysis of [3-(2,3-epoxypropoxy)propyl]-trimethoxysilane at 24.5 °C are consistent with kinetic data published by Pohl and Osterholtz (Polymer Science and Technology, 1985, 27, 157-170). The described study was not designed to monitor the subsequent condensation reaction involving the silanetriol hydrolysis product which has been shown by Pohl and Osterholtz (1985) to be acid-base catalyzed. Using their results, it was concluded that for the test material concentration (5x10-4 M) used during the study described herein,

condensation would not be significant on the timescale of the hydrolysis experiment.
TMSPGE is a highly reactive chemical and rapidly hydrolyzes to methanol and 3-glycidoxypropyl-silanetriol (R-Si(OH)3 where R = -(CH2)3OCH2CHOCH2).

Result : Nominal = 5x10-4 M (~110 mg/L)
Concentration not directly measured; rate constants extracted
from changes in analytical response for each component.

pH	5.0	7.0	9.0
t1/2 (hours) @			
10.0 °C:	0.29	18	0.11
24.5 °C:	0.15	6.5	0.13
37.0 °C:	0.087	3.3	0.053

Table 1. Kinetic Constants for Hydronium, Hydroxide, and Solvent
(H2O) Catalyzed Hydrolysis Reactions of [3-(2,3-epoxypropoxy)propyl]trimethoxysilane at 24.5 °C

Constant (units)	1st hydrolysis step	2nd step	3rd step
kH3O+ (M-1 s-1)	131	310	354
k-OH (M-1 s-1)	143	957	1850
k0, est. (s-1)	2.2x10-6	1.3x10-5	1.8x10-5

Over the pH range investigated, the intermediate silanol products
(the mono- and di-ol) were observed to hydrolyze more rapidly than
the original tri-alkoxysilane. Consequently, these breakdown products
can be considered transient. The stability of the methanol co-product
was not considered, but is probably stable under these conditions.

Source : SEHSC

Test condition : The consecutive hydrolysis reactions (@ pH 5.0, 7.0 and 9.0; at 10, 24.5 and 37.0 deg C) were followed by high performance liquid chromatography (HPLC) with element specific detection for silicon using inductively coupled plasma
atomic emission spectroscopy (ICP-AES) using acetate and tris(hydroxymethyl)aminomethane buffers of varying concentrations. The data was modeled by multiple linear regression to determine quantitatively the effect of pH, i.e. hydronium and hydroxide ion concentrations, and buffer concentration on rates of hydrolysis.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

The identity and purity of the test substance were determined during a separate characterization study conducted according to EPA TSCA Good Laboratory Practice Standards. The purity of the test material was measured as 99+%.

Conclusion : According to the definition put forth in the test guidelines,
the test material was found to be hydrolytically unstable

(t1/2<1 year) over a range of environmentally relevant pH and temperature conditions. At 24.5 °C, conversion to the final silanetriol was predicted to reach 99.9% in < 2.8 days.

Reliability : (2) valid with restrictions
Review of the study report and raw data indicate the results are scientifically defensible and adequate for assessing the stability in water of the test substance

Flag : Critical study for SIDS endpoint

24.03.2004 (56) (70)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product : yes
Method : other: in vitro hydrolysis
Year : 2001
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Experimental in vitro procedure for determining the approximate molecular weight distribution of test article hydrolysis products resulting from exposure to gastric juice simulant - no recognized guideline available.

Remark : An in vitro study was designed to approximate the molecular weight distribution of the reaction products that would result from the hydrolysis, and subsequent condensation, of test article when mixed with gastric juice. Quantitation was not conducted. Based on the qualitative analytical results, hydrolysis products from the test substance underwent continuous condensation reactions to produce higher molecular weight cyclic and linear siloxanes.
The study described above was not designed to monitor the subsequent (> 4 hrs) condensation reactions.

Result : The GPC chromatograms consisted primarily of one major low molecular weight peak, with a slight lower molecular weight shoulder, plus a partially resolved smaller peak of lower molecular weight.
The major peak was shifted to a higher molecular weight in the 4-hr sample in comparison to the 1- hr sample. In addition, the 4-hr sample showed a decrease in the relative size of the lower molecular weight shoulder and peak compared to the 1-hr sample.
At the 1-hr reaction time, the GPC chromatogram showed Mn=1102, Mw=1312 with 73 area % of the chromatogram higher than MW=1000. The 4-hr sample had an overall molecular weight of Mn=1269, Mw=1524 with 84 area % of the chromatogram higher than MW=1000.
ESI-MS analyses showed that some fully hydrolyzed products and trace amount of the partially hydrolyzed products were detected at both of the reaction times. The intensities of these hydrolysis products decreased over the time period, again, as a result of continuous condensation reactions.
The results of the ESI-MS were in good agreement with the NMR results. Both cyclic and linear condensation products were detected. Based upon the relative peak intensities in the ESI-MS spectra, the majority of the condensation

products observed are cyclics.
Based on the NMR results, all data agrees with the findings from the GPC and ESI-MS analyses-- that is the condensation reactions continued over the 4 hour period of time that the study was conducted.
Breakdown products from hydrolysis: methanol and silanol. The stabilities of methanol and silanol were not measured. However, silanols will undergo condensation reactions to form siloxanes in general. The stabilities of silanols lie in the order R3SiOH > R2Si(OH)2 > RSi(OH)3, with the bulkier R groups lending more stability to the SiOH function (Smith, A. L., The Analytical Chemistry of Silicones; Wiley, New York, 1991; 112, 12).

Quantitation was not conducted. Based on the qualitative analytical results, hydrolysis products from the test substance underwent continuous, condensation reactions to produce higher molecular weight cyclic and linear siloxanes.

Description of solubility : Soluble

Breakdown products: Yes, methanol and transient silanol materials

pH value: ~ 0.1 = pH of the test system
Concentration: ~ 23% v/v = Concentration of the test solution
Temperature °C: ~ 22 °C
Value (mg/L) at temperature °C: Quantitation was not conducted. Based on the qualitative analytical results, hydrolysis products from the test substance underwent continuous, condensation reactions to produce higher molecular weight cyclic and linear siloxanes.

Description of solubility : Soluble

pH value(a) and concentration(b) at temperature °C: pH = ~ 0.1 and 3.2 x 105 (mg/L)(c) of TMSGPE/1N HCL at ~ 22 °C

Breakdown products: Yes, methanol and transient silanol materials
(a)= pH of the test system
(b)= Concentration of the test solution
(c)= Calculation as follows:

Density of TMSGPE: 1.070 g/ml (obtained from Gelest Inc. catalog) 0.3 ml (TMSGPE)/1ml (1N HCL) x 1.070 g/ml x 99.18% x 1000 mg/g x 1000 ml/1L(1N HCL) = 3.2 x 105 mg/L

Source : Dow Corning Corporation

Test condition : Analytical procedures: 0.6 ml of the neat TMSPGE and 2.0 ml of 1N HCL [final concentration of test substance ~ 23% (v/v)] were mixed in a vial to simulating gastric conditions. The solution was allowed to equilibrate at room temperature for approximately 1 hr & 4 hrs prior to analysis.
Temperature: Room temperature (~ 22 °C)
Replicates: A single vessel (consisting of a glass bottle with a polystyrene-sealed screw caps) was used per time

point. Vessels were not sterilized.
Co-solvent: None.

Gel permeation chromatography (GPC) was used to determine the relative molecular weight distribution (MWD) of the hydrolysis and condensation products. The chromatographic equipment consisted of a Waters 600 pump, a Waters 717 autosampler and a Waters 410 differential refractometer. The separation was made with two PLgel 5 um Mixd-C columns (Polymer Laboratories, 300 mm x 7.5 mm, molecular weight separation range of 200 to 2,000,000), preceded by a PLgel 5 um guard column (50 mm x 7.5 mm).
The analyses were performed using certified grade THF flowing at 1.0 ml/min as the eluent, and the columns and detector were both heated to 35 °C.

Samples obtained at the 1-hr and 4-hr reaction times were analyzed by GPC .The GPC sample was prepared at ~ 1% (w/v) of the TMSGPE/1N HCl solution in THF, and filtered through a 0.45 um PTFE syringe filter into a glass autosampler vial. An injection volume of 100 ul was used and data was collected for 25 minutes per injection..

Characterization of the hydrolysis and condensation products was determined by both nuclear magnetic resonance spectroscopy (NMR) and electrospray ionization mass spectrometry (ESI-MS).

A Varian Mercury 400 MHz FT-NMR spectrometer equipped with a 16 mm silicon free multinuclear 13C/29Si probe was used. 1H, 13C and 29Si NMR spectra were acquired at the two reaction times on NMR sample of ~ 3.5:1 (v/v) of the TMSGPE/1N HCl solution and D2O.

The ESI-MS analyses were carried out with a PE Sciex API 300 triple quadrupole (QQQ) mass spectrometer and a Bruker Fourier transform ions cyclotron resonance mass spectrometer (FTICR-MS). ESI-MS analysis was conducted through direct infusion of a sample of ~1 ul:5 ml (v/v) of the TMSGPE/1N HCl solution and CHCl3/CH3CN (1:1, v/v) co-solvent at the two reaction times.

Data treatment: For GPC analysis, molecular weight averages were determined relative to a calibration curve (3rd order) created using polystyrene standards covering the molecular weight range of 580 to 2,3000,000. Also, the area percent values were not only relative to the polystyrene standards, but the responses of the higher and lower molecular weight species. Data collection and processing was performed using PE Nelson Access*SEC software.

Based on the NMR peak integration and chemical shift, percentages of each type of produced species at the two reaction times were determined.

The ESI-MS instrument was calibrated with a Hewlett Pakard ES tuning mix with molecular weight spanning a mass range of m/z 118- m/z 2722. Data acquired in the broadband mode were typically collected using 512 K data points.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No.

2530-83-8)

The identity and purity of the test substance were determined during a separate characterization study conducted according to EPA TSCA Good Laboratory Practice Standards. The purity of the test material was measured as 99+%.

Conclusion : The number-average and weight-average molecular weights of the test substance solution were determined by GPC as to be 1102 and 1312 with 73 area % of the chromatogram higher than 1000 molecular weight at the1-hr reaction time, respectively. At the 4-hr reaction time, its number-average and weight-average molecular weights increased to 1269 and 1524 with 84 area % of the chromatogram higher than 1000 molecular weight, respectively. The results in collaboration of the NMR and ESI-MS analyses indicated that the test substance underwent hydrolysis to form fully hydrolyzed products with trace amounts of partially hydrolyzed products. Continuously, those hydrolyzed products through condensation reactions, produced both cyclic and linear siloxanes with the majority being cyclics under the given condition. These condensation reactions continued over the time period. The test substance was found to be hydrolytically unstable at ~ 22 oC under the given pH condition.

Reliability : (2) valid with restrictions
13.12.2004 (71)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : other: Fugacity Model Level I, II and III
Media : other
Air : 0 % (Fugacity Model Level I)
Water : 100 % (Fugacity Model Level I)
Soil : 0 % (Fugacity Model Level I)
Biota : 0 % (Fugacity Model Level II/III)
Soil : 0 % (Fugacity Model Level II/III)
Method : other
Year : 2004

Method : The EQC model (ver. 2.02) was used for all fugacity calculations as recommended by EPA.

Remark : All simulations were conducted at a data temperature of 25 °C using default values of the model for compartment dimensions and properties. If chemical-specific data required for the simulations were not available, estimated values were obtained using structure activity relationship (SAR) models developed by the EPA Office of Pollution

Prevention Toxics and Syracuse Research Corporation, as provided with the EPI Suite (version 3.10) package. Level-I, -II, and -III fugacity models for a Type-1 chemical (i.e., chemicals that partition into all environmental media) were used for the simulations.

Physical and chemical properties of 3-gylcidoxypropyltrimethoxysilane (CAS No. 2530-83-8) used for fugacity calculations.

Property	Value	Comments
Molecular weight	236	
Data temperature (°C)	25	
Water solubility (g/m3)	1.0x106	Est.value (1)
Vapor pressure (Pa)	1.12	Extrapolated value (2)
Log Kow	-0.92	Est. value(3)
Melting point (°C)	-70	
Half-life in air (h)	5.8	Est. Value (4)
Half-life in water (h)	6.5	Measured at pH 7.0, 25 °C (5)
Half-life in soil (h)	63	Est. Value (5)
Half-life in sediment(h)	6.5	Est. Value (5)

(1) Water solubility of 3-glycidoxypropyltrimethoxysilane at 25 °C was estimated using the SAR Model WSKOW® (version 1.41). The model was used as received from the EPA.

(2) Vapor pressure of 3-glycidoxypropyltrimethoxysilane at 25 °C was extrapolated from a temperature-vapor pressure relationship that was developed using experimental data measured at temperatures ranging from 121-194 °C.

(3) Log Kow of 3-glycidoxypropyltrimethoxysilane at 25 °C was estimated using the SAR Model KOWWIN® (version 1.67). The model was used as received from the EPA.

(4) The half-life in air of 3-glycidoxypropyltrimethoxysilane at 25 °C was estimated using the SAR Model APOWIN® (version 1.91). The model was used as received from the EPA.

(5) The overall half-life of 3-glycidoxypropyltrimethoxysilane in soil and sediment were estimated as a function of the measured hydrolysis half-life and the estimated rate of biodegradation in water. Biodegradation was estimated using the SAR Model BIOWIN® (version 4.01), as received from the EPA. The BIOWIN result for ultimate biodegradation time frame (2.6595; "weeks-months") was converted to an estimated half-life in water (900 hours) using the EPA default conversion factors in EPI Suite. Biodegradation half-life in soil was assumed to be 2 times longer than the BIOWIN estimate for water. Biodegradation half-life in sediment was assumed to be 9 times longer than the BIOWIN estimate for water. The half-life in sediment was assumed to be equal to the measured hydrolysis half-life in water. Because of the decreased activity of water in soil, the hydrolysis half-life in soil was assumed to be 10 times longer than the measured half-life in water.

Result : Level-I Simulation.
Environmental Compartment

	Air	Water	Soil	Sediment
Distribution (%)	0.0	100	0.0	0.0

Level-II Simulation
Environmental Compartment

	Air	Water	Soil	Sediment
Distribution (%)	0.0	100	0.0	0.0
Reaction losses(%)	0.0	99.1	0.0	0.0
Advective losses(%)	0.0	0.9		0.0

Overall residence time(h) 9.3
Reaction residence time (h) 9.4
Advective residence time (h) 1000

Level-III Simulation
A. Emission Rates (kg/h): Air = 1000; Soil = 0; Water = 0
Environmental Compartment

	Air	Water	Soil	Sediment
Distribution (%)	1.4	1.9	96.7	0.0
Reaction losses(%)	11.2	14.2	73.6	0.0
Advective losses(%)	0.9	0.1		0.0

Overall residence time(h) 69
Reaction residence time (h) 70
Advective residence time (h) 6474

B. Emission Rates (kg/h): Air = 0; Soil = 1000; Water = 0
Environmental Compartment

	Air	Water	Soil	Sediment
Distribution(%)	0.0	0.8	99.2	0.0
Reaction losses(%)	0.0	14.2	93.0	0.0
Advective losses(%)	0.0	0.1		0.0

Overall residence time (h) 4
Reaction residence time (h) 4
Advective residence time (h) 5384

C. Emission Rates (kg/h): Air = 0; Soil = 0; Water = 1000
Environmental Compartment

	Air	Water	Soil	Sediment
Distribution (%)	0.0	100	0.0	0.0
Reaction losses (%)	0.0	99.1	0.0	0.0
Advective losses (%)	0.0	0.9		0.0

Overall residence time (h) 9.3
Reaction residence time (h) 9.4
Advective residence time (h) 1000

D. Emission Rates (kg/h): Air = 1000; Soil = 1000; Water = 1000
Environmental Compartment

	Air	Water	Soil	Sediment
Distribution (%)	0.6	6.9	92.5	0.0
Reaction losses (%)	3.7	40.1	55.5	0.0
Advective losses (%)	0.3	0.4		0.0

Overall residence time (h) 55
Reaction residence time (h) 55
Advective residence time (h) 7930

The measured hydrolysis half-life for 3-glycidoxypropyltrimethoxysilane at pH 7.0 is 6.5 hours at 25 °C. As such, 3-glycidoxypropyltrimethoxysilane will not exist in the environment but will rapidly hydrolyze to methanol and 3-glycidoxypropylsilanetriol. The

environmental fate, transport, and distribution of 3-glycidoxypropylsilanetriol were evaluated to provide a more realistic assessment of 3-glycidoxypropyltrimethoxysilane. Results from the simulation suggest that > 99% of the total steady-state mass of 3-glycidoxypropylsilanetriol will reside in the water and soil compartments, and will not be found in air or sediment. It is expected that 65-85% of the 3-glycidoxypropylsilanetriol produced by the steady-state hydrolysis of 3-glycidoxypropyltrimethoxysilane will degrade in about 20-35 days.

Source : SEHSC

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Upon contact with water or water vapor, 3-glycidoxypropyltrimethoxysilane generates methanol and the corresponding silanol, 3-glycidoxypropylsilanetriol. Depending upon concentration, 3-glycidoxypropylsilanetriol will condense to form a highly cross-linked polymeric gel.

Conclusion : Results from the multimedia model simulations indicate that 3-glycidoxypropyltrimethoxysilane will not persist in the environment, but will degrade to methanol and 3-glycidoxypropylsilanetriol. If released directly to air, about 11% of the steady-state emission is expected to degrade in air, 74% expected to partition to and degrade in soil, and 14% expected to partition to and degrade in water. When released to soil 93% of the steady-state emission is expected to degrade in soil and 7% expected to partition to and degrade in water. When released directly to water, essentially 100% of the steady-state emission will degrade in water. Advection from the local environment is expected to be insignificant (less than or equal to1% of the steady-state emission) for all emission scenarios. Global persistence of 3-glycidoxypropyltrimethoxysilane in the model system was about 3 days when released directly to air or soil, and about 0.5 days when released to water. If released simultaneously to all three compartments (i.e., air, water, and soil), essentially 100% of the steady-state emission degrades in about 2 days. Based on Level-III modeling, it is expected that > 99% of the total steady-state mass of 3-glycidoxypropyl-trimethoxysilane will reside in the water and soil compartments and will not be found in air or sediment.

Reliability : (2) valid with restrictions
Reliability: Klimisch Code 2, reliable with restrictions:
· The fugacity modeling was conducted using an accepted model.
· Measured and estimated data were both used for chemical-specific data required by the model.

Flag : Critical study for SIDS endpoint

15.09.2005 (56) (62) (67) (73) (74)

Type : fugacity model level III

Media :

Air : % (Fugacity Model Level I)

Water : % (Fugacity Model Level I)

Soil : % (Fugacity Model Level I)

Biota : % (Fugacity Model Level II/III)

Soil : % (Fugacity Model Level II/III)
Method : other: model
Year :

Method : Environmental distribution and overall persistence of 3 glycidoxypropyl-silanetriol CAS 51287 18 4), based on Level-III fugacity modeling.
The EQC model (ver. 2.02) was used for all fugacity calculations as recommended by EPA. All simulations were conducted at a data temperature of 25*C using default values of the model for compartment dimensions and properties. If chemical-specific data required for the simulations were not available, estimated values
were obtained using structure activity relationship (SAR) models developed by the EPA Office of Pollution Prevention Toxics and Syracuse Research Corporation, as provided with the EPI Suite (version 3.1011) package.
Estimated physical and chemical properties used for fugacity modelling of 3 glycidoxypropyl-silanetriol:

" Melting point (ºC) 110
" Boiling point (ºC) 356
" Vapor pressure (Pa) 1.48 10-5
" Water solubility (g/m3) 7.88 106
" Log KOW -2.61
" Henry's constant (atm·m3·mol-1) 1.18 10-16
" OH radical oxidation rate constants (cm3·mol-1·sec-1) 3.01 10-11
" Ultimate Biodegradation (d) 15
" Overall Reaction half life (h)
o air 12.8
o water 360
o soil 720
o sediment 3240

Result : Environmental Compartment

	Air	Water	Soil	Sediment
Emission Rates (kg/h): Air = 1000; Water = 0; Soil = 0				
" Distribution (%)	0.0	26.1	73.9	0.0
" Reaction losses (%)	0.0	34.1	48.2	0.0
" Advective losses (%)	0.0	17.7		0.0
" Overall persistence (h)	678			
o reaction persistence (h)	824			
o advective persistence (h)		3833		
Emission Rates (kg/h): Air = 0; Water = 1000; Soil = 0				
" Distribution (%)	0.0	99.8	0.0	0.2
" Reaction losses (%)	0.0	65.8	0.0	0.0
" Advective losses (%)	0.0	34.2		0.0
" Overall persistence (h)	342			
o reaction persistence (h)	520			
o advective persistence (h)		1002		
Emission Rates (kg/h): Air = 0; Water = 0; Soil = 1000;				
" Distribution (%)	0.0	22.2	77.8	0.0
" Reaction losses (%)	0.0	30.5	53.6	0.0
" Advective losses (%)	0.0	15.9		0.0
" Overall persistence(h)	716			
o reaction persistence (h)	851			
o advective persistence (h)		4512		

Emission Rates (kg/h): Air = 1000; Soil = 1000; Water =

1000

"	Distribution (%)	0.0	39.0	60.9	0.1
"	Reaction losses (%)	0.0	43.5	33.9	0.0
"	Advective losses (%)	0.0	22.6		0.0
"	Overall persistence (h)	579			
o	reaction persistence (h)	748			
o	advective persistence (h)		2564		

The overall persistence of 3 glycidoxypropyl-silanetriol in the environment, (based on Level-III fugacity modelling) is about 24 days

Source : Dow Corning Corporation
Reliability : (2) valid with restrictions
09.12.2004 (62)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other
Contact time : 28 day(s)
Degradation : = 37 (±) % after 28 day(s)
Result : other: not readily biodegradable
Deg. product :
Method : other
Year : 1993
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : DOC-DIE AWAY TEST (EWG Guideline 79/831/EWG, Appendix V, Part C (updated edition dated July 1990), Method C.4-A.

Result : Degradation % after time: Duplicates run with test article. Flask 1: Percent degradation after 0, 7, 14, 21, 27 and 28 days was 0, 31, 34, 31, 43 and 37%, respectively. Flask 2: Percent degradation after 0, 7, 14, 21, 27 and 28 days was 0, 31, 34, 35, 40, and 37%, respectively.

Results: Mean percent degradation for test article: 0, 31, 34, 33, 41, and 37% for 0, 7, 14, 21, 27, and 28 days, respectively.

Kinetic (for sample, positive and negative controls): For each time period %, sample % degradation for each time period noted above. For positive control, sodium benzoate, > 96% degradation was reported for each time period in both duplicate samples, and was 100% DOC reduction within 28 days. For the negative control, % degradation was not calculated, but raw data indicates no degradation at any of the time periods measured.

Breakdown products: DYNASYLAN GLYMO is known to be hydrolytically unstable. When added to water, it rapidly hydrolyzes, generating methanol and silanetriol derivatives.

Therefore, results from this study likely represent biodegradation of methanol rather than the parent material.

Source : SEHSC

Test condition : · Analytical method used to measure biodegradation: DOC analyses were in the form of a double determination of oxygen-enriched and de-gassed samples (removal of inorganic carbon), membrane filter with pore size of 0.2 µm. The DOC analysis was performed using two-point calibration in a carbon analyzer (Shimadzu).

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8); DYNASYLAN GLYMO, Purity 98%

Conclusion : DYNASYLAN GLYMO achieved a breakdown rate of 37%(DOC reduction) within 28 days. Based on these findings, DYNASYLAN GLYMO was determined as "not readily biodegradable". The control substance, sodium benzoate, achieved a breakdown rate of 99.5% (DOC reduction) within 10 days and 100% within 28 days. This leads to the conclusion that the culture used possessed adequate biological activity.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

29.03.2004 (24)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Elimination :

Method :

Year : 2004

GLP : no

Test substance : as prescribed by 1.1 - 1.4

Remark : Bioaccumulation is not anticipated since this material is hydrolytically unstable. Rapid hydrolysis of this material produces methanol and silanetriols. The epoxy group slowly reacts to form diols in water. The Si-C bond will not undergo further hydrolysis. The methoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield an epoxy functional silicone resin (oligomer resin).

If the silane is slowly released such that the concentration of the resulting epoxy-functional silanetriol is not high enough to result in polymerization, the silanetriol will exist largely as a monomer. The monomer is known to be water soluble by virtue of the three hydroxy groups on the silicon. It is expected that this silanetriol will have a low Kow because of these hydroxy groups and so is not expected to bioaccumulate. The water solubility of the silanetriol cannot be measured because of the tendency to condense at concentrations greater than 500480 ppm, (The equilibrium constant for the condensation of a 3-methacryloxypropylsilanetriol to the dimer is about 480 ppm, Osterholtz and Pohl, 1992). The estimated water solubility is 1 x 106 mg/L (USEPA, 2000). At higher concentrations, the silanetriol and small condensation

products will precipitate out of water due to formation of larger, water insoluble polymeric resins.

Reliability : (2) valid with restrictions
09.12.2004 (64)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 180
LC50	:	= 237
LC100	:	= 320
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	USEPA. 1975. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. Ecological Research Services, EPA-660/3-75-009. 61 p
Remark	:	The low dissolved oxygen concentrations of 3.5 mg/L were measured in the control chambers and test chambers for which no mortality was observed. It is not likely that the low dissolved oxygen concentrations had a significant impact on the outcome of the study.
Result	:	(mg/L nominal concentrations) ·96-h NOEC = 180 ·96-h LC10 = 198 (139-220; 95% CI) ·96-h LOEC = 240 ·96-h LC50 = 237 (208-268; 95% CI) ·96-h LC100 = 320 ·96-h LC90 = 283 (255-398; 95% CI) No mortality observed in controls. Sublethal effects (stressed, loss of equilibrium, air gulping) observed in 240 mg/L exposure (LOEC) at 72-h observation. Sublethal effects (dark pigmentation, quiescence) observed in 320 mg/L exposure (LC100) at 24-h observation.
Source	:	Dow Corning Corporation
Test condition	:	· Design: static exposure, no solution renewal · Dilution water: reconstituted soft-water prepared from glass-distilled water, EPA-660/3-75-009 (USEPA 1975) · Water chemistry: not documented, (except for pH and dissolved oxygen). Based on EPA-660/3-75-009, the expected hardness would be 40 to 48 mg CaCO3/L, expected alkalinity 3 to 35 mg CaCO3/L, and expected pH 7.2 to 7.6. Measured pH at test initiation ranged from 7.2 to 7.3 (mean 7.2). Hardness and alkalinity were not measured. Total organic carbon (TOC) was not measured but expected to be insignificant. · Test substance stability: test substance not stable in aqueous solutions; measured hydrolysis half-life is 8 min to 6.5 hours at 25ºC over the pH range of 5 to 9 · Exposure vessel: polyethylene-lined vessels containing 10 L of dilution water; vessels aerated prior to study initiation but not during study · Dosing solutions: no dosing solutions used; test material added directly to exposure vessels. Manner of addition of test substance to dilution water not documented. Time of test solution preparation and time of fish addition were not recorded for the definitive study. Not documented if fish

were added before or after addition of test substance.
· Carrier solvent: none
· Exposure concentrations: nominal - 0, 10, 32, 100, 135, 180, 240, 320, 1000 mg/L; measured - concentrations not analytically verified
· Replication: duplicate controls; single exposure concentrations
· Test system: juvenile rainbow trout having a mean total length of 7.1 cm (range 5.5-8.4 cm); fish were acclimated to laboratory conditions a minimum of two weeks before testing; loading rate of 10 fish per exposure vessel (9 fish in 135, 180, and 240 mg/L exposure concentrations); total of 97 fish
· Observation periods: 0, 24, 48, 72, 96 h after study initiation
· Photo-period: not specified
· Temperature: 12°C in water bath (mean and ranges not reported)
· Dissolved oxygen: initiation (t = 0 h): mean 12.5 mg/L (range 11.5-13.0 mg/L); termination (t = 96 h): mean 5.1 mg/L (range 3.5-7.0 mg/L)
· pH: initiation (t = 0 h): mean 7.3 (range 7.2-7.4); termination (t = 96 h): mean 7.3 (range 7.3-7.4)

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

Purity of the test substance was measured by gas chromatography and reported as 98%. The test substance is not stable in water and rapidly hydrolyzes to methanol and 3-glycidoxypropyl-silanetriol (R-Si(OH)3 where R = -(CH2)3OCH2CHOCH2). The measured hydrolysis half-life for the test substance is 8 min to 6.5 hours at 25ºC over the pH range of 5 to 9 (Kozerski et. al. 2001).

Conclusion : Based on results from the study (NOEC = 180 mg/L, LOEC = 240 mg/L, and LC50 = 237 mg/L), the test substance and hydrolytic degradation products are considered practically non-toxic (LC50 > 100 mg/L) to rainbow trout under the described conditions of exposure.

Reliability : (2) valid with restrictions
Study is considered to be reliable with the following restrictions:
· study was not conducted under GLP
· water chemistry not documented
· exposure concentrations were not analytical verified
· exposure concentrations were not replicated
· temperature not documented for entire study

Flag : Critical study for SIDS endpoint

09.12.2004 (10) (45) (56)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : = 32
LC50 : = 276
Limit test : no
Analytical monitoring : no
Method : other:EPA 660/3-75-009
Year : 1978
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : It was not documented if fish were added before or after addition of test substance.
This study was not conducted in full compliance with OECD 203. However, the study design, documentation of data, and results are considered scientifically defensible and adequate for assessing the acute toxicity of the test substance (CAS No. 2530-83-8) to freshwater fish. The study is considered to be reliable with the following restrictions:
- study was not conducted under GLP
- water chemistry not documented
- exposure concentrations were not analytical verified
- exposure concentrations were not replicated
- temperature not documented for the entire study
- fish size was not documented
- sublethal effects were not documented

Result : Results from the study were reported as follows (mg/L, nominal concentrations):

- 96-h NOEC = 32
- 96-h LOEC = 100
- 100% mortality = 1000
- 96-h LC10 = 59 (13-114; 95% CI)
- 96-h LC50 = 276 (152-572; 95% CI)
- 96-h LC90 > 1000 (610-8396; 95% CI)

Based on results from the study (NOEC = 32 mg/L, LOEC = 100 mg/L, and LC50 = 276 mg/L), the test substance and hydrolytic degradation products are considered practically non-toxic (LC50 > 100 mg/L) to bluegill sunfish under the described conditions of exposure.

Test condition : The static acute toxicity of the test substance to bluegill sunfish (Lepomis macrochirus) was determined in reconstituted soft water following guideline EPA-660/3-75-009 (USEPA 1975). Hardness, alkalinity, and total organic carbon (TOC) were not measured. Based on EPA-660/3-75-009, the expected hardness would be 40 to 48 mg CaCO3/L, expected alkalinity 3 to 35 mg CaCO3/L, and expected pH 7.2 to 7.6. Juvenile bluegill sunfish (size not documented) were exposed in single replicates (loading rate of 10 fish per vessel) to nominal concentrations of 0, 10, 32, 100, 320, and 1000 mg/L. The test substance was added directly to the exposure vessels (polyethylene-lined containers with 10 L of dilution water), a carrier solvent was not used. Manner of addition of test substance to dilution water was not documented. The non-GLP study was conducted at 22°C. Exposure concentrations were not analytically verified. Mean dissolved oxygen was 13.3 mg/L (range 13.0-13.5 mg/L) at test initiation and 8.5 mg/L (range 8.0-9.0 mg/L) at test termination. Mean pH was 7.2 (range 7.2-7.3) at test initiation and was not recorded at test termination.

Test substance : CAS No. 2530-83-8; purity reported as 98%)

Reliability : (2) valid with restrictions
This study was not conducted in full compliance with OECD 203. However, the study design, documentation of data, and results are considered scientifically defensible and adequate for assessing the acute toxicity of the test substance (CAS No. 2530-83-8) to freshwater fish. The study is considered to be reliable with the following restrictions:

· study was not conducted under GLP
· water chemistry not documented
· exposure concentrations were not analytical verified
· exposure concentrations were not replicated
· temperature not documented for the entire study
· fish size was not documented
. sublethal effects were not documented

09.12.2004 (10)

Type	:	semistatic
Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	= 30
LC50	:	= 55
LC100	:	= 100
Limit test	:	no
Analytical monitoring	:	yes
Method	:	Directive 92/69/EEC, C.1
Year	:	1996
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The concentrations are based on the substance. 24 hr LC50 = 58 mg/l (30-100) 48 hr LC50 = 55 mg/l (30-100) 72 hr LC50 = 55 mg/l (30-100) 96 hr LC50 = 55 mg/l (30-100) For the interpretation of the results, it has to be taken into account that DYNASYLAN GLYMO is sensitive to hydrolysis and that it possibly hydrolyzes during the preparation of the stock solution and during the exposure time.
Test condition	:	An initial solution was prepared in drinking water (Gelsenwasser AG), stirred for about 18 hours, and filtered. The resulting solution served as a stock solution. Groups of 10 fish/tank were exposed to the test material at concentrations of 0, 1, 3, 10, 30 and 100 mg/l. Fresh test solutions were prepared daily. Test parameters: Water hardness: approx. 11 deg dH Temperature: Mean = 20 deg C; min 19 deg C/max 20 deg C Aeration: continuous Light/dark: 16/8 hr Feeding: none pH during the test: 7.7 - 8.4 Oxygen values during the test: 75-110% saturation The measured analytical values of the stock solutions: The analysis was carried out by DOC measurements (TOC-500-infrared analyser, Shimadzu): 1st batch (0 hr): 1110 mg substance/l 2nd batch (24 hr): 1287 mg substance/l 3rd batch (48 hr): 1069 mg substance/l 4th batch (72 hr): 1012 mg substance/l
Test substance	:	DYNASYLAN GLYMO; purity 98% glycidyloxypropyl-trimethoxysilan

Reliability : (2) valid with restrictions
Conducted in accordance with testing guidelines, but non-GLP.

09.12.2004 (54)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= 250
EC50	:	= 710
EC100	:	= 1000
Limit Test	:	no
Analytical monitoring	:	no
Method	:	OECD Guide-line 202
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : OECD Guideline Number: 202, EC Guideline Number: Annex V - C.2., and OPPTS Draft Guideline Number: 850.1010
USEPA. 1975. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. Ecological Research Services, EPA-660/3-75-009. 61 p

Result : Biological observations:
o Number immobilized as compared to the number exposed: Number immobilized: 22, Number exposed: 140 (includes controls)
o Concentration response with 95% confidence limits: 710 mg a.i./L, with 95% confidence intervals of 500 to 1000 mg a.i./L
o Cumulative immobilization: No immobilization was observed among daphnids exposed to the 63, 250, and 500 mg a.i./L treatment levels. Immobilization of 100% was observed in the 1000 mg a.i./L treatment level. Immobilization of 5% was observed in the 130 mg a.i./L treatment level.
o Was control response satisfactory (yes/no/unknown): Yes. No immobilization or adverse effects were observed in daphnids exposed to the solvent control. Immobilization of 5% was observed in the control. Although immobilization of 5% was observed in the control, this is considered to be within the expected range of naturally occurring variability for acute tests (ASTM, 2000). In addition, since no associated sublethal effects were observed at these treatment levels, the immobilizations are not considered to be toxicant-related.

Source : SEHSC

Test condition : · Test organisms: Daphnia magna
o Source, supplier, any pretreatment, breeding method: Springborn Smithers culture facility. Daphnids were cultured in 1.0-L glass vessels containing 0.80 L of water. Water used to culture the daphnids was be prepared in the same manner and has the same characteristics as the dilution water. Daphnids were fed a unicellular green algae, Ankistrodesmus falcatus (4 x 107 cells/mL) and YCT (yeast, cereal leaves and flaked fish food) suspension, daily, at a

rate of 1 mL algae and 0.5 mL YCT solution per vessel per day. Daphnids were obtained by removing all immature daphnids from the culture vessel, thus isolating mature gravid daphnids 24 hours prior to initiating the test. Young produced by these organisms were subsequently pipetted into the test beakers.

o Age at study initiation: < 24 hours

o Control group: dilution water and solvent control

· Test conditions:

o Stock solutions preparation (vehicle, solvent, concentrations) and stability: A 1.0 mg a.i./mL stock solution was prepared by placing 2.375 mL (2.5413 g based on a density of 1.07 g/mL, 2.5108 g as active ingredient) of glycidoxy in a 3.8 L glass jar and diluting with 2500 mL of dilution water containing 0.250 mL dimethylformamide (DMF, CAS # 68-12-2). The solution was stirred for approximately 10 minutes with a magnetic stir bar and stir plate. Each test concentration was prepared by adding the appropriate amount of the 1.0 mg a.i./mL stock solution to an intermediate vessel and diluting to 1000 mL with dilution water.

o Test temperature range: 20 to 21 °C

o Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): The toxicity test was conducted in 250-mL glass beakers, each containing 200 mL of test solution. Four replicate test vessels were established for each treatment level and a dilution water and solvent control. No aeration was provided to the test vessels.

o Dilution water source: Fortifying well water based on the formula for hard water (U.S. EPA, 1975).

o Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): The dilution water had a total hardness and alkalinity as CaCO3 of 170 mg/L and 120 mg/L, respectively, a pH of 7.8 and a specific conductivity of 500 µmhos/cm. The TOC concentration of the dilution water source was 0.60 mg/L for the month of January 2002.

o Lighting (quality, intensity, and periodicity): The test area was illuminated with Sylvania Octron® fluorescent bulbs at an intensity range of 70 to 90 footcandles at the solutions' surface. The test area received a regulated photoperiod of 16 hours of light and 8 hours of darkness. Sudden transitions from light to dark and vice versa were avoided. Light intensity was measured once during the test.

o Water chemistry in test (D.O., pH), in the control, and at least one concentration where effects were observed: The dilution water and solvent control vessels had a measured DO concentration of 9.1 and 8.7 mg/L respectively, at test initiation and 8.4 and 8.5 mg/L respectively, at test termination. pH measured in the dilution water and solvent control vessels were both 7.9 at test initiation and both 8.0 at test termination. The 1000 mg a.i./L treatment level had a measured DO concentration of 8.6 mg/L at test initiation and 8.4 mg/L at test termination. pH measured in the 1000 mg a.i./L treatment level was 7.9 at test initiation and 8.0 at test termination.

· Element (unit) basis (i.e., immobilization): Immobilization

· Test design (number of replicates, individuals per replicate, concentrations): Twenty daphnids were

impartially selected and distributed to each concentration and the controls (five daphnids per replicate vessel). Test concentrations were 63, 130, 250, 500 and 1000 mg/L.
· Method of calculating mean measured concentrations (i.e., arithmetic mean, geometric mean, etc.): Not applicable.
· Exposure period: 48-hours
· Analytical monitoring: No analytical monitoring was conducted during this test. Test results are reported on nominal concentrations.

Test substance : 3-Glycidoxypropyltrimethoxysilane

Purity: 98.8%

Conclusion : Following 48 hours of exposure (test termination), no immobilization was observed among daphnids exposed to the 63, 250, and 500 mg a.i./L treatment levels or the solvent control. Immobilization of 100% was observed in the 1000 mg a.i./L treatment level. Several mobile daphnids in the 500 mg a.i./L treatment level were observed to be lethargic and swimming on the bottom of the test vessel. No adverse effects were observed among the mobile daphnids exposed to the remaining treatment levels (63, 130, and 250 mg a.i./L) or the control and solvent control. Immobilization of 5% was observed in the 130 mg a.i./L treatment level and the control. Although immobilization of 5% was observed in the 130 mg a.i./L treatment level and the control, this is considered to be within the expected range of naturally occurring variability for acute tests (ASTM, 2000). In addition, since no associated sublethal effects were observed at these treatment levels, the immobilizations are not considered to be toxicant-related.

The 48-hour EC50 for glycidoxy and daphnids was estimated using non-linear interpolation to be 710 mg a.i./L, with 95% confidence intervals (calculated by binominal probability) of 500 to 1000 mg/L. The No-Observed-Effect Concentration (NOEC) was determined to be 250 mg a.i./L.

Reliability : (2) valid with restrictions
The studies were conducted following a recognized guideline (OECD 202) and are sufficiently documented for assessment. The most significant restriction is the lack of analytical verification. A concentrated stock solution and carrier solvent were used to prepare the test solutions for the study. Under the conditions described for preparation of the concentrated stock solution, the test material 3-glycidoxypropyl-trimethoxysilane could have significantly hydrolyzed to 3-glycidoxypropyl-silanetriol, which could have condensed to insoluble siloxane resins. Nonetheless, the 48-h EC50 of 710 mg/L is similar to the predicted (ECOSAR; epoxide structural class) 48-h EC50 of 850 mg/l for 3-glycidoxypropyl-trimethoxysilane and 6,400 mg/L for 3-glycidoxypropyl-silanetriol.

Flag : Critical study for SIDS endpoint

09.12.2004 (11) (61)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC0 : = 299
EC50 : = 473

EC100 : = 598
Limit Test : no
Analytical monitoring : yes
Method : Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year : 1993
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : 24-hr EC50 > 842 mg/l
48-hr EC50 = 473 mg/l

The concentrations are based on the substance.

For the interpretation of the results, it has to be taken into account that DYNASYLAN GLYMO is sensitive to hydrolysis and that it possibly hydrolyzes during the preparation of the stock solution and during the exposure time.

Test condition : For the preparation of a stock solution, 1 g/l of the test material was equilibrated in synthetic fresh water, stirred for about 18 hr and filtered. The resulting solution served as a stock solution. Groups of daphnia (< 24 hours old; 4 replicates of 5 daphnia/test concentration) were exposed to the test material at concentrations of 0, 103, 150, 206, 299, 421, 598, and 842 mg/l.

Test parameters:
Temperature: 20 +/- 1 deg C
Aeration: none
Light/dark: dark
Feeding: none
pH during the test: 7.4
Oxygen during the test: 6.5-7.1

Analysis: The analyses were carried out by measurement of dissolved organic carbon. The DOC content was determined with a Shinadzu TOC Analyzor 500. The measured analytical value was
428 mg DOC/l corresponding to 935 mg of substance/l.

Test substance : DYNASYLAN GLYMO; purity 98%
glycidyloxypropyl-trimethoxysilan

Reliability : (2) valid with restrictions
09.12.2004 (52)

Type : static
Species : other: Simocephalus vetulus
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = 100
EC50 : = 324
LOEC : = 250
Analytical monitoring : no
Method : other: EPA-660/3-75-009
Year : 1978
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Methods: Probit analysis (Finney 1952)
USEPA. 1975. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. Ecological Research Services, EPA-660/3-75-009. 61 p

Result : (mg/L nominal concentrations)
96-h NOEC = 100 96-h EC10 = 248 (212-272; 95% CI)

96-h LOEC = 250 96-h EC50 = 324 (301-343; 95% CI)

96-h EC100 = 500 96-h EC90 = 422 (393-474; 95% CI)

Source : Dow Corning Corporation

Test condition :
- Test design: static exposure, no solution renewal
- Dilution water: reconstituted hard-water; glass-distilled water reconstituted with 192 mg/L NaHCO3, 120 mg/L CaSO4, 120 mg/L MgSO4, and 8 mg/L KCl (pH adjusted to 7.5 with NaOH)
- Water chemistry: not documented
- Test substance stability: test substance not stable in aqueous solutions; estimated hydrolysis half-life of 4 hours at pH 7
- Exposure vessel: 250-mL glass beakers containing 200 mL of dilution water; vessels aerated prior to but not after study initiation; vessels covered with Saran WrapÒ during exposure
- Dosing solutions: no dosing solutions used; neat test material added directly to exposure vessels
- Carrier solvent: none
- Exposure concentrations: nominal - 0, 100, 250, 300, 350, 400, 450, 500 mg/L; measured - concentrations not analytically verified.
- Replication: duplicate controls and exposure concentrations
- Test system: Simocephalus vetulus neonates (age not documented) from laboratory cultures maintained under testing conditions; loading rate of 10 organisms per exposure vessel; total of 160 organisms
- Observation periods: 0, 24, 48 h after study initiation
- Photo-period: 18-h light/6-h dark; 600 foot-candle
- Temperature: 23 ± 1°C in environmental chamber
- Dissolved oxygen: not documented
- pH: mean 7.5 (range 7.4-7.7)

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

Purity of the test substance was measured by gas chromatography and reported as 98%. The test substance is not stable in water and rapidly hydrolyzes to methanol and 3-glycidoxypropyl-silanetriol (R-Si(OH)3 where R = -(CH2)3OCH2CHOCH2). The hydrolysis half-life for the test substance is estimated to be 4 hours at pH 7 (Pohl and Osterholtz 1985).

Conclusion : The test substance is considered practically non-toxic (LC50 > 100 mg/L) to Simocephalus vetulus (Family Daphnidae) under the described conditions of exposure.

Based on results from the study (NOEC = 100 mg/L, LOEC = 250 mg/L, and EC50 = 324 mg/L) the test substance and hydrolytic degradation products are considered practically non-toxic (LC50 > 100 mg/L) to Simocephalus vetulus (Family Daphnidae) under the described conditions of exposure.

Reliability : (2) valid with restrictions
Study is considered to be reliable with the following restrictions:
- study was not conducted under GLP
- exposure concentrations were not analytical verified

· age of neonates not documented
· sublethal effects not documented
· dissolved oxygen not documented

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4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 130
EC50	:	= 350
Limit test	:	no
Analytical monitoring	:	no
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	OPPTS Draft Guideline Number 850.5400, OECD Guideline Number 201, and EC Guideline Number Annex V - PART C.3. Statistical methods:Shapiro-Wilks' Test , Bartlett's Test , Williams' Test, Kruskal-Wallis' Test, Bonferroni's test
Result	:	96 hour EC50 (cell density) = 260 mg/l; 96 hour ErC50 = 350 mg/l. 72 hour EbC50 (biomass) = 250 mg/l; NOEC = 130 mg/l (biomass, cell density and growth rate).
Source	:	SEHSC
Test condition	:	·Test Organisms: Pseudokirchneriella subcapitata, formerly Selenastrum capricornutum, strain 1648, Class Chlorophyceae. The alga was obtained from Carolina Biological Supply Co., Burlington, North Carolina, and was maintained in stock culture at Springborn Smithers. The stock cultures were maintained within the following conditions: a shaking rate of 100 ± 10 rpm, a temperature of 24 ± 1 °C and continuous illumination at the surface of the medium with an intensity of approximately 300 to 500 footcandles (3200 to 5400 lux). Lighting was supplied by Duro-Test® Vita-Lite® fluorescent bulbs. Culture flasks were agitated continuously on an orbital shaker. ·Test Conditions: static oTest temperature range: 23 to 24 °C oGrowth/test medium: The culture medium used was Algal Assay Procedure (AAP) medium prepared with sterile, deionized water. oExposure vessel type: The test was conducted in sterile 250-mL Erlenmeyer flasks containing 100-mL of test solution. All test vessels were fitted with stainless steel caps which permit gas exchange. oWater chemistry in test: TOC concentration of the AAP sample collected in January 2002 was 0.47 mg/L. The dilution water and solvent control vessels both had a specific conductivity of 90 mmhos/cm at test initiation and at test termination. pH measured in the dilution water and solvent control vessels were 7.3 and 7.1 respectively, at

test initiation and 8.4 and 8.5 respectively, at test termination. The 1000 mg a.i./L treatment level had a specific conductivity of 70 mmhos/cm at test initiation and 80 mmhos at test termination. pH measured in the 1000 mg a.i./L treatment level was 7.0 at test initiation and 7.2 at test termination.
oStock solution preparation: A 1000 mg a.i./L stock solution was prepared by placing 1.889 mL (2.0212 g based on a density of 1.07 g/mL, 1.9969 g as active ingredient) of glycidoxy in a 2000 mL volumetric flask and diluting to volume with sterile AAP medium containing 0.10 mL/L of dimethyl formamide (DMF, CAS No. 68-12-2). The resulting stock solution was stirred using a magnetic stir plate and stir for 15 minutes. Nominal test concentrations were prepared from dilutions of the 1000 mg a.i./L stock solution.
oLight levels and quality during exposure: 340 - 440 footcandles (3700 - 4700 lux). The photosynthetically-active radiation (PAR) of the test area measured at test initiation ranged from 50 to 69 µE/m2/s.
·Test Design: Approximately 30 minutes after the test solutions were added to the test flasks (100 mL per flask), a 0.216-mL inoculum of Pseudokirchneriella subcapitata cells, at a density of approximately 464 x 104 cells/mL, was aseptically introduced into each flask. This inoculum provided the required initial (0 hour) cell density of approximately 1.0 x 104 cells/mL. Three replicate test vessels were established for each treatment level, the dilution water control and the solvent control. Test concentrations were 31, 63, 130, 250, 500 and 1000 mg a.i./L.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Purity: 98.8% Lot 17108Ci, Expiration: not available

Conclusion : · Cell Density
Cell densities in the 31, 63, 130, 250, 500 and 1000 mg a.i./L treatment levels averaged 83, 136, 137, 89, 11 and 0 x 104 cells/mL, respectively. Statistical analysis based on Williams' Test determined a significant reduction in cell density in all treatment level tested as compared to the pooled control. Based on Williams' Test the NOEC was determined to be <31 mg a.i./L. Additional statistical analysis (Bonferroni's Test) determined a significant reduction in cell density in the 31, 250, 500 and 1000 mg a.i./L treatments. The effect on the 31 mg a.i./L treatment level is not considered treatment-related since the two higher concentrations (63 and 130 mg a.i./L) were not affected and were less than 10% inhibited. Therefore, the NOEC was determined to be 130 mg a.i./L. The 96 hour EC50 for cell density was calculated to be 260 mg a.i./L, with 95% confidence intervals of 190 and 360 mg a.i./L.

· Biomass
Biomass in the 31, 63, 130, 250, 500 and 1000 mg a.i./L treatment levels averaged 35, 53, 37, 20, 3.6 and 0.7 cells·days/mL, respectively. Statistical analysis (Williams' Test) determined a significant difference in biomass in the 250, 500 and 1000 mg a.i./L any treatment levels tested when compared to the biomass in the pooled

control. Therefore, the NOEC was determined to be 130 mg a.i./L. The 72 hour EbC50 was calculated to be 250 mg a.i./L, with 95% confidence intervals of 140 and 450 mg a.i./L.

Growth Rate
The 0- to 72 hour growth rate in the 31, 63, 130, 250, 500 and 1000 mg a.i./L treatment levels averaged 1.17, 1.37, 1.24, 0.99, 0.32 and -0.6 days-1, respectively. Statistical analysis (Kruskal-Wallis' Test) did not determine a significant reduction in any treatment level tested when compared to the growth rate in the pooled control. Since the Kruskal-Wallis' Test did not provide a reasonable NOEC (1000 mg a.i./L), the NOEC was empirically estimated to be 130 mg a.i./L, the highest concentration with less than 10% inhibition. The 72 hour ErC50 was calculated to be 350 mg a.i./L, with 95% confidence intervals of 170 and 720 mg a.i./L.

Reliability : (2) valid with restrictions
The studies were conducted following a recognized guideline (OPPTS 850.5400) and are sufficiently documented for assessment. The most significant restriction is the lack of analytical verification. A concentrated stock solution and carrier solvent were used to prepare the test solutions for the study. Under the conditions described for preparation of the concentrated stock solution, the test material 3-glycidoxypropyl-trimethoxysilane could have significantly hydrolyzed to 3-glycidoxypropyl-silanetriol, which could have condensed to insoluble siloxane resins.

Flag : Critical study for SIDS endpoint
09.12.2004 (48)

Species	:	Anabaena flos-aquae (Algae)
Endpoint	:	
Exposure period	:	7 day(s)
Unit	:	mg/l
NOEC	:	= 0
LOEC	:	= 50
EC10	:	= 40
EC50	:	= 119
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : EPA-670/4-73-00 (USEPA 1973)

Statistical Methods: Probit analysis (Finney 1952); calculations as described by Stein (1973)

Result : Final Yield (mg/L nominal concentrations)

7-d NOEC = 0 7-d EC10 = 26 (11-46; 95% CI)

7-d LOEC = 50 7-d EC50 = 268 (185-370; 95% CI)
7-d EC90 = 2742 (1777-5003; 95% CI)

Growth Inhibition (mg/L nominal concentrations)

7-d NOEC = 0 7-d EC10 = 40 (29-49; 95% CI)
7-d LOEC = 50 7-d EC50 = 119 (101-147; 95% CI)
7-d EC90 = 357 (259-595; 95% CI)

Source : Dow Corning Corporation

Test condition :
- Test design: static exposure, no solution renewal
- Growth medium: sterile algal broth prepared from glass-distilled water and powdered nutrient media (DifcoÒ Laboratories); source of dilution water not documented
- Water chemistry: not documented
- Test substance stability: test substance not stable in aqueous solutions; estimated hydrolysis half-life of 4 hours at pH 7
- Exposure vessel: 125-mL polycarbonate Erlenmeyer flasks containing 40 mL of sterile algal broth; aseptic technique used throughout study
- Dosing solutions: no dosing solutions used; neat test material added directly to exposure vessels
- Carrier solvent: none
- Exposure concentrations: nominal - 0, 50, 100, 1000, 10,000 mg/L; measured - concentrations not analytically verified
- Replication: triplicate controls and exposure concentrations
- Test system: Anabaena flos-aquae, 1.00´104 cells/mL at test initiation, laboratory culture (original source and method of cultivation not documented)
- Observation periods: 0, 3, 4, 5, 6, 7 d after study initiation
- Photo-period: 18-h light/6-h dark; 600 foot-candle
- Temperature: 23 ± 1°C in environmental chamber
- pH: not documented

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8).

Purity of the test substance was measured by gas chromatography and reported as 98%. The test substance is not stable in water and rapidly hydrolyzes to methanol and 3-glycidoxypropyl-silanetriol (R-Si(OH)3 where R = -(CH2)3OCH2CHOCH2). The hydrolysis half-life for the test substance is estimated to be 4 hours at pH 7 (Pohl and Osterholtz 1985).

Conclusion : Based on results from the study for final yield (NOEC = 0 mg/L, LOEC = 50 mg/L, and EC50 = 268 mg/L) and growth inhibition (NOEC = 0 mg/L, LOEC = 50 mg/L, and EC50 = 119 mg/L), the test substance and hydrolytic degradation products are considered practically non-toxic (LC50 > 100 mg/L) to Anabaena flos-aquae (blue-green algae) under the described conditions of exposure.

Reliability : (2) valid with restrictions
Study is considered to be reliable with the following restrictions:
- study was not conducted under GLP
- original supplier of the test system not documented
- cultivation methods for laboratory culture not documented
- source of dilution water not documented
- water chemistry not documented
- exposure concentrations not analytical verified

17.03.2004 (10) (45) (66)

Species : Scenedesmus subspicatus (Algae)
Endpoint : biomass

Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= 53
EC10	:	= 91
EC50	:	= 255
Limit test	:	no
Analytical monitoring	:	yes
Method	:	Directive 92/69/EEC, C.3
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	On the basis of cell growth: 72-hr EbC50 = 255 mg/l 72-hr EbC10 = 91 mg/l NOEC = 53 mg/l On the basis of the growth rate: (0-72-hr) ErC50 > 420 mg/l (0-72-hr) ErC10 = 190 mg/l The concentrations are based on the substance. For the interpretation of the results, it has to be taken into account that DYNASYLAN GLYMO is sensitive to hydrolysis and that it possibly hydrolyzes during the preparation of the stock solution and during the exposure time.
Test condition	:	Exponentially growing cultures of green algae were exposed at concentrations of 0, 29, 53, 84, 147, 252, and 420 mg/l over several generations under exact defined conditions. For the preparation of the stock solution, 1 g/l of the test item was equilibrated in deionized water, stirred for 18 hours, and filtered. The resulting solution served as a stock solution. The analyses were carried out by measurement of dissolved organic carbon. The DOC content was determined with a Shinadzu TOC Analyzer 500. Test parameters: Temperature: 24 +/- 2 deg C Test medium: as described in guideline 92/69/EEC C.3. (1992) Culture apparatus: The algae were cultured in sterile-aerated Erlenmeyer flasks on a light-table. Light intensity: approximately 8000 lux, white pH during the test: 6.9-7.6 (beginning of test); 8.3-8.9 (end of test) The measured analytical value was 482 mg DOC/l corresponding to 1051 mg of substance/l.
Test substance	:	DYNASYLAN GLYMO; purity 98% glycidyloxypropyl-trimethoxysilan
Reliability	:	(2) valid with restrictions

13.12.2004 (51)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	other

Species	:	Pseudomonas putida (Bacteria)
Exposure period	:	5 hour(s)
Unit	:	
Method	:	other
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Bacteria EC10 = 1520 mg/l (related to the density of 1.07 g/m³)
Result	:	EC10 = 1.4 ml/l
Test condition	:	Four 100-ml von Loh bottles with ground glass stoppers were coated with the culture solution, the bacterial suspension, and the test substance in staged concentrations (0, 500, 1000, 1500 and 2000 ul/l), were sealed without air, and were incubated for approximately 5 hours at approximately 25 deg C. Two were treated with HgCl2 solution to kill the bacteria, and serve to determine auto-oxidation grades of the test substance. Nine control bottles without the test substance were used as reference; four of these contained HgCl2 to determine the final oxygen content. At the end of testing HCl was added to stop biochemical processes. The differential between the oxygen content of the solutions stored in the individual containers at the initial time (0) and after the incubation period reveals the bacterial oxygen consumption. Comparison of the amounts of oxygen consumed in the reference and test preparations provides information regarding the concentration-related influence on oxygen consumption by the test substance.
Test substance	:	DYNASYLAN GLYMO; purity 97.3% glycidyloxypropyl-trimethoxysilan

09.12.2004 (50)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	Daphnia magna (Crustacea)
Endpoint	:	reproduction rate
Exposure period	:	21 day(s)
Unit	:	mg/l
NOEC	:	>= 100
LOEC	:	> 100
Analytical monitoring	:	yes
Method	:	OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"
Year	:	1997
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The concentrations are based on the substance. NOEC >= 100 mg/l LOEC > 100 mg/l The analytical verification of the stock solution was carried out after 0, 2 and 5 days by measurement of

dissolved organic carbon. The analytical values showed deviations < 20% from the freshly prepared concentrations. It was concluded that the test item (or possible hydrolysis products) is present over the whole exposure time.

For the interpretation of the results, it has to be taken into account that DYNASYLAN GLYMO is sensitive to hydrolysis and that it possibly hydrolyzes during the preparation of the stock solution and during the exposure time. The concentrations are based on the substance.

The highest tested concentration at which no negative effects were observed on the reproduction rate with respect to the survival of the parent animals: NOEC >= 100 mg/l
The lowest tested concentration at which the first significant effects were observed on the reproduction rate with respect to survival of the parent animals: LOEC > 100 mg/l

Summary of Results of Mortality and Reproduction Rate of Daphnia Magna

Conc. (mg/L)	Control	2.5	6	16	40	100
Living MT	10	10	9	9	10	8
Inhibition MT (%)	0	0	10	10	0	20
Living JT*						
Parent:1	68	69	79	88	74	77
2	75	52	-	89	60	38
3	65	73	71	-	76	80
4	54	81	76	82	51	74
5	80	56	62	76	76	54
6	63	73	66	80	71	45
7	77	69	65	70	92	69
8	65	68	67	67	78	-
9	82	69	67	92	47	-
10	85	95	92	102	73	85
Sum JT	714	705	645	746	698	522
Std Dev	9.9	12	9.4	11.1	13.5	17.4
Repro. Rate	71	71	72	83	70	65
Inhibition JT(%)	-	0	-1	-17	1	8
Max Value	85	95	92	102	92	85
Min Value	54	52	62	67	47	38
Variat. Coeff.	14	17	13	13	19	27
t-Test	-	ns	>BI	>BI	ns	ns

where:
MT = mothers
JT = young
JT* = Living JT from the living mothers after 21 days
ns = not significant
>BI = reproduction rate > reproduction rate of the control, no t-test performed

pH and Oxygen Content (% Saturation) in the Test Solutions

Conc. (mg/l)	Day0 fresh		Day2 2-d old		Day9 fresh		Day12 3-d old		Day14 fresh		Day16 2-d old	
	pH	O2	pH	O2	pH	O2	pH	O2	pH	O2	pH	O2
contrl	8.5	88	8.2	107	8.2	93	8.1	99	8.4	87	8.0	97
2.5	8.5	91	8.1	105	8.3	91	8.0	97	8.5	84	8.0	97
6.0	8.4	91	8.1	105	8.3	91	8.0	96	8.5	86	7.9	96
16	8.5	90	8.2	104	8.3	88	8.0	95	8.5	84	7.9	95
40	8.4	91	8.1	104	8.3	91	8.0	96	8.5	83	7.8	89
100	8.4	90	8.1	104	8.3	90	7.9	93	8.4	85	7.7	86

The pH of the freshly made up and 2-dad and 3-day old solutions of test item frequently deviated by more than 0.3 units. Since this did not affect the reproduction rate, this pH change is not considered as reducing the quality of the results.

The analytical verification of the stock solution was carried out after 0, 2 and 5 days by measurement of dissolved organic carbon. The concentrations of the freshly prepared test batches were determined.The stock solution analytical values showed deviations < 20% from the freshly prepared concentrations. It was concluded that the test item (or possible hydrolysis products) is present over the whole exposure time.

For the interpretation of the results, it has to be taken into account that DYNASYLAN GLYMO is sensitive to hydrolysis and that it possibly hydrolyzes during the preparation of the stock solution and during the exposure time.

Test condition : For the preparation of a stock solution, 1 g/l of the test item was equilibrated in deionized water, stirred for about 18 hours, and filtered. The resulting solution served as a stock solution. Groups of daphnia (10/dose level) were exposed to the test material at concentrations of 0, 2.5, 6.0, 16, 40 and 100 mg/l. The test solutions were changed 3 times per week.

Test parameters:
Temperature: 20 +/- deg C
Test water: Synthetic fresh water, M4-medium as described by Elendt (1990)
Experimental set-up: 5 concentrations and 1 control; 1 individual per replicate
Animal density: approximately 60 ml per individual
Light/dark: 16/8 hr, with a light ratio of approximately 600/100 lux. 58 W fluorescent lamps.
Feeding: Daily with ELENDT-algae (Scenedesmus subspicatus); Day 0 to 6: 0.5 x 10E7 cells/daphnia; Day 7 to 21: 1.0 x 10E7 cells/daphnia

The analyses were carried out by measurement of dissolved organic carbon.

Test substance : DYNASYLAN GLYMO; purity 98% glycidyloxypropyl-trimethoxysilan

Reliability : (1) valid without restriction

13.12.2004 (53)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 7.5 ml/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	50
Vehicle	:	
Doses	:	3.9, 5.0, 6.3, 10.0 and 12.6 ml/kg
Method	:	other
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Piloerection and lethargy within 1 hour of administration, followed by coma and death. All deaths occurred within 48 hours of administration: 1/10, 3/10, 3/10, 7/10 and 8/10 rats died at 3.9, 5.0, 6.3, 10.0 and 12.6 ml/kg dose levels, respectively. All survivors were generally asymptomatic after this time. LD50=7.5 (6.00-9.37).
Source	:	Dow Corning Corporation
Test condition	:	Each rat received a single dose of the test substance. The rats weighed 200 + 2 grams at dosing and were fasted overnight prior to test substance administration. Rats received 3.9, 5.0, 6.3, 10.0 or 12.6 mL/kg of undiluted test substance, equivalent to 3.6, 4.7, 5.9, 9.3 and 11.8 g/kg. Rats were observed immediately after dosing and daily thereafter for fourteen days. Gross necropsies were not performed. ·Age: Not specified (weight of animals approximately 200 g) ·Doses: 3.9, 5.0, 6.3, 10.0 and 12.6 ml/kg ·Doses per time period: Single Dose ·Volume administered or concentration: Material used as supplied ·Post dose observation period: 14 Days
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Conclusion	:	The acute combined male/female LD50 was determined to be 7.5 ml/kg with 95% confidence level of 6.00-9.37 ml/kg in rats.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

09.12.2004 (28)

Type	:	LD50
Value	:	> 5 ml/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	no data
Doses	:	no data

Method : other
Year : 1978
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Not specified, Generally consistent with OECD Guideline 401
Result : Value: LD50 > 5.0 ml/kg
Source : SEHSC
Test condition : ·Age: Young adult, weight 200 + 2g.

·Doses per time period: One administration

·Post dose observation period: 14 days
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Conclusion : The LD50 for Gamma-Glycidyloxypropyltrimethoxysilane is greater than 5 ml/kg.
Reliability : (2) valid with restrictions
24.03.2004 (22)

Type : LD50
Value : = 7010 mg/kg bw
Species : rat
Strain : Wistar
Sex : male/female
Number of animals : 50
Vehicle : other: cottonseed oil
Doses : 3.6, 4.7, 5.9, 9.3 and 11.8 g/kg
Method : other
Year : 1976
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The design of the study generally conforms to that described in OECD Health Effects Test Guideline No. 401 (February 24, 1987).
Remark : This is a range-finding study, which preceded the conduct of a full LD50 study.
Result : Value [LD50 or LC50] with confidence limits: The acute median lethal dose (LD50) with 95% confidence limits, calculated by the method of Litchfield and Wilcoxon, J. Pharm. Exp. Thera., 96, 99 (1949) was 7.01 (5.61-8.76) g/kg.

Number of deaths at each dose level: No deaths occurred on the dose range-finding study.
Source : SEHSC
Test condition : Route of administration: Oral via gastric intubation (gavage). Each rat received a single dose of the test substance. The rats weighed 200 + 2 grams at dosing and were fasted overnight prior to test substance administration. Rats received 2.5, 5.0 or 12.5 mL/kg of a 20% test substance mixture in cottonseed oil or 5.0 mL/kg of undiluted test substance, equivalent to dose levels of 0.47, 0.93, 2.34 and 4.76 g/kg. Rats were observed for seven days.
Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Conclusion : Although this study was not conducted in full conformance with OECD test guidelines, it is more than adequate to assess the acute oral toxicity study of the test substance. The test substance has a very low order of toxicity in rats

by the oral route of exposure.

Reliability : (2) valid with restrictions
Valid with restrictions. Based on a review of the report, the study was judged to be scientifically defensible.

13.12.2004 (28)

Type : LD50
Value : = 8400 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 32
Vehicle :
Doses : 4.6, 6.8, 10.2 15.4 g/kg
Method : other
Year : 1963
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : LD50 calculated based on techniques published by Weil, C.S., Biometrics, Sept 1952; Thompson, W.R., Bact. Rev., Nov 1947; Thompson W.R. and Weil, C.S., Biometrics, March 1952.

Result :
· Time of death (provide individual animal time if less than 24 hours after dosing): Not conducted.
· Description, severity, time of onset and duration of clinical signs at each dose level: Slight to moderate ataxia approximately two minutes after dosing in all dose groups. The ataxia lasted 5-10 minutes followed by moderate to severe sedation. In addition, animals in the 10.2 and 15.4 g/kg dose groups displayed muscular weakness and hypernea approximately 10 minutes after administration of the test material. The reactions persisted 24 hours or until death intervened. Deaths occurred 20 minutes to 18 hours after dosing.
· Necropsy findings, included doses affected, severity and number of animals affected: No significant gross pathological alterations.
· Potential target organs (if identified in the report): Not specified.
· If both sexes tested, results should be compared: Not specified.

Source : Dow Corning Corporation

Test condition :
·Age: Not specified. Animals average body weight was ~110 g.
·Doses: 4.6, 6.8, 10.2 15.4 g/kg
·Volume administered or concentration: Material used as supplied.
·Post dose observation period: 14 days.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Conclusion : The acute combined male/female LD50 was determined to be 8.4 g/kg.

Reliability : (2) valid with restrictions

24.03.2004 (27)

Type : LD50
Value : = 22.6 ml/kg bw
Species : rat
Strain : other

Sex	:	male
Number of animals	:	15
Vehicle	:	other
Doses	:	8.0, 16.0, 32.0 ml/kg
Method	:	other: similar to OECD Guide-line 401
Year	:	1962
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Although this study was not conducted in full conformance with OECD test guidelines, it is more than adequate to assess the acute oral toxicity study of the test substance. The test substance has a very low order of toxicity in rats by the oral route of exposure. The calculated LD50 (22.6 ml/kg) exceeds the current OECD and EPA limit test level more than four-fold. Animals became sluggish after dosing. Four of the five deaths occurred within twenty-four hours post dosing. All animals in the two lower doses groups gained weight during the study. Gross necropsy disclosed congestion of the lungs and the abdominal viscera plus mottled livers with prominent acini.
Test condition	:	Strain: Carworth Farms-Elias. Each rat received a single dose of the test substance. The rats weighed 90 - 119 grams at dosing and were five to six weeks of age. The rats were not fasted prior to dosing. Rats were weighed prior to dosing and at study termination. Three groups of rats received 32.0, 16.0, or 8.0 ml/kg of the undiluted test substance. Rats were observed immediately after dosing and daily thereafter for fourteen days. Gross necropsies were only performed on the animals that died during the study. The method of moving average for calculating the median-effective dose (LD50) was applied to the 14-day mortality data.
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Reliability	:	(2) valid with restrictions

09.12.2004 (63)

Type	:	LD50
Value	:	= 16900 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	no data
Number of animals	:	
Vehicle	:	no data
Doses	:	14.0, 14.4, 15.5, 16.3, 17.1, or 18.0 g/kg
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	In an acute oral toxicity study in rats conducted in 1978, six groups of ten to twelve rats received oral doses of the test substance of 14.0, 14.4, 15.5, 16.3, 17.1, or 18.0 g/kg. The rats were observed for 14 days and those that died were necropsied.
Result	:	Mortalities were 0%, 0%, 9%, 40%, 58% and 80%, respectively, at the above dosages. The LD50 was 16.9 g/kg with 95% confidence limits of

16.4-17.4 g/kg. Remarkable clinical signs seen at the higher dosages were reductions in spontaneous activity, reactivity and respiration and loss of motor coordination. Dark areas on the liver margins and some hemorrhaging in the lungs were seen in some rats that died. The test substance has a very low order of toxicity in rats by the oral route.

Reliability : (2) valid with restrictions
09.12.2004 (7)

Type : other
Value :
Species : rat
Strain :
Sex : female
Number of animals : 5
Vehicle :
Doses : 2000 mg/kg bw
Method : other
Year : 2000
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Five fasted female Sprague-Dawley rats were dosed with 2000 mg/kg TMSPGE mixed with activated charcoal as a tracer. After 20 or 30 minutes the animals were sacrificed, and the stomachs and gastrointestinal tracts examined for presence of test article. The study was also repeated in the absence of the activated charcoal tracer.

Remark : The lack of clinical signs of toxicity following acute or repeated dosing is likely related to the hydrolysis of TMSPGE and subsequent polymerization of the hydrolysis products, and thus, the lack of bioavailability.

Result : In all cases, the hydrolysis product(s) of the test article were found in the stomach contents or in the upper gastrointestinal tract, and was observed to have the consistency of a siloxane gel. In cases where the stomach contents included food, small waxy particles of test article were observed. Both the gel-like substance and waxy particle forms of the hydrolysis products of the test article observed in the stomach and upper gastrointestinal tract support the rapid polymerization of TMSPGE under oral (gavage) conditions, as the test article exists as a clear, water like liquid. In either case, little or no absorption of test article appeared to have occurred. In contrast, there was no liquid present in the stomachs of animals gavaged with an equivalent dose of water and sacrificed after 30 minutes.

Test substance : 98.92% TMSPGE
Reliability : (2) valid with restrictions
09.12.2004 (75)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50
Value : > 5.3 mg/l
Species : rat
Strain : Fischer 344

Sex	:	male/female
Number of animals	:	30
Vehicle	:	
Doses	:	0.8, 1.9, and 5.3 mg/L
Exposure time	:	4 hour(s)
Method	:	other
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	OECD Health Effects Test Guideline No. 403 (May 12, 1981)
Result	:	A median lethal concentration (LC50) could not be calculated because less than 50% of the animals died at the highest exposure level, however, the four-hour inhalation LC50 in rats can be estimated to be greater than 5.3 mg/L. No deaths occurred at the two lower concentrations (1.9 and 0.8 mg/L). At the highest concentration (5.3 mg/L), three rats died, one male on day 1, one female on day 1 and one female on day 2. Following exposures, all rats exhibited varying amounts of test substance contamination on the fur. Clinical signs included excessive lacrimation, dry and moist rales, nasal discharge, and yellow staining in the anal-genital area. These signs were considered to be dose-related and were not generally observed during the second week following exposure. There was also a transient dose-related body weight depression seen in all groups (including the control) during the first week, however, mean body weights exceeded pre-exposure values by day 14 in all groups. Discolored lungs and autolytic changes were seen in the three rats that died. There were no gross abnormalities noted at the necropsy of survivors.
Source	:	Dow Corning Corporation
Test condition	:	Each rat received a single exposure to the aerosolized test substance. The duration of the exposures was four hours plus the period of time required for the aerosol to clear from the chambers prior to animal removal. The rats were approximately 11 weeks of age and weighed 242 + 9 grams (males) and 149 + 5 grams (females) at exposure. Exposure concentrations were 0 (air control), 0.8, 1.9 and 5.3 mg/L. Exposure concentrations were measured using gravimetric methods. Analysis of concomitant test atmosphere samples by gas chromatography was also performed. The gas chromatographic data were considered secondary due to recovery inefficiencies, however, gas chromatographic values averaged 85% of the gravimetrically determined concentrations. Mass median aerodynamic diameter was determined hourly by cascade impaction for each exposure level and ranged from 1.4 to 2.0 microns. Average chamber temperature and relative humidity ranges were 71-73 °F and 69-78%, respectively. The rats were observed during the four hour period immediately following completion of exposure and daily thereafter for 14 days. All rats were weighed 1, 2, 4 or 5, 7 and 14 days after exposure. Surviving animals were euthanized on day 14. Gross necropsies were performed on all rats
Test substance	:	3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

Conclusion	:	The test substance has a very low order of toxicity in rats by inhalation. The estimated LC50 exceeds current OECD and EPA limit test exposure levels.
Reliability	:	(1) valid without restriction Based on a review of the report, the study was judged to be scientifically defensible.

24.03.2004 (4)

Type	:	LC50
Value	:	> 2.7 mg/l
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	24
Vehicle	:	no data
Doses	:	0.7 1.4, 2.7 mg/L (saturated)
Exposure time	:	4 hour(s)
Method	:	other
Year	:	1963
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	·Description, severity, time of onset and duration of clinical signs at each dose level: No deaths or untoward behavioral reactions. ·Necropsy findings, included doses affected, severity and number of animals affected: No significant gross pathological alterations.
Source	:	Dow Corning Corporation
Test condition	:	·Age: Young adult. Average body weight of 250 g. ·Doses: 0.7 1.4, 2.7 mg/L (saturated) ·Doses per time period: 1 ·Volume administered or concentration: Material used as supplied ·Post dose observation period: 14 days ·Exposure duration (for inhalation studies): 4 hours
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Conclusion	:	4 hour LC50 > 2.7 mg/L
Reliability	:	(2) valid with restrictions

24.03.2004 (27)

Type	:	other
Value	:	
Species	:	rat
Strain	:	other
Sex	:	female
Number of animals	:	6
Vehicle	:	other
Doses	:	.56 mg/l
Exposure time	:	8 hour(s)
Method	:	other
Year	:	1962
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The calculated concentration, based on weight loss of sample in relation to dilution air, were 0.56 mg/liter. There was no mortality during the study and all animals gained weight

during the subsequent two-week observation period and were normal in all respects at sacrifice on the 14th day

Test condition : Concentrated vapor was generated at approximately 21 deg C by passing dried air at the rate of 2.5 liters/minute through a fritted glass disc immersed to a depth of at least one inch in 50 ml of test substance. The concentration of the nine-liter exposure chamber was calculated based on weight loss of sample in relation to dilution air. The duration of exposure was eight hours. Animals were observed daily during a 14-day post-exposure observation period. Animals were weighed prior to test initiation and at test termination.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Conclusion : This study was not conducted in conformance with OECD test guidelines and the calculated LC50 is approximately ten-fold lower than current the OECD limit test level for acute inhalation.

Reliability : (3) invalid

09.12.2004 (63)

5.1.3 ACUTE DERMAL TOXICITY

Type : other
Value : = 6800 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 32
Vehicle :
Doses : 4.6, 6.8 , 10.2 15.4 g/kg (24 hours)
Method : other
Year : 1963
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The acute mean lethal dose (LD50) of the test material was determined by using the techniques of Weil, C.S., Biometrics, Sept. 1952.; Thompson, W.R. , Bact. Rev., Nov. 1947; Thompson, W.R. and Weil C.S., Biometrics, March, 1952.

Result : LD50 = 6.8 g/kg Standard Deviation of LD50 = 0.9 g/kg

I.Time of death - Death occurred 18-24 hours following dermal application of test material.
II.Description, severity, time of onset and duration of clinical signs at each dose level: Animals in all dose groups displayed mild to moderate hypoactivity approximately two to three hours following application of the test material. This hypoactivity persisted for 48 hours or until death intervened.
III.Necropsy findings, included doses affected, severity and number of animals affected: No significant gross pathological alterations.

Source : Dow Corning Corporation

Test condition : I.Age: Young adult. Average body weight 2.5 kg.
II.Doses: 4.6, 6.8 ,

10.2 15.4 g/kg (24 hours)
·Doses per time period: 1
·Volume administered or concentration: Undiluted
III. Post dose observation period: 14 days
IV.Exposure duration: 24 hours
Twenty four hours prior to the test material application, the backs of the rabbits were shaved free of hair with electric clippers. Following twenty-four hour waiting period, the rabbits received skin applications of the undiluted test material at selected dose levels. The exposure sites were covered by wrapping the trunk with an impervious plastic sheeting which was secured by tape. The test material remained in contact with the skin for twenty-four hours. Behavior reactions were observed and recorded during the contact period, after which the plastic sheet was removed from each test rabbit. The exposure sites were examined for local reactions. Observations for mortality and behavioral abnormalities were made for up to fourteen days following skin application.

Test substance : [3-Glycidoxypropyltrimethoxysilane(CAS#2530-83-8)]

No information of purity of the material is provided.

Conclusion : LD50 = 6.8 g/kg

Reliability : (2) valid with restrictions
The study was not conducted according to GLPs.

13.07.2004 (27)

Type : LD50
Value : = 3.97 ml/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 8
Vehicle :
Doses : 2.5 and 5.0 ml/kg
Method : other: similar to OECD Guide-line 402
Year : 1962
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Erythema and slight necrosis were observed. Deaths occurred on the first and second day after application of the test substance. Necropsy findings included congested lungs, mottled livers with prominent acini, and off-color kidneys with internal congestion. All survivors gained weight during the study. LD50 3.97 (2.93-5.37) ml/kg

Test condition : The rabbits weighed 2240 - 2730 grams at dosing and were three to five months of age. The rabbits were weighed prior to dosing and at study termination. Each rabbit received a single dermal application of the test substance and polyethylene sheeting was used to retain the dose in contact with the clipped skin of the trunk for the 24-hour skin contact period. The rabbits were immobilized during the 24-hour skin contact period. Two groups of rabbits were dosed at 5.0 or 2.5 ml/kg of the undiluted test substance. After 24 hours, the polyethylene sheeting was removed and the animals were caged for the remainder of the 14-day observation period. The animals were observed immediately after dosing and daily thereafter for fourteen days. Gross necropsies were only performed on the animals that died

during the study. The method of moving average of calculating the LD50 was used.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Conclusion : Although this study was not conducted in full conformance with OECD test guidelines, it is more than adequate to assess the acute dermal toxicity of the test substance. The test substance has a very low order of toxicity in rabbits by the dermal route of exposure. The calculated LD50 exceeds the current the OECD and EPA limit test level.

Reliability : (2) valid with restrictions

09.12.2004 (63)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	1.94
Result	:	slightly irritating
Classification	:	
Method	:	other: Draize
Year	:	1982
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Result : All six rabbits treated with the test material developed well-defined erythema at 24 and 48 hours post application, which remained at the 72-hour observation and persisted through 96 hours in all animals. The erythema was not accompanied by edema. The test material was classified as a mild dermal irritant based on a PII of 1.94. No irritation was observed at the untreated sites of all animals. Significant irritation was observed in the positive control animals which had a PII score of 5.22

Source : Dow Corning Corporation

Test condition : I.Age: 10-12 weeks old
II.Doses: 0.5 ml
III.Doses per time period: Single dose
IV.Volume administered or concentration: 0.5 ml (total)
V.Post dose observation period: 8 days
VI.Exposure duration (for inhalation studies): 24 hours
Six rabbits were closely clipped over the back and sides with clippers. A 0.5 ml sample of test liquid was applied to a surgical gauze patch, two single layers thick, with a 1.0 ml tuberculin syringe. The gauze patch was then placed on the test site and secured with strips of Blenderm surgical tape. The positive control gauze patch was wet with 0.5 ml of 1.0% sodium lauryl sulfate after which it was applied the appropriate skin site. At the end of the 24-hour exposure period, the wrappings and patches were removed. Observations were made one hour after removal of the patches

and up to 192 hours after test material application..
Erythema and edema were evaluated and scored according to the technique of Draize. Primary Dermal Irritation Indices were calculated using only the 24 hour, 48 and 72-hour irritation values.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Conclusion : The test material was classified as a mild dermal irritant based on a PII of 1.94.

Reliability : (2) valid with restrictions
The study was conducted in 1982 and appeared to comply with GLPs. The report was audited by the Quality Assurance Unit.

17.03.2004 (39)

Species : rabbit
Concentration : undiluted
Exposure : Semiocclusive
Exposure time : 24 hour(s)
Number of animals : 4
Vehicle :
PDII : .06
Result : not irritating
Classification : not irritating
Method : other
Year : 1976
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : FDA Handbook Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics, 1959 p.47

Result : The test material was found to be a non-irritant under the conditions of the study. The Primary Irritation Index (PII)= 0.06

Source : Dow Corning Corporation

Test condition : A 0.5 ml sample of the test material was applied to areas of both intact and abraded skin. These areas were occluded by gauze pads. After 24 hours the patches were removed and the skin reaction were evaluated according to the Draize scale.
·Age: Not specified
·Doses : 0.5 ml
topical/24 hours
·Doses per time period: 0.5 ml (total)
·Volume administered or concentration: 0.5 ml
·Post dose observation period: 72 hours

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

No information of purity of the material.

Conclusion : PII=0.06 (Non-irritant)

Reliability : (2) valid with restrictions
The study was not conducted according to GLP standards.

24.03.2004 (28)

Species : rabbit
Concentration : undiluted
Exposure : no data
Exposure time : 24 hour(s)
Number of animals : 4
Vehicle :
PDII : 1.8

Result : slightly irritating
Classification :
Method : other
Year : 1963
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : The undiluted test material when applied to intact and abraded skin of albino rabbits was found to produce mild irritation. The Mean Irritation Score = 1.8 (combined)
Source : Dow Corning Corporation
Test condition : The mean Draize scores for the 24 and 72-hour grading periods were averaged to obtain separate mean irritation grades for both intact and abraded skin. The latter two means were averaged to give a combined average irritation score
·Age: Not specified
·Doses : 0.5 ml
topical/ 24 hours
·Doses per time period: 0.5 ml (total)
·Volume administered or concentration: 0.5 ml
·Post dose observation period: 72 hours
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Conclusion : The test material is a mild irritant in albino rabbits.
Reliability : (2) valid with restrictions
The study was not conducted according to GLPs

17.03.2004 (27)

Species : rabbit
Concentration : undiluted
Exposure : Open
Exposure time : 24 hour(s)
Number of animals : 5
Vehicle :
PDII :
Result :
Classification :
Method : other
Year : 1962
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes, Draize, et. al., J. Pharm. & Exp. Ther. 82, 4, December 1944.
Result : Moderate to marked capillary injection was noted on the five animals, corresponding to a grade 3 in the 10-grade rating system.
Test condition : The mean scores for the 24 and 72-hour grading periods were averaged to obtain separate mean irritation grades for both intact and abraded skin. The latter two means were averaged to give a combined average irritation score
·Age: Not specified
·Doses: 0.5 ml
topical/ 24 hours
·Doses per time period: 0.5 ml (total)
·Volume administered or concentration: 0.5 ml
·Post dose observation period: 72 hours

Uncovered application of 0.01 ml of the test substance to the clipped skin of the rabbit belly was evaluated in five rabbits.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

No information of purity of the materials provided.

Conclusion : The protocol of this study was not conducted in full conformance with OECD test guidelines and does not meet important criteria of the current standard methods (dose volume; un-occluded contact).

Reliability : (3) invalid

09.12.2004 (63)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle : other
PDII :
Result : slightly irritating
Classification :
Method : other
Year : 1958
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Single exposures of undiluted material and the 10% solution in Dowanol 50B caused no irritation. However, prolonged and repeated contact produced slight irritation on intact and abraded skin of rabbits. This material did not appear to be absorbed through the skin in toxic amounts.

Source : Dow Corning Corporation

Test condition : Doses : Single and repeated
Volume administered or concentration: undiluted plus 10% in Dowanol 50B

VI.Exposure duration:
Single, prolonged and repeated exposures (up to 10 applications) of undiluted material and the 10% solution in Dowanol 50B to intact and abraded skin. Material was also applied on ear.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Conclusion : The test material caused a slight irritation and exfoliation to the skin of rabbits.

Reliability : (3) invalid
The study was conducted in 1958 and it was not in compliance with GLPs.

17.03.2004 (26)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : other: undiluted and 5% solution in water

Dose	:	.1 ml
Exposure time	:	
Comment	:	
Number of animals	:	18
Vehicle	:	other: some applications diluted with water
Result	:	irritating
Classification	:	
Method	:	other
Year	:	1982
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	In unwashed eyes treated with undiluted test material, blinking and tearing were observed in all eyes within minutes after instillation. Pannus of the cornea developed in 2 of the 6 animals. Corneal opacities, covering a minimal area of the cornea, persisted for 21 days in the animals which developed pannus. Conjunctival redness was also observed in several test eyes. In the washed eyes, treated with undiluted test material and washed 20 seconds later, minimal signs of irritation reported. No irritation was observed in the washed and unwashed eyes of rabbits exposed to 5% of the test material in water.
Source	:	Dow Corning Corporation
Test condition	:	I.Age: 10-12 weeks II.Doses : 0.1 ml of undiluted and 0.1 ml of 5% test material in water. III.Doses per time period: Single IV.Volume administered or concentration: 0.1 ml V.Post dose observation period: Up to 21 days The amount of 0.1 ml of the undiluted test material was administered topically to the eyes of 9 rabbits. The contralateral eye served as an untreated control. Twenty seconds after instillation, the treated eyes of 3 of the 9 rabbits were washed for 1 minute with tap water. Eyes were examined up to 21 days after exposure. A second group of 9 rabbits was treated similarly with a 5% solution of the test material diluted in water. The eyes of the second group of rabbits were examined up to 7 days after exposure. The scoring of ocular irritation was performed according to Draize scale.
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8) Purity of test article was > 99%
Conclusion	:	The test material was considered to be an eye irritant according to the Federal Hazardous Substances Act (FHSA).
Reliability	:	(2) valid with restrictions Major elements of GLP were followed. The report was audited, and signed by Quality Assurance.

24.03.2004 (38)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	
Number of animals	:	6
Vehicle	:	none
Result	:	slightly irritating

Classification	:	
Method	:	other
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	FDA Handbook Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics, 1959 p49
Result	:	The test material elicited only very mild eye irritation in those animals in which the treated eyes remained unwashed. This irritation was confined to slight erythema and edema of the conjunctiva which did not persist beyond 48 hours after instillation. At no time was the cornea or iris of any animal affected.
Source	:	Dow Corning Corporation
Test condition	:	·Doses : 0.1 ml (The eyes of 3 rabbits were washed 4 seconds after installation) ·Volume administered or concentration: Material used as supplied ·Post dose observation period: Up to 7 days
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8) No information of purity of the material provided.
Conclusion	:	The test material was found to be a very mild eye irritant
Reliability	:	(2) valid with restrictions The study was not conducted according to GLP standards.

17.03.2004 (28)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	
Number of animals	:	5
Vehicle	:	none
Result	:	slightly irritating
Classification	:	
Method	:	other
Year	:	1963
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Exactly 0.1 ml of undiluted test material was instilled into conjuctiva sac of the right eye of each test rabbit, The left eye of each animal served as a control. At 1, 24, 48, 72 96 hours and 7 days following instillation, the cornea, iris and palpebral conjunctiva were examined individually and graded for irritation and injury according to the standard scoring system.
Result	:	No irritation was observed after 1 hour. Material was considered minimally irritating.
Source	:	Dow Corning Corporation
Test condition	:	·Age: Not specified. Young adult ·Doses : 0.1 ml ·Volume administered or concentration: Material used as supplied ·Post dose observation period: Up to 7 days.
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

No information of purity of the material provided.
Conclusion : Material was considered minimally irritating.
Reliability : (2) valid with restrictions
The study was not conducted according to GLPs
17.03.2004 (27)

Species : rabbit
Concentration : undiluted
Dose : .5 ml
Exposure time :
Comment :
Number of animals : 5
Vehicle : none
Result :
Classification :
Method : other (calculated)
Year : 1962
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : One rabbit eye was unharmed while four others had traces of diffuse corneal necrosis. Injection of the eyelids was also noted. Grade 2 in the 10-grade rating system.
Test condition : Instillation of an excess (0.5ml) of the undiluted test substance to the one eye was evaluated in five rabbits.
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Conclusion : The study was not conducted in compliance with the OECD guideline (dose volume) and the scoring criteria are inappropriate compared to current procedures.
Reliability : (3) invalid
09.12.2004 (63)

Species : rabbit
Concentration : undiluted
Dose :
Exposure time :
Comment :
Number of animals : 1
Vehicle : none
Result :
Classification :
Method : other
Year : 1981
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Slight pain and very slight conjunctival redness was observed in both eyes immediately following exposure. Conjunctival redness persisted for 24 hours. No irritation was observed after 48 hours.
Source : Dow Corning Corporation
Test condition : I.Age: Not specified
II.Doses : Two drops of
the undiluted material was administered into each eye. Left eye was washed for 2 minutes with tepid water after instillation.
III.Doses per time period: N.A.
IV.Volume administered or concentration: Material was used

as supplied.
V.Post dose observation period: Up to 48 hours.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

No information of purity of the material reported.

Conclusion : The test material produced slight conjunctival irritation which may persist for several hours.

Reliability : (3) invalid
The study was not conducted according to GLPs.

17.03.2004 (32)

Species : rabbit
Concentration : undiluted
Dose :
Exposure time :
Comment : no data
Number of animals :
Vehicle : other
Result :
Classification :
Method : other
Year : 1958
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : The undiluted test material has a very slight effect on the eye. Contact with eyes was moderately painful but no corneal damage or serious conjunctival injury occurred. The 10% solution in propylene glycol was only slightly painful and slightly irritating to the eyes.

Source : Dow Corning Corporation
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Conclusion : The test material caused moderate pain with essentially no irritation to the washed or unwashed eyes.

Reliability : (4) not assignable
The study was conducted in 1958 and it was not in compliance with GLPs.

17.03.2004 (26)

5.3 SENSITIZATION

Type : Patch-Test
Species : human
Concentration : 1st: Induction 1 %
2nd: Challenge 1 %
3rd:
Number of animals : 111
Vehicle : other: none
Result : not sensitizing
Classification : not sensitizing
Method : other
Year : 2000
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : One hundred eleven subjects between the ages of 20 and 75

years, with a mean age of 47.9, were enrolled in the study. The majority of subjects were Caucasian women. One hundred subjects completed the study, six were lost to follow-up, one voluntarily withdrew, and four reported non-test article-related adverse events. No dermal reactions were noted during induction or challenge with the test article. Based on the conditions employed in this study and the elicited individual dermatological response grades, there was no evidence of sensitization to the test article.

Source : Dow Corning Corporation

Test condition : The study population consisted of males and females from the general population with different ethnic backgrounds. Inclusion criteria were as follows: 1) Individuals 18 years of age or older; 2) Individuals free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, would interfere with the study results; 3) Individuals of any skin type or race providing the skin pigmentation allowed discernment of erythema; 4) Individuals who completed a patch study Medical Screening form as well as a Medical/Personal History form; and 5) Individuals who read, understood and signed an informed consent agreement. Exclusion criteria were as follows: 1) Individuals with any visible skin disease at the evaluation site which, in the opinion of the investigative personnel, would interfere with the evaluation of the study material; 2) Individuals receiving systemic or topical drugs or medication which, in the opinion of the investigative personnel, would interfere with the study results; 3) Individuals with psoriasis and/or active atopic dermatitis/eczema; 4) Females who were pregnant, planned to become pregnant during the study, or were breast-feeding a child; 5) Individuals with a known sensitivity to cosmetics, skin care products or topical drugs as related to the material being evaluated; and 6) Individuals who were being treated for asthma.

A previously conducted range-finding primary irritation patch test was conducted with the test article to determine its ability to irritate the skin of human volunteer subjects using an occlusive primary irritation patch test. Under the conditions employed in the study (0.2 mL; 48-hour exposure period), the test article caused definite irritation when applied undiluted and at concentrations of 75%, 50% and 25% in methanol. The irritation was not clinically significant at concentrations of 1% and 10% in methanol. Based on the results of this study, the 1% dose level was chosen for repeated insult patch testing of the test article.

Study Design
The study extended over a 6-week period and involved 3 phases, Induction, Rest, and Challenge. The Induction Phase consisted of 9 consecutive applications of the study material and subsequent evaluations of the patch sites. The test article/acetone solution and the acetone vehicle were applied under semi-occlusive patch conditions and the pad was affixed with hypoallergenic tape. A sodium lauryl sulfate (SLS) solution was applied under occlusive conditions to assess compliance by evaluation of the positive control application site. The patches were applied to the infrascapular area of the back, either to the right

or left of the midline. The subjects were required to remove the patches approximately 24 hours after application. All subjects were told to avoid wetting the patches and were asked not to engage in activities that caused excessive perspiration. They were instructed to report any adverse events and concomitant medications and to notify the staff if they experienced any discomfort beyond mild itching or observed any adverse changes at the evaluation sites while on the study or within two weeks of completing the study. They returned to the facility at 48-hour intervals to have the sites evaluated and identical patches applied to the same sites. Dermatological responses were graded at the time of examination using a scale outlined by the International Contact Dermatitis Group. When the positive control site to assess subject compliance had a grade of +D (indicating definite erythema and damage to the epidermis), application of the sodium lauryl sulfate (SLS) 0.1% aqueous solution control was discontinued. Patches applied on Friday were removed by subjects after 24 hours and sites were evaluated on the following Monday, i.e., 72 hours after patch application. Following the ninth evaluation, the subjects were dismissed for a 10-15 day rest period. Subjects who were absent once during the 3-week, 9-patch induction phase received a make-up (MU) patch at the last induction visit. The MU applications were graded 48 hours later at the MU visit or were recorded as N9G (no ninth grading). The Rest Phase lasted for approximately 2 weeks. The Challenge Phase was initiated during the sixth week of the study. Identical patches were applied to sites previously unexposed to the study material. The subjects removed the patches after 24 hours and the sites were graded after additional 24-hour and 48-hour periods (i.e., 48 and 72 hours after application). To be considered a completed case, a subject must have had 9 applications and no fewer than 8 subsequent readings during induction and 1 application and 2 readings during challenge. Only completed cases were used to assess sensitization.

Test substance : Gamma-Glycidoxypropyltrimethoxysilane (CAS#2530-83-8)

Purity: >98%

Conclusion : Appropriate concurrent negative and positive compliance controls were included and the expected responses were observed. The test substance, Gamma-Glycidoxypropyltrimethoxysilane, did not demonstrate evidence of sensitization.

Reliability : (1) valid without restriction
Based on a review of the report, the study was judged to be scientifically defensible.

13.06.2003 (72)

Type : Buehler Test
Species : guinea pig
Concentration : 1st: Induction 100 %
2nd: Challenge 100 %
3rd:
Number of animals : 18
Vehicle :
Result : not sensitizing
Classification : not sensitizing
Method : other

Year : 1982
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Buehler method, Delayed contact hypersensitivity in the guinea pigs was used (Arch. Dermatol. 91: 171-175 (1965).
Result : Although some irritation was seen in negative control animals, no skin sensitization was demonstrated for DMSO. The test material exhibited no potential of dermal sensitization in guinea pigs. Animals treated with DNCB (a known sensitizer) exhibited clear evidence of sensitization. Toxic Response/Effects by Dose Level: Not a sensitizer in guinea pigs
Source : Dow Corning Corporation
Test condition : Test Subjects
I.Age at study initiation: Not reported. Animals weighed 296-499 g at the induction of treatment.
II.No. of Animals per sex per dose: 10 males/group for main study. 8 males/group for irritation controls.

Study Design
I.Vehicle: Induction: 80% ethanol; challenge: Acetone
II.Clinical observations performed and frequency: Only mortality, morbidity and signs of toxicity were observed weekly.
The dermal sensitizating capabilities were evaluated in Buehler test in guinea pigs. A range finding study was performed to determine the highest concentration which produced mild irritation (for induction) and the highest non-irritating concentration (for challenge). Undiluted test material was selected for both induction and challenge phases. Positive, 2,4-dintro chlorobenzene (DNCB) and negative, dimethyl sulfoxide and irritation controls were incorporated into the study. All animals were observed prior to treatment and on days 7, 14, 21, 28, 35 and 45 for mortality, morbidity and signs of toxicity. Evaluation of the dermal responses was made at 24 and 48 hours after administration of each challenge dose. Erythema and edema were scored according to the Draize scale.

Dose Levels: Induction: 0.2 ml 100% Test Material; 0.2 ml 100% DMSO for negative control; 0.2 ml 2,4-dinitrochlorobenzene (DNCB) at 0.5% in 80% ethanol as positive control. Challenge: Same concentrations as that of induction for both test material and negative control; 0.1% DNCB in acetone for positive control.

Frequency of Treatment: 3 times/week for 3 weeks induction phase; one 6 hour exposure was used for each challenge and re-challenge phase.

Control Group and Treatment: 100% DMSO

Post Exposure Observation Period: Two days following challenge and re-challenge.
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Purity of the test material was not reported.
Conclusion : Under the conditions of this study, the test material was

not a sensitizer in guinea pigs.

Reliability : (2) valid with restrictions
The study was conducted in 1982, most probably under GLPs.

18.03.2004 (43)

Type	:	Guinea pig maximization test
Species	:	guinea pig
Number of animals	:	20
Vehicle	:	peanut oil
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1984
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Magnusson and Klingman/OECD Guide-line 406
Result	:	No evidence of skin irritation or skin sensitization was observed in any of the animals following challenge phase. Body weight: No obvious effects on body weight gains or food consumption were noted.
Source	:	Dow Corning Corporation
Test condition	:	Test Subjects I.Age at study initiation: Young adult, weighing approximately 450 g II.No. of Animals per sex per dose: 20 females in the test group and 10 females in the control group. Study Design I.Vehicle: Peanut oil
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8) Purity of the test material was not reported.
Conclusion	:	Under the conditions of the study, the test material was not a skin sensitizer.
Reliability	:	(2) valid with restrictions The study was conducted under GLPs and the conduct and report were audited by Quality Assurance Unit. Characterization of the test material was not specified in the report. Positive control substance was not included in the study.

18.03.2004 (44)

Type	:	Buehler Test
Species	:	guinea pig
Concentration	:	1st: Induction undiluted occlusive epicutaneous 2nd: Induction undiluted occlusive epicutaneous 3rd: Induction undiluted occlusive epicutaneous
Number of animals	:	30
Vehicle	:	
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Result	:	There were no substance related effects or influence on body weight in either test or control animals. There was no erythema or edema observed during Induction Phase I, II or III; no skin irritation was observed in the control animals. There was no skin irritation observed in either test or control animals in the Challenge Phase.
Test condition	:	In the definitive test, a test group of 20 animals was induced with 100% test substance on days 0, 7 and 14 and subsequently challenged with 100% test substance on day 28. A control group of 10 animals was induced and challenged with MEH 56 corn oil.
Test substance	:	DYNASYLAN GLYMO; purity 98% glycidyloxypropyl-trimethoxysilan
Reliability	:	(1) valid without restriction
09.12.2004		(49)

Type	:	Buehler Test
Species	:	guinea pig
Concentration	:	1st: 1 % 2nd: 3rd:
Number of animals	:	
Vehicle	:	other
Result	:	ambiguous
Classification	:	
Method	:	other
Year	:	1982
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Buehler modified method for delayed contact hypersensitivity in the guinea pigs.
Result	:	No significant signs of gross toxic effects were noted. One animal in the test material group died on day 4. The death did not appear to be test material related. The test material produced a very slight sensitizing reaction in guinea pigs. The positive control material produced a sensitizing reaction. Toxic Response/Effects by Dose Level: Very weak sensitizer in guinea pigs.
Source	:	Dow Corning Corporation
Test condition	:	During induction phase, the test material (1% in DMSO) was applied topically 0.5 ml) once per week for 3 weeks. Animals in the positive control group received 0.5 ml of 2% paraphenylenediamine (PPD) in 80% ethanol while animals in negative control received 0.5 ml of DMSO. All applications were contained on multilayer 2 cm2 gauze patches for an exposure period of 6 hours. After the completion of the 14-day rest period, animals in all groups received 0.5 ml materials over the shaved left/flank area with which the induction applications had been made. All applications sites were occluded. Twenty four hours after application of the challenge dose, dermal irritation readings for all sites were recorded at 24, 48 and 72 hours using the Draize scale. Test Subjects I.Age at study initiation: 4-12 weeks old and weighed 300-500 g. II.No. of Animals per sex per dose: 10 males per material.

Study Design
I.Vehicle: DMSO/80% ethanol.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Purity of the test material not reported.

Conclusion : Under the conditions of this study, the test material was a very slight sensitizer in the guinea pigs.

Reliability : (3) invalid
The study was conducted in 1982, most probably not under GLPs.

1) This study found 30% test material in DMSO irritating while another study (Bio/Dynamics) has used 100% test material and found no skin irritation.
2) This study uses ertheyma only as a criteria for sensitization. A swelling parameter should have been scored because sensitization is often accompanied by slight edema.
3) No description of nature of redness was included in the report, since type of redness is usually different between irritation and sensitization.
4) The study uses 24 hours exposure during challenge applications, although no range-finding skin irritation data available for 24 hour exposure for comparison. The long exposure period for test material in vehicle (DMSO) most probably the irritation response from DMSO and not the delayed allergic reaction.

05.04.2004 (36)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	28 days
Frequency of treatm.	:	5 consecutive days per week for 4 weeks
Post exposure period	:	Not applicable
Doses	:	40, 400 and 1000 mg/kg/day
Control group	:	yes
NOAEL	:	> 1000 mg/kg
Method	:	OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : As our experience and knowledge associated with the issues surrounding the testing of TMSPGE increased, it has become apparent that it is not stable by the oral route.
Specifically, TMSPGE readily hydrolyzes to methanol and silanols (Note: methanol is included in the EPA HPV Challenge Program). pH has a significant effect on the rate of hydrolysis, and at pH 4, the hydrolysis is complete within 2.5 minutes. Slight changes in pH affect the rate of

hydrolysis, which may result in administration of differing forms of the test article with each dosing. The hydrolysis rate is susceptible to the presence of trace acid and/or base.

A non-GLP study was conducted to examine the fate of TMSPGE following oral (gavage) exposure. Five fasted female Sprague-Dawley rats were dosed with 2000 mg/kg TMSPGE mixed with activated charcoal as a tracer. After 20 or 30 minutes the animals were sacrificed, and the stomachs and gastrointestinal tracts examined for presence of test article. The study was also repeated in the absence of the activated charcoal tracer. In all cases, the hydrolysis product(s) of the test article were found in the stomach contents or in the upper gastrointestinal tract, and was observed to have the consistency of a siloxane gel. In cases where the stomach contents included food, small waxy particles of test article were observed. Both the gel-like substance and waxy particle forms of the hydrolysis products of the test article observed in the stomach and upper gastrointestinal tract support the rapid polymerization of TMSPGE under oral (gavage) conditions, as the test article exists as a clear, water like liquid. In either case, little or no absorption of test article appeared to have occurred. In contrast, there was no liquid present in the stomachs of animals gavaged with an equivalent dose of water and sacrificed after 30 minutes.

The lack of clinical signs of toxicity following acute or repeated dosing is likely related to the hydrolysis of TMSPGE and subsequent polymerization of the hydrolysis products, and thus, the lack of bioavailability.

Result : There were no test substance-related mortalities. One 40 mg/kg/day male and two 1000 mg/kg/day males died during the course of the study. However, necropsy of these rats revealed test substance to be present in the lungs and thus the deaths were associated with dosing trauma. There were no test substance-related effects on clinical condition, behavior, body weight, body weight changes or food consumption, nor were there any test substance-related effects on hematological, blood biochemical or urinalysis parameters; some statistical differences from control values were present in these data, but all values for the treated groups were within normal ranges. No test substance-related organ weights effects or gross or microscopic pathological changes were observed.

Under the conditions of this study, the NOAEL (No Observed Adverse Effect Level) for the test substance was found to be 1000 mg/kg/day or greater when administered orally five days per week for four weeks to male and female rats.

Source : Dow Corning Corporation

Test condition : There were 9-11 rats per sex in each group. Young adult rats weighed 260 + 21 grams (males) and 219 + 15 grams (females) at initiation of dosing. No vehicle was used; the test substance was administered undiluted. Observation for mortality and clinical condition was performed daily. Individual body weights and food consumption were measured every four days. Hematological (all animals), blood biochemical (all animals) and urine analysis (5/sex/group)

studies were carried out at the end of the treatment period. Hematological parameters evaluated were erythrocyte count, hemoglobin level, hematocrit, reticulocyte count, platelet count and total and differential leukocyte counts. Blood chemistry parameters were alkaline phosphatase, glutamic pyruvic transaminase, glutamic oxalacetic transaminase, blood urea nitrogen, lactic dehydrogenase, total protein, total bilirubin, total cholesterol, creatinine, Ca, Na, K, Cl, P, glucose, albumin and globulin. Urinalysis parameters were specific gravity, glucose, bile pigments, ketone bodies, protein, pH, occult blood and bilirubin. All rats received a gross pathological examination that included all major tissues, organs, orifices and the cranial, abdominal and pelvic cavities and their viscera. Fresh organ weights were recorded for liver, brain, kidneys, lungs, heart, spleen, adrenals, testes and ovaries. Paired organs were weighed separately. The following organs/tissues were collected from all rats and preserved in 10% neutral buffered formalin: liver, kidneys, brain, sciatic nerve, mesenteric lymph node, urinary bladder, heart, lungs, gonads, spleen, pituitary, prostrate/uterus, thyroid, parathyroid, adrenals, stomach, small and large intestines, bone, seminal vesicles, epididymides and gross lesions. All of these tissues from the control and high dose groups were examined microscopically.

Statistical Methods: Statistical comparisons between the control and treated groups were carried out where appropriate. Body weights, food consumption, hematology values, blood chemistry values and absolute and relative organ weights were analyzed by a one-way analysis of variance. Group means were compared to control values using Dunnett's multiple t-test. Where appropriate, a non-parametric analysis of variance by ranks was used to evaluate these parameters. The 95% ($P < 0.05$) confidence level was chosen as the criteria of significance.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Conclusion : The test substance has a low order of toxicity in rats by repeated oral administration. The NOAEL exceeds current OECD and EPA maximum dose level requirements for studies of this type.
Reliability : (1) valid without restriction
Based on a review of the report, the study was judged to be scientifically defensible.

18.06.2003 (33)

Type : Sub-acute
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : 2 weeks
Frequency of treatm. : Nine exposures of 6 hours per day, 5 exposures during week 1 and 4 exposures during week 2.
Post exposure period : None, rats were necropsied on the day after exposure.
Doses : Target concentrations were 0, 75, 225 and 750 mg/m3.
Control group : yes
Method : other
Year : 1982
GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Remark : Under the conditions of this study, the No Observed Adverse Effect Concentration is 0.225 mg/l.

Result : Actual dose levels:
males - 0, 77, 226, 707 mg/m3
females - 0, 73, 226, 734 mg/m3

No deaths occurred in the controls or in animals treated with 75 or 225 mg/m3 test material. However, six rats at the high exposure level (5 males and one female) either died or were sacrificed in a moribund state from three to five days after initiation of the study. The animals had no evidence of acute tissue toxicity but appeared to have succumbed to inanition. The mid and high exposure level groups exhibited signs of nasal discharge and dry and moist rales and body weight depressions following a dose-response pattern. The body weight decrease was noted only at 750 mg/m3. Males lost about 13% and females lost 2.6% in the first week. In the second week, however, no body weight loss was observed in the females but males lost 3.7% body weight.
Microscopic examination of the tissues revealed no histopathological evidence of a systemic or localized (respiratory tract) effect of the test material.

Source : Dow Corning Corporation

Test condition : Test Subjects
I. Age at study initiation: 7-8 weeks
II. No. of Animals per sex per dose: 10

Study Design
I. Vehicle: None
II. Whole body exposure
III. Clinical observations performed and frequency: Daily for unusual conditions and viability and weekly for detailed physical assessment. Food consumption was not measured.
IV. Organs examined at necropsy (macroscopic and microscopic): A complete examination of internal organs and tissues was conducted. At gross necropsies, brain, kidneys, lungs with trachea, livers, spleen, heart, testes, and ovaries were weighed. Selected organs and tissues including nasal turbinates and paranasal sinuses were preserved in formalin except eyes and testes which were fixed initially in Bouin's solution, then preserved in formalin. Microscopic examinations were performed for both dead and surviving animals in all groups.
V. Aerosol inhalation study. Chamber aerosol concentrations were measured hourly for each exposure level and aerosol particle size was determined once a day.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

No purity of the test material reported.

Conclusion : The authors concluded that under the conditions of this study and on the basis of histopathology results, the test material was considered to be non-toxic systemically and non-irritating to the respiratory tissue.

Reliability : (2) valid with restrictions
The study appeared to comply with GLP's and was approved by the Quality Assurance Unit.

09.12.2004 (42)

Type	:	Sub-acute
Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	6 hours/day
Frequency of treatm.	:	Five days per week for three weeks followed by four days of exposure during the fourth week for a total of 19 exposures over a 4-week period
Post exposure period	:	Not applicable
Doses	:	0 or 150 mg/m3
Control group	:	yes
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS

Method	:	The data for continuous, parametric variables were intercompared for the exposure and control groups by use of Levene's test for homogeneity of variances and by t-tests. If Levene's test indicated homogeneous variances, the groups were compared by pooled variance t-tests. If Levene's test indicated heterogeneous variances, the groups were compared by separate variance t-test. Frequency data were compared using Fisher's exact tests. All statistical tests, except the frequency comparisons, were performed using BDMP Statistical Software (Dixon, 1985). The frequency data tests are described in Biometry (Sokal and Rohlf, 1969). The probability value of $p < 0.05$ (two-tailed) was used as the critical level of significance for all tests.
Result	:	A mean TMSPGE-hydrolysate gravimetric concentration of 119 mg/m3 was obtained. The MMAD was 2.93 microns with a sg of 1.71. No mortality or exposure-related clinical signs were observed during the study. Decreases in absolute body weight and/or body weight gain were observed for the TMSPGE-hydrolysate treated animals during each week of the study. At the end of the study the percent decrease in mean body weight of the TMSPGE hydrolysate exposed group compared to the control group was 11%. At the end of the study the percent decrease in mean body weight gain of the TMSPGE hydrolysate exposed group compared to the control group was 29%. No gross or microscopic lesions that could be attributed to TMSPGE-hydrolysate aerosol exposure were noted.
Test condition	:	The inhalation chambers used in the study were constructed of stainless steel with glass windows for animal observations. Chamber volume was approximately 1300 liters and the airflow was approximately 300 L/min (13.5 air changes per hour). Chamber temperature and relative humidity were determined at least twelve times per exposure. A 2% TMSPGE-hydrolysate solution was prepared daily and was metered from a piston pump into an atomizer fitted with a liquid nozzle and an air nozzle. The atomizer was inserted into the top of the inhalation chamber turret where the liquid aerosol was dispersed throughout the chamber by filtered chamber supply air. The operating pressure of the atomizer used to generate the TMSPGE-hydrolysate was 20 psig. Chamber concentrations of TMSPGE-hydrolysate were determined by gravimetric methods. Four samples were obtained from the TMSPGE-hydrolysate aerosol exposure

chamber each day. The nominal concentration was calculated daily by dividing the total amount of material delivered to the chamber by the total airflow rate. The particle size distribution was measured using a TSI Aerodynamic Particle Sizer and a 20:1 diluter. These determinations were made once a day for the duration of the study. The data collected were analyzed by probit analysis to obtain the mass median aerodynamic diameter (MMAD) and the geometric standard deviation (sg).

There were 15 rats each in the TMSPGE-hydrolysate treated and control groups. Five of the fifteen animals in each group were assigned to a satellite group destined for ultrastructural evaluation of the larynx; however, electron microscopic examination was not performed. The rats (41 days of age) weighed 131.2 + 9.0 grams at the initiation of exposure. The rats were observed daily during exposure and observations were recorded on a group basis. Preceding and following each exposure, observations were recorded for animals exhibiting overt clinical signs. At the time of body weight collection and just preceding necropsy, detailed observations were performed on all animals. On non-exposure days, animals were observed once a day for overt clinical signs and mortality. Individual body weights were measured prior to initiation of the first exposure, weekly and immediately prior to sacrifice. Ten animals of the TMSPGE-hydrolysate treated and control groups were sacrificed on the day following the 19th exposure. A complete necropsy was performed on these animals and the following tissues were fixed in 10% neutral buffered formalin for histologic evaluation: gross lesions, larynx, lungs, trachea, nasal turbinates and kidneys. The satellite group (5 TMSPGE-hydrolysate treated and 5 control animals) was sacrificed on the day following the 18th exposure. The larynges of three control animals and five TMSPGE-hydrolysate treated animals were taken and immersion-fixed in 2% glutaraldehyde for possible electron microscopic examination. The remaining two rats from the control group were subjected to a complete necropsy and perfusion-fixed with 5% methanol-free EM grade formaldehyde. The perfusion-fixation was performed to allow comparison of these control rats with rats from another silane group that was also perfusion-fixed. The larynges from these two rats were then further immersion-fixed in 2% glutaraldehyde. Other organs, including brain, spinal cord, and peripheral nerves, were taken from these control animals and processed for light microscopic evaluation.

Test substance : 3-Glycidoxypropyltrimethoxysilane hydrolysate
Conclusion : Repeated exposure of rats to 119 mg/m3 of aerosol generated from TMSPGE-hydrolysate did not produce any evidence of laryngeal granuloma formation.
Reliability : (2) valid with restrictions
09.12.2004 (16)

Type : Sub-acute
Species : rat
Sex : male
Strain : other
Route of admin. : dermal
Exposure period : Approximately 1.25 hours/day

Frequency of treatm.	:	Two days (W, F) for the first week, three days (M, W, F) for the second week, and two days (M, W) for the third week for a total of 7 applications over 17 days
Post exposure period	:	Not applicable.
Doses	:	0 or 1 ml/kg
Control group	:	yes
NOAEL	:	> 1 ml/kg bw
Method	:	
Year	:	1975
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Statistical comparisons were performed by the homogenicity and analysis of variance procedures.
Result	:	There was no mortality or remarkable differences in body weight or absolute/relative liver or kidney weights. Abnormal skin responses (desquamation, and fissures) were noted on the test substance-treated rabbits. No abnormal skin responses were noted on the control animals.
Test condition	:	Groups of four male albino rabbits, between 2.0 - 2.3 kg, received 7 dermal applications over a 17 day period. The dermal LD50 was determined to be 3.97 mL/kg, one-quarter of the LD50, or 1.0 ml/kg, was selected as the dose level for this study. The dose was gently massaged, using a glass test tube as the applicator, into the clipped skin on the belly, and on the flanks as the size of the dose necessitated. As the dose of the test substance was so large that it could not be applied in one application, one-half of the dose was applied for one minute during two separate 15-minute periods. As skin irritation resulted with the test substance, the subsequent dose was applied to an intact area of skin. One hour after the last application, the skin was gently blotted with cleansing tissue to remove any unabsorbed liquid. The rabbits were weighed before study initiation, before each daily dose, and two days following the final application (study termination). The liver and kidney were weighed at study termination.
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Conclusion	:	The no-observed-effect-level (NOEL) for systemic effects was determined to be greater than 1.0 mL/kg/application of the test substance to rabbits under the conditions employed in this study.
Reliability	:	(3) invalid

09.12.2004 (18)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella typhimurium TA97, TA98, TA100
Test concentration	:	8, 40, 200, 1000, and 5000 ug/plate
Cycotoxic concentr.	:	>5000 ug/plate
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1988
GLP	:	yes

Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Not specified, but generally consistent with OECD Guide-line 471
Result	:	·Frequency of reversions/mutations/aberrations, polyploidy as appropriate: The treatment of strain TA100 with GLYMO gave rise to numbers of revertants/plate at least five times that of the solvent control in the absence and presence of S-9. GLYMO treatment of strain TA97 in the absence and presence of S-9 also produced increases in revertant numbers but only about twice the background level.
Source	:	SEHSC
Test condition	:	·Test Design: ØNumber of replicates: One ØFrequency of dosing: Once ØPositive and negative control groups and treatment: Positive controls: 9-aminoacridine, 2-nitrofluorene, Sodium azide, were used for strains TA97, TA98, TA100, respectively. 2-aminoanthracene was used for all strains in the positive controls. Negative controls used ethylene glycol dimethyl ether (EGDME). ØNumber of metaphases analyzed: Not applicable ·Solvent: EGDME ·Description of follow up repeat study: A follow up study was not performed. ·Criteria for evaluating results (e.g. cell evaluated per dose group): Analysis of variance (F-test) and regression analysis.
Test substance	:	3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)
Conclusion	:	Mutagenic in Salmonella typhimurium strains TA97 and TA100 both in the absence and presence of S-9.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.07.2004 (23)

Type	:	Bacterial reverse mutation assay
System of testing	:	Bacterial
Test concentration	:	0.001, 0.1, 1.0, 5.0, 10.0 and 20.0 µl/plate
Cycotoxic concentr.	:	Not reported
Metabolic activation	:	with and without
Result	:	positive
Method	:	OECD Guide-line 471
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Quantity: 0.1 to 0.15 ml of a 9000 x g supernatant of rat liver homogenate per ml of reaction mixture Induced or Not Induced: Yes; Arochlor 1254
Result	:	The test substance was clearly mutagenic in the TA-100 and TA-1535 strains, both with and without metabolic activation. Dose-related increases in the numbers of revertants were seen for TA-100 at treatment concentrations of 1 and 5 µl/plate (the highest levels tested for this strain). Dose-related increases in the numbers of revertants were seen for the TA-1535 strain at treatments concentrations of 5.0, 10.0 and 20.0 µl/plate. In addition, the numbers of TA-1535 revertants at treatments of 0.1 and 1.0 µl/plate

(activation assay) were approximately two times the solvent control. No evidence of mutagenic activity was present for any of the other strains that were tested.

Source : SEHSC
Test condition : The control and test substances were administered once. The solvent (negative control) for all treatments/strains was dimethylsulfoxide (DMSO), 50 µl/plate.
Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Conclusion : Appropriate concurrent negative and positive controls were included, and the expected responses were observed. The test substance, 3-glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8), induced mutagenicity in the TA-100 and TA-1535 strains, both with and without metabolic activation. No mutagenic activity was seen in any of the other strains that were tested. The results indicate that the test substance induces missense mutations and does not require metabolic activation to be genetically active.
Reliability : (2) valid with restrictions
The study was not conducted according to GLPs.

29.03.2004 (60)

Type : Bacterial reverse mutation assay
System of testing : Bacterial
Test concentration : 0.5, 5, 100 and 500 ul/plate
Cycotoxic concentr. : Not reported
Metabolic activation : with and without
Result : positive
Method : other
Year : 1979
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Genotoxic effects with metabolic activation: positive in TA-1535 and TA 100 (500 ul/plate)

Genotoxic effects without activation: positive in TA1535 and TA-100 (100 ul/plate)

Source : SEHSC
Test condition : · Test Design:
Ø Number of replicates: Only one plate per concentration was used. However, results are given as the average of ten replicate counts on each plate.
Ø Positive and negative control groups and treatment: Anthramine was the positive control agent for the activation assay (all strains). In the nonactivation assay, the positive control substances were sodium azide (TA-1535 and TA-100), 2-nitrofluorene (TA-1538 and TA-98) and 9-Aminoacridine (TA-1537). All positive control treatments were 100 ug/plate.

· Solvent: The solvent (negative control) for all treatments /strains was DMSO, 50ul/plate.
· Criteria for evaluating results (e.g. cell evaluated per dose group): The plates were incubated for 48 hours at 37 degrees centigrade, then counted. Approximately 108 cells from a 16 hour culture of each strain were evaluated. Revertants per plate for positive control substances ranged from 62 to more than 1000, depending on the agent and strain.
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No.

2530-83-8)

Conclusion : The test material exhibited genetic activity in Salmonella strains TA-1535 and TA-100 with and without activation.

Reliability : (2) valid with restrictions
The study was not conducted according to GLPs.

29.03.2004 (30)

Type : Bacterial reverse mutation assay
System of testing : Bacterial
Test concentration : 5, 50, 100 and 500 ug/plate
Cycotoxic concentr. : Not reported
Metabolic activation : with and without
Result : positive
Method : other
Year : 1977
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Ames et al. Mutation Research 31:347, 1975
Result : A dose-related increase in mutation frequency was observed between 5-500 ug/plate in strains TA-1535 and TA-100 with and without metabolic activation.
Source : Dow Corning Corporation
Test condition : · Test Design:
Ø Number of replicates: Only one plate per concentration was used. However, results are given as the average of ten replicate counts on each plate.
Ø Frequency of dosing:
Ø Positive and negative control groups and treatment: Positive controls for non-activation: Methylnitrosoguanidine (MNNG), 9-Aminoacridine (AA), 2-Nitrofluorene (NF). Positive controls for activation: 2-Anthramine (ANTH), 9-Aminoquinoline (AMQ), 2-Aminofluorene (AF).
Ø MNNG treatment was 10 ug/plate. All others were 100 ug/plate.
· Solvent: The solvent (negative control) for all treatments/studies was DMSO 50 ul/plate
· Criteria for evaluating results (e.g. cell evaluated per dose group): The plates were incubated for 48 hours at 37 degrees centigrade, then counted. Approximately 108 cells from a 16 hour culture of each strain were evaluated. Revertants per positive control substances ranged from 18-566.
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

No information of purity of the material provided
Conclusion : The test material exhibited genetic activity in Salmonella typhimurium strains TA-1535 and TA-100 with and without activation.
Reliability : (2) valid with restrictions
The study was not conducted according to GLPs.

29.03.2004 (29)

Type : other: cell transformation
System of testing : Balb/3T3 cells
Test concentration : 37.3, 149.0, 224.0, 280.0 and 350.0 nl/ml
Cycotoxic concentr. : survival ranged from 0.1% at
395 nl/ml to approximately 103 to 111% over the 97.7 to 1.53 nl/ml range

Metabolic activation :
Result : negative
Method : other
Year : 1982
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Kakunaga, T. (Int. J. Cancer 12: 463-473, 1973)
Statistical methods: Bailey's modification of the student's t-test (Bailey, NTJ. Statistical Methods in Biology; Wiley and Sons, Inc. NY, pg 50, 1959).

Result : In the dose range-finding study, treatment resulted in survivals ranging from 0.1% at 395 nl/ml to approximately 103 to 111% over the 97.7 to 1.53 nl/ml range. No survivors were observed for treatments with 781 nl/ml and higher. Based on these results, concentrations of 350.0, 280.0, 224.0, 149.0, and 37.3 nl/ml were chosen for the transformation assay. This concentration range corresponded to approximately 5-10% to nearly 100% survival in the preliminary cytotoxicity test.

In the transformation assay, treatment with the negative control induced a total of 3 foci among the 42 negative control flasks, for an average of 0.07 focus/flask. The positive control treatments with 5.0 µg/ml MCA induced a total of 106 foci among the 27 positive control flasks, for an average of 3.9 focus/flask. Log10 analysis of these data showed that the positive control frequency of 0.654 foci/flask was highly significant ($p < 0.01$) compared to the negative control value of 0.022 focus/flask, indicating the sensitivity of the test. One focus each was induced at 280.0 nl/ml and at 149.0 nl/ml. No transformations were noted at 37.3, 224.0, or 350.0 nl/ml. After log10 analysis, the average number of foci/flask ranged from zero at 350, 224 and 37.3 nl/ml to 0.014 at 280 and 249 nl/ml. Compared to the negative control value, none of the frequencies of transformed foci observed for the test material treatments achieved the 95% confidence level of being significantly altered. In addition, no evidence of a dose-related response was observed

Source : SEHSC

Test condition : Dosage Selection: The solubility of the test chemical in growth medium was determined at fifteen concentrations ranging from 1.5 to 25,000 nl/ml. Each dose was applied to three culture dishes seeded 24 hours earlier with 200 cells per dish. After an exposure period of 72 hours, the cells were washed and incubated in growth medium for an additional 3-5 days. The surviving colonies were stained and counted and a relative survival for each dose was obtained by comparing the number of colonies surviving treatment to the colony counts in negative control dishes. The highest dose chosen for the subsequent transformation assay caused no more than a 90% reduction in colony forming ability. Four lower doses (usually including one dose with little apparent toxicity) were also selected for the main study.

Transformation Assay: Twenty-four hours prior to treatment, a series of 60 mm dishes were seeded with 104 cells/dish and incubated. At least 20 dishes were then treated for each of the following conditions: Five pre-selected doses of test

chemical; positive control (3-methylcholanthrene at 5.0 µg/ml); and negative control (growth medium). The dishes were incubated for a 72-hour exposure period; the cells were washed and incubation was continued for approximately four weeks with re-feeding twice a week. The assay was terminated by fixing the cell monolayers with methanol and staining with Giemsa. The stained dishes were examined to determine the number of foci of transformed cells.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Conclusion : The test material was considered to be inactive in the Balb/3T3 in vitro transformation assay.
Reliability : (2) valid with restrictions
13.07.2004 (57)

Type : Bacterial reverse mutation assay
System of testing : Bacterial
Test concentration : 0.1, 1.0, 5.0, 10.0, 25.0, 50.0, 100.0, and 150.0 µl/plate (same concentrations for activated and non-activated conditions)
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1983
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : The test substance was mutagenic in the TA-100 and TA-1535 strains, both with and without metabolic activation.
Dose-related increases in the numbers of revertants were seen for TA-100 at treatment concentrations of 0.1 up to 150 µl/plate (the highest level tested for this strain).
Dose-related increases in the numbers of revertants were seen for the TA-1535 strain at treatments concentrations of 100.0 and 150.0 µl/plate without activation and 50.0 to 150.0
with activation. No evidence of mutagenic activity was present for any of the other strains that were tested.
Source : SEHSC
Test condition : The control and test substances were administered once. The solvent (negative control) for all treatments/strains was distilled water, 10-22 µl/plate. Tests conducted with one plate per test concentration. Report indicates that the test material is 3-Glycidoxypropyl-trimethoxysilane (CAS No. 2530-83-8), ingredients F and L, but there is no specification of percentages or identity of F and L.
Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Report indicates that the
test material is 3-Glycidoxypropyl-trimethoxysilane (CAS No. 2530-83-8), ingredients F and L, but there is no specification of percentages or identity of F or L.
Conclusion : Appropriate concurrent negative and positive controls were included, and the expected responses were observed. The test substance, 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8), induced mutagenicity in the TA-100 and TA-1535 strains, both with and without metabolic activation. No mutagenic activity was seen in any of the other strains that were tested. The results indicate that the test substance induces mis-sense mutations and does not require metabolic activation to be genetically active.
Reliability : (3) invalid

The full report for this study was unavailable and insufficient information was given in the available summary to adequately identify the test substance. Report indicates that the test material is 3-Glycidoxypropyl-trimethoxysilane (CAS No. 2530-83-8), ingredients F and L, but there is no specification of percentages or identity of F or L.

24.03.2004 (58)

Type : Mouse lymphoma assay
System of testing : in vitro L1578Y mouse lymphoma TK +/- cells
Test concentration : 100, 300, 500, 1000, 2000, 3000 nl/ml (non activation), 2000, 4000, 5000, 6000, 8000 nl/ml (with S9 activation)
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1983
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : Appropriate concurrent negative and positive controls were included, and the expected responses were observed. Under non-activation conditions, a dose-dependent increase in mutant frequency was induced and exceeded the minimum criteria for mutagenicity (83.4 X 10-6) at 2000 nl/ml and 3000 nl/ml. Low to moderate toxicity was induced (percent relative growth 97% - 37.7%).

In the presence of metabolic activation a wide range of toxicities was observed (percent relative growth 91.2% - 8.9%). All the assayed treatments exceeded minimum criterion of 68.0 X 10-6. However, relative growth was dramatically inhibited at concentrations of 5000 nl/ml or greater.

Source : SEHSC
Test condition : Stock solutions were prepared and then 1:10 dilutions were introduced into the media containing cells. The control and test substances were administered once. The solvent (negative control) for all treatments/strains was water. Solvent control for non-water soluble materials was DMSO. No indication of the quantity of S9 was given for the activation study.

Positive Control Agents and Doses (µg/plate)
Ethylmethane sulfonate (EMS) at 0.5 µl/ml was the positive control for tests lacking S9 activation.
Dimethylnitrosamine (DMN) was used at concentrations of 0.15 and 0.3 µl/ml for studies with S9 activation.

To select the appropriate doses ranges for cloning, cells are exposed to the test chemical for 4 hours and then are washed, placed in growth medium for 2-3 days to allow recovery, growth, and expression of the TK -/- phenotype. Cell counts were performed daily and appropriate dilutions were made to allow optimum growth rates. After the cloning doses were selected, 3 X 10^-6 cells for each dose level were seeded onto soft agar plates with selection medium. Resistant (mutant) colonies were counted after 10 days of incubation. A portion of the cell suspension was cloned in

normal medium. The ratio of resistant colonies to total viable cell number was the calculated mutant frequency.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Conclusion : The test substance, 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8), induced mutations in mouse lymphoma L1578Y TK cells, both with and without metabolic activation.
Reliability : (2) valid with restrictions
A generic study protocol was included with the report, but the conditions specific to the conduct of this study were not given. The methods used in this study are scientifically defensible.

24.03.2004 (59)

Type : Bacterial reverse mutation assay
System of testing : Bacterial, TA 100
Test concentration : 2.5 mg/plate
Cycotoxic concentr. : Substance was not cytotoxic at 2.5 mg
Metabolic activation : with and without
Result :
Method : other
Year : 1981
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Ames et al, Mutation Research 31: 347-364, 1975
Remark : It is well known that this class of compounds (i.e., epoxides) are subject to metabolic inactivation by the enzyme epoxide hydrase present in mammalian tissues. Therefore, it is reasonable to assume that the mutagenicity of [3-Glycidoxypropyltrimethoxysilane] would be reduced in a mammalian system. This study was designed to test this hypothesis by adding increasing amounts of cellular homogenate from rat and rabbit tissues to [3-Glycidoxypropyltrimethoxysilane] and then assaying its mutagenic activity in the Ames test.
Source : Dow Corning Corporation
Test condition :
· Test Design:
Ø Number of replicates: All treatments were plated in duplicate.
Ø Frequency of dosing: The control and test substance were administered once.
Ø Positive and negative control groups and treatment: Benzo(a)pyrene (2.5 ug) and
p-Chlorophenylglycidyl ether (50 ug) were used as reference standards.
Ø Number of metaphases analyzed:
· Solvent: DMSO
· Description of follow up repeat study:
· Criteria for evaluating results (e.g. cell evaluated per dose group): The plates were incubated for up to 72 hours at 37 degrees centigrade, then counted. The number of cells evaluated per treatment group was not reported.
Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

No information of purity of the material provided.
Conclusion : The mutagenicity of [3-Glycidoxypropyltrimethoxysilane] and other alkyl epoxides observed in the standard Ames Reverse Mutation Assay may not reflect its mutagenic potential in a mammalian system due to the presence of enzymes capable of

inactivating the reactive epoxide moiety.

Reliability : (3) invalid
29.03.2004 (34)

Type : other: cell transformation
System of testing : Secondary hamster embryo cells
Test concentration : 20 - 200 µg/ml
Cycotoxic concentr. :
Metabolic activation : no data
Result : ambiguous
Method : other
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Although the results of this test were determined to be inconclusive, a complete copy of this study was not available for review
Result : The positive controls yielded inconsistent results. The test material, tested at concentrations of 20 through 200 µg/ml, also yielded inconsistent results. The results of this test were inconclusive.
Source : SEHSC
Test condition : The test material was dissolved in DMSO. Secondary hamster embryo cells were grown for three days after which samples of 750 cells were cultured for toxicity and 5 x 104 for transformation. Cells were exposed to the test material for 6 days and then grown in culture with media changes every 4 days. On day nine, toxicity was determined while transformation was determined at periods up to 28 days (Casto et al., Canc. Res. 37:3508-3515, 1977). At this time, the cells were fixed in formalin with Giemsa stain. These cultures were then closely inspected for the appearance of morphologically transformed colonies.
Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Reliability : (3) invalid
13.07.2004 (9)

Type : other: cell transformation
System of testing : BALB/3T3 Cells
Test concentration : 8.3, 12.5 and 16.6 ug/ml
Cycotoxic concentr. : Not reported
Metabolic activation : no data
Result : negative
Method : other
Year : 1981
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Kakunagam Int. J. Cancer 12:463, 1973

The test material was incubated for 72 hours at 37 degrees centigrade with exponentially growing BALB/3T3 (CL-A31) cells. After incubation, the medium was discarded and the target cells washed with fresh medium. Approximately 9-11 days after the initiation of the experiment, plates designated for cytotoxicity were fixed, stained and scored for surviving colonies in order to determine plating efficiency. Approximately 30-40 days after the initiation of the experiment, plates were fixed, stained, and scored for

the morphologically-transferred phenotype

Source : Dow Corning Corporation

Test condition : I. Test Design:
A. Number of replicates: 12
B. Frequency of dosing: The controls and test substance were administered once.
C. Positive and negative control groups and treatment: Negative controls (DMSO) added to the test system in the preparation of dilutions of the test material (2.5 x 10^3 ug/ml). Positive control (N-Methyl-N-nitro-N-nitrosoquanidine (MNNG) prepared in sterile distilled water (0.5 ug/ml).
D. Number of metaphases analyzed: N.A.
II. Solvent: DMSO
III. Description of follow up repeat study: N.A.
IV. Criteria for evaluating results (e.g. cell evaluated per dose group): Approximately 1x10^4 cells per 60 mm dish were seeded for determination of the phenotype transformation effects of each treatment.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

Purity of the test material not reported

Conclusion : The authors concluded that at the concentrations tested, the test material did not induce cell transformation in BALB/3T3 CL-A31.

Reliability : (3) invalid
The study was not conducted according to GLPs. There was no evidence that the maximum cell concentration tested was high enough and there is no indication that positive and solvent controls gave the appropriate responses.

13.07.2004 (31)

Type : Bacterial reverse mutation assay

System of testing : Bacterial

Test concentration : 0.05, 0.1, 0.5, and 1.0 mg/plate

Cycotoxic concentr. : No information provided

Metabolic activation : without

Result : positive

Method : other

Year : 1982

GLP : no

Test substance : as prescribed by 1.1 - 1.4

Method : Ames (Mutation Research 31: 347-364, 1975)

Responses (number of revertants) to the test substance were compared to concurrent negative and positive controls.

Result : The test material induced a dose-related response at all doses tested. Under the conditions of this study, the test material was found to be mutagenic under non-activation conditions.

Source : Dow Corning Corporation

Test condition : -Criteria for evaluating results: The number of revertant, colony producing, bacteria were counted after a forty-eight hour growth period. A dose-related increase in revertants over spontaneous background was considered a positive test result.
Dimethylsulfoxide (DMSO) was used to prepare the dilutions of the test material and as a negative (solvent) control (50 µl/plate). Sodium azide (1.0 µg/plate) was used as the

positive control.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

No information of purity of the material provided

Conclusion : The test material exhibited genetic activity in Salmonella strain TA-100 without activation.

Reliability : (3) invalid
This study does not meet important criteria of today's standard methods

29.03.2004 (4)

Type : Mammalian cell gene mutation assay
System of testing : mouse lymphoma cell line (derived from L5178Y)
Test concentration : 0.33, 0.65, 1.30, 2.60, and 5.20 µl/ml
Cycotoxic concentr. : 5.2 ul/ml
Metabolic activation : without
Result : positive
Method : other
Year : 1976
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Modification of that reported by Clive and Spector (Mutat. Res 31: 17-20, 1975)

Result : The results show a mutagenic response four times the negative control at the high dose of the test material and the data show a dose response over the three highest concentrations. The test material was cytotoxic at 5.20 µl/ml.

Source : SEHSC

Test condition : Only non-activation conditions were employed since preliminary studies with bacteria indicated that the test material was mutagenic without metabolic activation from a rat liver S9 preparation.

The mouse lymphoma cell line used in this study was derived from L5178Y. The mouse lymphoma cells were maintained in Fischer's Medium for leukemic cells of mice with 10% horse serum and sodium pyruvate. Cloning medium consisted of Fischer's medium with 20% horse serum, sodium pyruvate, and 0.37% agar. Selection medium was made from cloning medium by the addition of 5.0 mg of BUdR to 100 ml of cloning medium. The solubility, toxicity, and doses were determined prior to screening. Toxicity was measured as loss in growth potential of the cells induced by a four-hour exposure to the chemical followed by a 24-hour expression period in growth medium. A minimum of four doses was selected from the range of concentrations by using the highest dose that showed no loss in growth potential as the penultimate dose and by bracketing this with one higher dose and at least two lower doses. Toxicity produced by test article treatment was monitored during the experiment. Based on preliminary screening, the test article was evaluated at 0.33, 0.65, 1.30, 2.60, and 5.20 µl/ml in the main assay. The solvent in which the test article was dissolved was used as a negative control. The solvent in this experiment was the tissue culture medium. The positive reference mutagen, ethylmethanesulfonate (EMS at 300 µg/ml), was included to test the responsiveness of the cells in the absence of a mouse liver activation system.

Non-activation assay: The procedure used is a modification of that reported by Clive and Spector (Mutation Research, 31:17-29, 1975). Prior to treatment, cells were cleaned of spontaneous TK-/- by growing them in a medium containing thymidine, hypoxanthine, methotrexate, and glycine (THMG). The test article was added to the cleansed cells in growth medium at the predetermined doses for five hours. The treated cells were washed, fed, and allowed to express in growth medium for three days. At the end of this expression period, TK -/- mutants were detected by cloning the cells in the selection medium for 10 days. Surviving cell populations were determined by plating diluted aliquots in nonselective growth medium. The mutation index was derived by dividing the number of clones formed in the BUdR-containing selection medium by the number found in the same medium without BUdR. The ratio was then compared to that obtained from other dose levels and from positive and negative controls. Colonies were counted on an Artek colony counter that resolves all colonies greater than 200 microns in diameter.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Reliability : (3) invalid
This study does not meet important criteria of today's standard methods

29.03.2004 (1)

Type : Bacterial reverse mutation assay
System of testing : TA1535
Test concentration : 1, 5, 10, 50, 100, 500 and 1000 ul/ml
Cycotoxic concentr. : 1000 ul/mL
Metabolic activation : without
Result : positive
Method : other
Year : 1976
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical methods: Responses (number of revertants) to the test substance were compared to concurrent negative and positive controls
Result : The test material was mutagenic at the 50, 100 and 500 µl/ml concentrations, as evidenced by dose-related increases in the numbers of revertants, and possibly at 10 µl/ml, where the number of revertants was nearly two times the solvent control. Cytotoxicity was observed at 1000 µl/ml.
Source : SEHSC
Test condition : An overnight culture of S. typhimurium strain TA-1535 grown in complete nutrient medium was concentrated to approximately 1010 cells per ml. The cells were washed and maintained in 0.9% saline. The cells were diluted in 0.67M sodium phosphate buffer pH 7.4 to a concentration of 108 cells/ml. Approximately 1.5 ml of this suspension was added to individual vessels for treatment. Aliquots of the test material were added to the suspensions to provide the concentration range identified above. Additional buffer was added in the negative control. The two lowest doses were prepared by diluting the test material 1:10 in DMSO and then adding aliquots into the test system. DMSO is not mutagenic in this assay. Concentrations were based on previous

experience with the test material in bacteria assays. The vessels were shaken at 37oC for 60 minutes. The contents were then either diluted and plated on complete agar plates to establish surviving populations or plated undiluted onto selective agar plates to establish mutant counts. After incubation at 37oC for three days, the plates were scored and mutation frequencies calculated for the control and each test concentration.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Reliability : (3) invalid
This study does not meet important criteria of today's standard methods

29.03.2004 (1)

Type : Bacterial reverse mutation assay
System of testing : Bacterial
Test concentration : 0.05, 0.1, 0.5, and 1.0 mg/plate
Cycotoxic concentr. :
Metabolic activation : without
Result : positive
Method : other
Year : 1982
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Ames (Mutation Research 31: 347-364, 1975)

Responses (number of revertants) to the test substance were compared to concurrent negative and positive controls.

Result : The test material induced a dose-related response at all doses tested. Under the conditions of this study, the test material was found to be mutagenic under non-activation conditions.

Source : SEHSC
Test condition : Dimethylsulfoxide (DMSO) was used to prepare the dilutions of the test material and as a negative (solvent) control (50 µl/plate). Sodium azide (1.0 µg/plate) was used as the positive control.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Reliability : (3) invalid
This study does not meet important criteria of today's standard methods

18.03.2004 (4)

Type : Bacterial reverse mutation assay
System of testing : S. typhimurium, TA-98, TA-100, TA-1535, TA-1537 and TA-1538
Test concentration : 5, 50, 500 and 5000 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result :
Method : other
Year : 1978
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : A doubling of the mutant frequencies, (revertants/total colonies) x 106, accompanied by dose response constituted a positive response.

Ames et al, Mutation Research 31: 347-364, 1975

Remark : The authors of this report incorrectly concluded that the test substance did not increase the number of revertants in any strains tested. Clear, dose-responsive, multi-fold increases in the numbers of revertants were present for the TA-100 and TA-1535 strains at concentrations of 500 and 5000 µg/plate, both with and without metabolic activation. No increase in mutation frequency was observed for the other strains or concentrations that were tested.

Result : Clear, dose-responsive, multi-fold increases in the numbers of revertants were present for the TA-100 and TA-1535 strains at concentrations of 500 and 5000 µg/plate, both with and without metabolic activation. No increase in mutation frequency was observed for the other strains or concentrations that were tested.

Test condition : In a study conducted in 1978, the mutagenic potential of the test substance was evaluated in a reverse mutation assay using five strains of S typhimurium, TA-98, TA-100, TA-1535, TA-1537 and TA-1538. Concentrations of 5, 50, 500 and 5000 µg/plate were tested, both with and without a mammalian activation system (Aroclor 1254-induced rat liver [S-9]). Dimethylsulfoxide was used to prepare the dilutions of the test material and as a negative (solvent) control. Appropriate positive controls were included.

Conclusion : Not genotoxic

Reliability : (2) valid with restrictions

09.12.2004 (2)

Type : Bacterial reverse mutation assay

System of testing : Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, and TA-100

Test concentration : 5, 50, 100 and 500 mg/plate

Cycotoxic concentr. :

Metabolic activation : with and without

Result : positive

Method : other

Year : 1979

GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Method : The test substance was one of four materials included in this 1979 evaluation of mutagenic potential using the Salmonella typhimurium reverse mutation assay. Bacteria (TA-1535, TA-1537, TA-1538, TA-98, and TA-100 strains) were exposed to the test substance in the presence or absence of a mammalian activation system (Aroclor 1254-induced rat liver [S9]). Four concentrations of the test substance (5, 50, 100, and 500 mg/plate) were tested. Dimethylsulfoxide was used to prepare the dilutions of the test material and as a negative (solvent) control (50 µl/plate). Appropriate positive controls were included.

Result : There was an increase in mutation frequency in strains TA-1535 and TA-100 at 500 mg/plate both with and without metabolic activation, for the TA-1535 strain at 100 mg/plate (activation assay) and for the TA-100 strain at 100 mg/plate (non-activation assay). It was concluded that the test substance induced bacterial mutations and did not require

metabolic activation to be genetically active.

Reliability : (2) valid with restrictions

09.12.2004 (30)

Type : Mammalian cell gene mutation assay
System of testing : Chinese Hamster Ovary cells
Test concentration : 10 to 1000 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1979
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : There was no increase in mutation rate observed at any dose tested. The positive controls showed measurable response.

Test condition : The test material was dissolved in DMSO. Methylmethansulfonate and dimethylnitrosoamine were used as positive controls. CHO cells were exposed to five concentrations of the test material and the cultures split after 24 hours. Seven days later the toxicity of the test material was determined. On day nine, the cells were harvested and plated for cloning efficiency and mutagenicity measured as a resistance to thioguanine toxicity (Hsie et al., Somatic Cell Genetics 1:247-261, 1975).

Reliability : (2) valid with restrictions
The report did not provide the results of the toxicity of the test article on the test system. A toxicity test was included in the test protocol.

14.07.2004 (3)

Type : Sister chromatid exchange assay
System of testing : Chinese Hamster Ovary cells
Test concentration : .02, .04, .06, .08 and .1 mg/ml
Cycotoxic concentr. : greater than .1 mg/ml
Metabolic activation :
Result : positive
Method : other
Year : 1982
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : In a study conducted in 1982, the test substance was evaluated for its ability to induce sister chromatid exchanges (SCE) in Chinese hamster ovary (CHO) cells. The test substance was diluted in dimethylsulfoxide, which was also used as the negative control (0.1 ml/flask). A positive control group (mitomycin-C, 3 x 10 -8 M) was included. CHO cells were exposed to the test substance (0.02, 0.04, 0.06, 0.08, and 0.1 mg/ml). At the end of a two hour incubation period, the medium was discarded and cells were washed with sterile saline. Fresh medium was added together with bromodeoxyuridine (BrdU; 10 ml). After approximately 27 hours, the mitotic cells were harvested, fixed, and dropped onto microslides for staining and SCE analysis.

Result : The test material produced increases in SCE in a dose-related manner in CHO cells at the 0.04, 0.06, 0.08 and 0.10 concentrations. Although the actual numbers of SCE

were low (less than a two-fold increase over untreated controls), the concentrations of the test material were also low (higher concentrations were cytotoxic) and the increases were statistically significant (as well as dose-responsive). Therefore, it was concluded that the test article was a moderate in vitro inducer of SCE.

Source : Epona Associates, LLC
Reliability : (2) valid with restrictions
29.03.2004 (5)

Type : Sister chromatid exchange assay
System of testing : Peripheral lymphocytes
Test concentration : .05, .1, .2 mg/ml
Cycotoxic concentr. :
Metabolic activation :
Result : positive
Method : other
Year : 1999
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Blood samples from naïve animals were harvested, fixed, stained, and SCE enumerated in accordance with standard operating procedures. The lymphocytes were exposed for one hour to the test substance at concentrations of 0.05, 0.1, and 0.2 mg/ml.
Result : Statistically significant increases in SCE frequencies were present at the 0.10 and 0.20 mg/ml concentrations.
Source : Epona Associates, LLC
Reliability : (2) valid with restrictions
29.03.2004 (8)

Type : other
System of testing :
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result :
Method :
Year : 1982
GLP :
Test substance : as prescribed by 1.1 - 1.4

Remark : This report, written in 1982, provides an overview of the genetic toxicity of the test substance based on the review of numerous in vitro and in vivo studies. It concludes that the test substance does not pose a significant genetic risk in intact animals.
Source : Epona Associates, LLC
Reliability : (4) not assignable
The complete study report was not reviewed.
20.06.2003 (6)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : mouse

Sex : male/female
Strain : CD-1
Route of admin. : gavage
Exposure period : Doses were administered on a split-dose schedule at time 0 and at 24 hours
Doses : 0.5, 1.67 and 5.0 g/kg of undiluted test substance
Result : negative
Method : other
Year : 1982
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Increases in the frequency of micronucleated cells were compared between the treated and negative control group using the Student T-test. Analysis of the data was made for males only, females only and combined male plus female data.

Result : All test substance-treated mice survived to the scheduled euthanization. There were no statistically significant increases of the micronucleus frequency in any of the treated groups, relative to the untreated (water) control group. The positive control induced an approximate eight-fold and statistically significant increase of the micronucleus frequency.

The No Observed Adverse Effect Level (NOAEL) for chromosomal aberration was greater than 5 g/kg orally in mice under the conditions of this assay.

Summary(1) of Micronucleus Assay Data By Exposure Group

	Percent PCE With Micronuclei		
Dose Group	Male	Female	Combined Data Male & Female
High (5 g/kg)	0.42	0.50	0.46
Mid. (1.67 g/kg)	0.48	0.46	0.47
Low (0.5 g/kg)	0.52	0.48	0.50
Negative Control	0.53	0.44	0.47
Positive Control	3.70*	4.06*	3.88*

(1)Mean Values
* Significant at p = .05

Source : Dow Corning Corporation
Test condition : Young adult (7-12 weeks old) mice weighing between 20 and 40 grams were used. There were 10 mice per group (five per sex). The test substance was administered undiluted.

A water-dosed negative control group and a positive control group were also included. The positive control group received triethylemelamine by intraperitoneal injection (1 g/kg). All doses were given using the previously described split schedule. Six hours after the last dose was given, the mice were euthanized using CO2 and femoral bone marrow smears were prepared. Aspirated bone marrow was transferred to centrifuge tubes (one per mouse) containing fetal calf serum. Following centrifugation, a portion of the resultant pellet was spread on a glass slide and allowed to air dry. The slides were stained in May-Gruenwald solution and Giemsa.

One thousand polychromatic cells per animal were scored. The slides were coded and analyzed blindly with respect to treatment.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)
Conclusion : The test substance, 3-glycidoxypropyltrimethoxysilane, did not induce chromosome damage in the bone marrow cells of mice following oral administration of a very high dose, i.e., 5 g/kg.
Reliability : (2) valid with restrictions
According to the guideline, animals should not be killed to obtain bone marrow before 12 hours after the last dose was administered, and in this assay mice were killed 6 hours after the second and final dose (which followed the first dose by 24 hours). In addition, information about the ratio of normochromatic to polychromatic cells was not available. Based on a review of the report, the study was judged to be scientifically defensible.
Flag : Critical study for SIDS endpoint
09.12.2004 (35)

Type : Sister chromatid exchange assay
Species : other: rats and rabbits
Sex : no data
Strain : no data
Route of admin. : inhalation
Exposure period : 6 hours/day for 9 days
Doses : 77, 226, 707 mg/m3
Result : negative
Method : other
Year : 1982
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : None (The procedure followed was given in the test laboratory SOP # GEN-018)
Result : Summary of SCE Frequencies in Rat Peripheral Lymphocytes Before, During and After the Prylog Exposure - Rat

Trtmnt	Animal No.	Experimental Day -14 to -13	-7 to -6	6	15	22
Neg. Control	462	.203 ±.015		.181 ±.013		
	464	.171(1) ±.019	.195 ±.014		.194 ±.014	
	473	.235 ±.015		.210 ±.014		
	476	PG PG	.155 ±.012		.193 ±.014	
Prylog low-dose (77 mg/m3)	455	PG PG	.250 ±.015	.215 ±.014		
	459	PG PG	.236 ±.015	.175 ±.013	PG PG	
	471	.211 ±.015	.202(2) ±.027	.198 ±.016	PG PG	
	475	.267 ±.016		.202 ±.014	PG PG	
Prylog						

mid-dose
(226 mg/m3)
457 PG .292 PG
PG ±.016 PG
461 PG .226 .222
PG ±.014 ±.015
470 .191 .179 .211
±.014 ±.013 ±.014
472

Prylog
high-dose
(707 mg/m3)
458 .180(3) .258**
±.019 ±.015
460 .170 .183 .206
±.013 ±.013 ±.015
467 PG .227 .193
PG ±.014 ±.021
469 PG .225 .211 .253
PG ±.014 ±.014 ±.016
Pos.
Control
MMC (1 mg/kg)
465 PG .196 PG .603** NS
PG ±.014 PG ±.033 NS
466 .203 .445** NS
±.014 ±.033 NS
468 PG .156 .569** NS
PG ±.012 ±.034 NS
474 PG .496(4)** NS
PG ±.028 NS
PG= poor growth
NS= not scored
(1)Only 11 cells scored (3)Only 12 cells scored
(2)Only 7 cells scored (4)Pre-exposure bloods did not grow, but the significance is nevertheless clear.
**Indicates a value significantly elevated (P < 0.01) when compared to the negative control using Student's t-test (twotailed). Similar results were obtained on Days 1, 5, 11 and 12. These data were not included in this Table.
The test material failed to induce SCEs in circulating lymphocytes of either rats or rabbits, but it did so when these cells were exposed directly, in-vitro. The results indicate that when lymphocytes are exposed to test article concentrations as low as 0.01%, highly significant (P<0.01) increases in SCE frequency are induced in both species.
Summary of SCE Frequencies in Peripheral Lymphocytes Before, During and After the Prylog Exposure - Rabbit Experiment I
Experimental Day
Trtmnt Animal -14 -6 1 8 14 21
No.
Negative
Control 771 .099 - .108 .135** - NS
±.009 - ±.010 ±.011 - -
774 .118 - .162** - .144 -
±.010 - ±.012 -±.011 -
780 .128 - - .155 .145 NS
±.011 - - ±.012 ±.011 -
Prylog

(77 mg/m3)
Low-Dose 775 - .129 .124 .107 - .119
- ±.011 ±.010 ±.010 - ±.010
776 - .125 .151 .146 PG -
- ±.010 ±.011 ±.011 - -
781 - .148 - - .139 .119
- ±.011 - PG ±.011 ±.010
Prylog
(226 mg/m3)
Mid-Dose 770 .101 .115 PG .122 - .123
±.009 ±.010 PG ±.010 - ±.010
777 .122 PG .116 - .129 -
±.010 PG ±.010 - ±.011 -
782 .120 .120 - .108 .128 .116
±.010 ±.010 - +/-.010 ±.010 ±.010
Prylog
(707 mg/m3)
High Dose 772 - .116 .128 .149 - .110
- ±.010 ±.011 ±.011 - ±.010
773 .156 .132 .145 - .144 -
±.012 ±.011 ±.011 - ±.011 -
778 - .121 - .137 .127 PG
- ±.010 - ±.011 ±.010 -
Positive
Control 779 .145 .137 .185** - - NS
±.011 ±.011 ±.013 - - -
783 - - - .269** .261** -
- - - ±.015 ±.015 -

NS = Not scored
PG = Poor growth

Source : Dow Corning Corporation

Test condition : Two in-vivo experiments were conducted. In the first in-vivo experiment, both rats and rabbits were used, while in the second in-vivo experiment only rabbits were employed.
In the first in-vivo experiment, 5 rats and 5 rabbits were placed in each group prior to initiation of the assay. The negative control groups were not treated. The positive control animals were not chambered, but were injected i.p. with mitomycin-C (1 mg/kg) on study days 0 and 7. The animals were exposed to test article concentration of 75, 225 and 750 mg/m3 for 6 hours a day for 9 days. All animals were bled once prior to initiation of the study treatment, various times during and after the exposure period. Slides made from blood samples were scored for SCEs.
In the second in-vivo experiment, only rabbits were employed. All the details of the experiment were the same as described in the first experiment. The second experiment was intended to score only controls and the high dose animals. However, the high dose proved toxic so the mid-dose slides were scored instead.

- Age at study initiation: Not reported
- No. of animals per dose: 5
- Vehicle: None
- Duration of test: 9 days
- Frequency of treatment: 5 days exposure in the first week and 4 days in the second week
- Sampling times and number of samples: Various time

intervals
· Control groups and treatment: Chamber air
· Clinical observations performed (clinical pathology, functional observations, etc.): No
· Organs examined at necropsy (macroscopic and microscopic): No
· Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): The number of lymphocytes evaluated was not reported.
· Criteria for selection of MTD: Not reported

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Test article > 99% purity was used.

Conclusion : Based on the results, the authors concluded that repeated inhalation of the test substance is unlikely to reach blood concentrations required to induce systemic genetic damage.

Reliability : (2) valid with restrictions
The study was not conducted according to GLPs.

10.12.2004 (41)

Type : Sister chromatid exchange assay
Species : rabbit
Sex : male
Strain : New Zealand white
Route of admin. : i.p.
Exposure period : One injection per day for 2 weeks
Doses : 30 and 100 mg/kg
Result : negative
Method : other
Year : 1982
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : None. Test Laboratory SOP GEN-018 was used for procedure.
Result : The test substance failed to induce significant increases in SCE frequency in a consistent, dose-related manner.
Source : Dow Corning Corporation
Test condition : Six rabbits were injected intraperitoneally with test substance once per day for 2 weeks. Samples of blood were taken from an ear vein before, during and after the exposure period for subsequent culture and SCE analysis. One in-vitro study was also conducted. Rabbit lymphocytes were exposed in-vitro to test substance for one hour at 0.05, 0.10 and 0.2 mg/ml concentrations and harvested 48 hours later for SCE analysis.
·Age at study initiation: Approximately 2-2.5 kg
·No. of animals per dose: 6 males
·Vehicle: DMSO
·Duration of test: 2 weeks
·Frequency of treatment: Once/day, 5 days/week for 2 weeks
·Sampling times and number of samples:
·Control groups and treatment: Negative control (DMSO, 2 ml/injection); mitromycin-c was used as a positive control, 1 mg/kg

·Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): The number of lymphocytes evaluated was not

reported.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Purity of test material was not reported.

Conclusion : The test material produced no biologically significant effect in peripheral lymphocytes chromosomes when rabbits were exposed by intraperitoneal (i.p.) injection.

Reliability : (2) valid with restrictions
The study was not conducted according to GLPs

18.03.2004 (40)

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : ICR
Route of admin. : i.p.
Exposure period : Single dose, with animals killed at 24 or 48 hours post-dosing
Doses : 500, 1000, and 2000 mg/kg BW as a suspension in distilled water
Result : positive
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical methods: Kastenbaum-Bowman, 1970 binomial distribution

Remark : The half lives for hydrolysis of TMSPGE at 25 deg C at various pH values:

pH	Half life
3	3 sec
4	30 sec
5	5 min
6	49 min
7	4 hours
8	45 min
9	4.6 min
11	2.7 sec

The route of exposure (intraperitoneal injection) is not relevant to worker exposure or consumer exposure hazard identification. In addition, TMSPGE is a highly reactive chemical and is subject to rapid hydrolysis. It is therefore unlikely that the animals were actually exposed to this glycidoxy material.

Result : One replacement group female died within 5 hours of dosing. All other mice survived to scheduled termination. Clinical signs included lethargy and piloerection at 1000 and 2000 mg/kg.

Moderate to severe reductions of 22 to 59% in the ratio of polychromatic erythrocytes to total erythrocytes were observed in the test article-treated groups relative to the vehicle control animals. Moderate reductions (22- 37%) were observed in male and female dose groups 24 hours after treatment with 500, 1000, and 2000 mg/kg and severe reductions (45-59% were observed in male and female mice 48 hours post-treatment. A reduction greater than 90% in the number of polychromatic erythrocytes was evident 48 hours post-treatment in 2 males at 2000 mg/kg. The number of PCEs

was not enumerated in these cases. A significant increase in micronucleated PCEs was observed in male and female mice 24 hours post-dosing in the 500, 1000, and 2000 mg/kg dose groups and at 48 hours post-dosing in the 2000 mg/kg dose group. The positive control substance also induced a significant increase in micronucleated PCEs.

Summary of Bone Marrow Micronucleus Study - 24 hrs

			PCE/Total Micronucleated PCEs	
# Treatment	Sex	Erythrocytes Mice	Control (Mean+/-sd) (%)	#/1000 PCEs Mean(+/-1sd)	#/PCEs Scored
Water(1)	M	5	.54+/- .01	--	0.3+/-0.27	3/10000
Water(1)	F	5	.55+/- .03	--	0.3+/-0.27	3/10000
TMSPGE						
500 mg/kg	M	5	.40+/- .08	-26	3.2+/-1.04	*32/10000
500 mg/kg	F	5	.42+/- .01	-24	3.9+/-3.31	*39/10000
1000 mg/kg	M	5	.35+/- .08	-35	8.8+/-1.82	*88/10000
1000 mg/kg	F	5	.43+/- .10	-22	14.7+/-5.51	*147/10000
2000 mg/kg	M	5	.34+/- .05	-37	24.3+/-7.03	*243/10000
2000 mg/kg	F	5	.38+/- .07	-31	24.1+/-8.39	*241/10000
CP(2)	M	5	.35+/- .08	-35	25.7+/-6.62	*257/10000
CP(2)	F	5	.38+/- .09	-31	24.3+/-5.09	*243/10000

1 = 20 mL/kg
2 = 50 mg/kg
* = p<0.05 (Kastenbaum-Bowman Tables)

Summary of Bone Marrow Micronucleus Study - 48 hrs

			PCE/Total Micronucleated PCEs		
# Treatment	Sex	Erythrocytes Mice	Control (Mean+/-sd) (%)	#/1000 PCEs Mean(+/-1sd)	#/PCEs Scored
Water(1)	M	5	.51+/- .05	--	0.1+/-0.22	1/10000
Water(1)	F	5	.53+/- .05	--	0.3+/-0.27	3/10000
TMSPGE						
2000 mg/kg	M	5	.21+/- .15	-59	3.3+/-1.61(3)	*20/60003
2000 mg/kg	F	5	.29+/- .12	-45	6.1+/-6.64	*61/10000

(1) = 20 mL/kg
(2) = 50 mg/kg
(3) = due to severe reduction in number of PCEs, MPCE out of 2000 PCE was not enumerated for two male mice. Values determined using three mice.
* = p<0.05 (Kastenbaum-Bowman Tables)

Source : Dow Corning Corporation

Test condition : Young adult (26-33.3 g (M) and 22.6 - 26.8g (F)) mice were used. There were 10 mice per group (five per sex). The test substance was administered in sterile distilled water. Additional animals, designated as potential replacement animals, were included at the 2000 mg/kg dose level.

A distilled water-dosed negative control group and a positive control group were also included. The positive

control group received cyclophosphamide in distilled water by intraperitoneal injection (50 mg/kg). 24 hours (positive and negative control) or 48 hours (negative control) after the last dose was given, the mice were euthanized by CO2 asphyxiation and femoral bone marrow smears were prepared. Aspirated bone marrow was transferred to centrifuge tubes (one per mouse) containing fetal calf serum. Following centrifugation, a portion of the resultant pellet was spread on a glass slide and allowed to air dry. The slides were stained in May-Gruenwald solution and Giemsa.

Two thousand polychromatic cells per animal were scored. The slides were coded and analyzed blindly with respect to treatment. The proportion of polychromatic erythrocytes was also recorded per 1000 erythrocytes.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

100% Pure

Conclusion : The test substance, 3-glycidoxypropyltrimethoxysilane, induced chromosome damage in the bone marrow cells of mice following i.p. administration of the test substance at all three dose levels tested.

Reliability : (2) valid with restrictions

13.12.2004 (13)

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : NMRI
Route of admin. : i.p.
Exposure period : Single dose, with animals killed at 24 or 48 hours post-dosing
Doses : 1600 mg/kg bw as a suspension in corn oil
Result : negative
Method : other
Year : 1994
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Methode B.12 Mutagenität, Mikrokerntest (1992)

Remark : Although only one dose level was used, it approximated the MTD and therefore represented a limit dose. The percent PCE with micronuclei was significantly increased for males and females in the positive control group. However, the PCE:NCE ratio only achieved statistical significance for the positive control female mice. In males, one male with a low PCE:NCE value resulted in a lack of statistical significance for the positive control males as a group.

Result : Two of 20 animals died following dosing with 1600 mg/kg BW, thereby indicating that this dose is very close to the MTD. Although there was a statistically significant increase of the micronucleus frequency in males only at the 24-hour sacrifice time point only, this was determined to be due to an extremely low incidence in the concurrent control group. The increase observed approximated the historic control level for this strain of mouse in this laboratory. The report authors concluded that the small increase was not biologically significant. The positive control induced a statistically significant increase of the micronucleus frequency.

Results of the Micronucleus test, Cyclophosphamide (24 hours)
MALES

	NCE Total No. examined	NCE with micronuclei (absolute)	NCE (%)	PCE Total No. examined	PCE with micronuclei (absolute)	PCE (%)	PCE:NCE
Total	24444	11	-	10018	449	-	
Mean		0.05			4.48	0.56	
Std. Dev.		0.04			1.69	0.27	
Signif.					***	ns	

***= p<0.001
ns=not significant

FEMALES

	NCE Total No. examined	NCE with micronuclei (absolute)	NCE (%)	PCE Total No. examined	PCE with micronuclei (absolute)	PCE (%)	PCE:NCE
Total	17508	9	-	10014	263	-	
Mean		0.05			2.63	0.68	
Std. Dev.		0.07			1.02	0.25	
Signif.					***	**	

**=0.001<p<0.01

Results of the Micronucleus test, Vehicle control (Corn oil)
MALES

	NCE Total No. examined	NCE with micronuclei (absolute)	NCE (%)
24 hours:			
Total	18953	0	-
Mean		0.00	
Std. Dev.		0.00	
48 hours:			
Total	16480	10	-
Mean		0.06	
Std. Dev.		0.05	

PCE

	Total No. examined	with micronuclei (absolute)	(%)	PCE:NCE
24 hours:				
Total	10030	9	-	
	Mean	0.09	0.56	
	Std. Dev.	0.05	0.18	
48 hours:				
Total	10009	19	-	
	Mean	0.19	0.65	
	Std. Dev.	0.07	0.20	

FEMALES

NCE

	Total No. examined	with micronuclei (absolute)	(%)
24 hours:			
Total	8646	2	-
	Mean	0.02	
	Std. Dev.	0.03	
48 hours:			
Total	11666	4	-
	Mean	0.03	
	Std. Dev.	0.04	

PCE

	Total No. examined	with micronuclei (absolute)	(%)	PCE:NCE
24 hours:				
Total	10029	15	-	
	Mean	0.15	1.24	
	Std. Dev.	0.03	0.35	
48 hours:				
	10014	11	-	
	Mean	0.11	0.96	
	Std. Dev.	0.06	0.29	

Results of the Micronucleus test, Dynasylan Glymo

MALES

NCE

	Total No. examined	with micronuclei (absolute)	(%)
24 hours:			
Total	15388	2	-
	Mean	0.02	
	Std. Dev.	0.02	
48 hours:			
Total	14628	4	-
	Mean	0.03	
	Std. Dev.	0.04	

PCE

	Total No. examined	with micronuclei (absolute)	(%)	PCE:NCE
24 hours:				

Total 10005 23 -
Mean 0.23 0.69
Std. Dev. 0.13 0.20
Signif. * ns
48 hours:
Total 10010 15 -
Mean 0.15 0.74
Std. Dev. 0.11 0.24
Signif. ns ns
*=0.01<p<0.05
ns=not significant

FEMALES

	NCE		
	Total No. examined	with micronuclei (absolute)	(%)
24 hours:			
Total	13395	5	-
		Mean	0.04
		Std. Dev.	0.05
48 hours:			
Total	19645	13	-
		Mean	0.06
		Std. Dev	0.05

	PCE			PCE:NCE
	Total No. examined	with micronuclei (absolute)	(%)	
24 hours:				
Total	10025	13	-	
		Mean	0.13	0.76
		Std. Dev.	0.06	0.11
		Signif.	ns	**
48 hours:				
Total	10012	13	-	
		Mean	0.13	0.84
		Std. Dev.	0.08	0.53
		Signif.	ns	ns

**=p<0.001

Historical Controls for NMRI mice (Huls AG since 7/1992)
1. Frequency of PCE harbouring micronuclei (%) - Approx. 2000 PCE/animal were scored:

	CPA 24m	CPA 24f	Oil 24m	Oil 24f	Oil 48m	Oil 48f
Sample size	44	45	35	35	35	35
Ave.	3.51	3.14	0.21	0.14	0.21	0.15
Median	3.35	2.90	0.20	0.10	0.20	0.15
Variance	1.64	1.44	0.20	0.01	0.01	0.01
Std. Dev.	1.28	1.20	0.12	0.10	0.10	0.09
Std. Err.	0.19	0.18	0.02	0.02	0.02	0.01
Min	1.79	1.40	0.00	0.00	0.05	0.00
Max	7.99	6.34	0.55	0.45	0.40	0.4
Range	6.20	4.94	0.55	0.45	0.35	0.4

Historical Controls (continued):

	H2O 24m	H2O 24f	H2O 48m	H2O 48f
Sample size	10	10	10	10
Ave.	0.14	0.15	0.22	0.13
Median	0.10	0.13	0.23	0.13
Variance	0.01	0.01	0.01	0.01
Std.Dev.	0.08	0.10	0.12	0.08
Std. Err.	0.03	0.03	0.04	0.02
Min	0.05	0.05	0.05	0.05
Max	0.30	0.40	0.45	0.25
Range	0.25	0.35	0.40	0.20

2. PCE:NCE ratios:

	CPA 24m	CPA 24f	Oil 24m	Oil 24f	Oil 48m	Oil 48f
Sample size	45	45	35	35	35	35
Ave.	0.30	0.47	0.51	1.05	0.67	1.14
Median	0.25	0.43	0.45	0.98	0.55	0.92
Variance	0.03	0.05	0.04	0.13	0.11	0.33
Std. Dev.	0.18	0.22	0.21	0.36	0.33	0.57
Std. Err.	0.03	0.03	0.04	0.06	0.06	0.10
Min	0.12	0.13	0.19	0.30	0.19	0.53
Max	0.87	1.13	1.10	1.82	1.53	2.80
Range	0.75	1.00	0.91	1.52	1.34	2.27

PCE:NCE ratios (continued):

	H2O 24m	H2O 24f	H2O 48m	H2O 48f
Sample size	10	10	10	10
Ave.	0.49	0.84	0.75	0.93
Median	0.42	0.86	0.73	0.90
Variance	0.02	0.05	0.17	0.12
Std. Dev.	0.14	0.23	0.41	0.35
Std. Err.	0.04	0.07	0.13	0.11
Min	0.35	0.55	0.32	0.47
Max	0.73	1.12	1.76	1.57
Range	0.38	0.57	1.44	1.10

Source : SEHSC

Test condition : Increases in the frequency of micronucleated cells were compared between the treated and negative control group using chi2 test of heterogeneity. Pearson's contingency, with Yates correcting factor for homogeneous groups; one-sided Student T-test was used in the case of in homogeneity. Analysis of the data was made for males only, females only and combined male plus female data. Young adult (34.6 + 6.9 g (M) and 28.5 + 5.7g (F)) mice were used. There were 10 mice per group (five per sex). The test substance was administered as a suspension in corn oil.

A corn oil-dosed negative control group and a positive control group were also included. The positive control group received cyclophosphamide in saline by intraperitoneal injection (50 mg/kg). 24 hours (positive and negative control) or 48 hours (negative control) after the last dose was given, the mice were euthanized by cervical dislocation and femoral bone marrow smears were prepared. Aspirated bone marrow was transferred to

centrifuge tubes (one per mouse) containing fetal calf serum. Following centrifugation, a portion of the resultant pellet was spread on a glass slide and allowed to air dry. The slides were stained in May-Gruenwald solution and Giemsa.

Two thousand polychromatic cells per animal were scored. The slides were coded and analyzed blindly with respect to treatment

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Dynasylan GLYMO 98.4% pure

Conclusion : The test substance, 3-glycidoxypropyltrimethoxysilane, did not induce chromosome damage in the bone marrow cells of mice following i.p. administration of a high dose, 1600 mg/kg BW, which approached the MTD.

Reliability : (2) valid with restrictions
13.12.2004 (21)

5.7 CARCINOGENICITY

Species : mouse
Sex : male/female
Strain : C3H
Route of admin. : dermal
Exposure period : Lifetime
Frequency of treatm. : 3 applications/week
Post exposure period : Not applicable
Doses : 25 µl of 25% TMSPGE in acetone/application
Result : negative
Control group : yes
Method : other
Year : 1981
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : The mean survival time of the TMSPGE group was 482 days versus 502 days for the acetone controls. The difference was not statistically different. The mean survival time in the methylcholanthrene (MC) group was 204 days reflecting the early mortality associated with the high incidence of skin tumors.

Tumor data are summarized in the following table:

	TMSPGE	MC	Acetone
Concentration	25%	0.1%	100%
Volume (ul)	25	25	25
Mean survival time (days)	482	204	502
Animals w/papillomas	0	2	0
Animals w/carcinomas	0	37	0
Animals with subcutaneous sarcomas	0	0	2
Time to first skin tumor (days)	0	31	0
Time to median skin			

tumor (days) 0 92 0

No epidermal or subcutaneous tumors were observed in the TMSPGE group. Eight animals had hyperkeratosis (compared to the acetone controls) suggesting a possible irritating effect on the epidermis. No epidermal tumors were observed in the group treated with acetone though two mice had subcutaneous sarcomas outside the treatment area (one subcutaneous fibrosarcoma of the left foreleg and one subcutaneous lymphosarcoma over the left hip). One mouse had epidermal hyperplasia. The positive control (MC) group had 39 animals with skin tumors including 33 with confirmed squamous cell carcinomas, two mice with papillomas four mice had gross carcinomas that were not confirmed histologically because of cannabilism. These results confirm the sensitivity of the animals to a known skin carcinogen.

Test condition : This study was designed to determine the dermal carcinogenic potential of TMSPGE by applying it to the skin of male C3H/HeJ mice over the period of their lifetime and determining the gross and microscopic appearance of the resulting lesions.

The 120 C3H/HeJ male mice used in this study were culled at random from a larger population of mice. The mice were housed 5 per cage in stainless-steel suspended cages. Food and water were provided ad libitum. The mice were identified by toe-clip according to pre-assigned, unique identification numbers. The mice were weighed individually and as cage mates of 5. The weights of 5 cage mates were used to randomize the mice into test groups. Prior to the start of testing the fur was clipped from the backs of the mice and they were checked for general health status.

Male C3H/HeJ mice, approximately 51 to 76 days of age, were obtained from Jackson Laboratories, Bar Harbor, ME. The mice were randomized into groups of 40 animals. Each group of 40 male mice received either the test chemical (25 µl dose of 25% TMSPGE in acetone) or a control material (25 µl dose of 0.1% methylcholanthrene in acetone or acetone alone) three times per week (on Mondays, Wednesdays, and Fridays, excluding holidays) applied by an Eppendorf pipette to the clipped skin of the back (on Tuesday and Thursday of each the fur was clipped from the back of each mouse). The mice were observed daily for mortality and were carefully examined for lesions of the skin once per month.

A necropsy was performed on all dead mice and on moribund mice, which were sacrificed. A necropsy consisted of a careful examination of the skin and body cavities. All observations were recorded. The dorsal skin and any suspect internal tumors from all non-autolyzed mice were fixed in 10% neutral buffered formalin. Tissues fixed in formalin were carefully trimmed, embedded, sectioned and stained with hematoxylin and eosin for examination by a pathologist. All neoplastic and non-neoplastic lesions discovered during the histopathologic examination were recorded and tabulated.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

The test substance was analyzed for purity four times during

the study. Analytical data indicate that the percent purity was 96.5%, 96.1%, 95.4%, and 95.5%

Conclusion : TMSPGE was not considered tumorigenic when applied to the skin of C3H mice under the conditions of this study.

Reliability : (2) valid with restrictions

09.12.2004 (14)

5.8.1 TOXICITY TO FERTILITY

Type : One generation study
Species : rat
Sex : male/female
Strain : Wistar
Route of admin. : gavage
Exposure period : Males: Exposed for a 70-day pre-pairing period, during pairing and until the last litter reached day 7 post-partum. Females: Exposed during pairing and until the last litter reached day 7 post partum.
Frequency of treatm. : once daily
Premating exposure period
Male : 70 days
Female : 14 days
Duration of test : until the last litter reached day 7 post partum
No. of generation studies : 1
Doses : 0, 250, 500 and 1000 mg/kg bw/d
Control group : yes, concurrent vehicle
NOAEL parental : = 500 mg/kg bw
NOAEL F1 offspring : = 1000 mg/kg bw
Result : No reproductive effect at the highest dose tested
Method : OECD Guide-line 415 "One-generation Reproduction Toxicity Study"
Year : 2004
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : PARENT ANIMALS
General Tolerability:
All males survived until scheduled necropsy and no clinical signs that were attributable to treatment with the test item were noted.

All females survived until scheduled necropsy. At 1000 mg/kg bw/d, starting during early/mid gestation, all females displayed signs of discomfort after dosing (pushing head through bedding). This behavior was noted as long as the females were dosed (i.e., one day prior to scheduled necropsy).

Mean food consumption of males and females was not affected by treatment with the test substance.

At 1000 mg/kg bw/d, mean body weight gain of males during the prepairing period was slightly decreased, resulting in a slightly lower mean body weight at the end of the prepairing period (375 g compared with 409 g in the vehicle control). Although statistical significance was only reached on single days, this reduction was considered to be test item related. During the pairing and after pairing period, lower absolute body weights at 1000 mg/kg bw/d persisted, while body weight

gain was similar to that of the vehicle control.

Body weight development of females was not affected by treatment with the test item.

Reproduction Data:
For both generations, the fertility rate was high resulting in at least 23 litters per group for evaluation of reproduction data. At all dosages, there were no treatment related effects on mean or median precoital time, fertility indices, mean duration of gestation and number of implantations, post-implantation loss, pup survival or litter size from birth through to weaning.

OFFSPRING
No test-item related findings or clinical signs were noted at first litter check on day 0 post partum or during the lactation period. Pup weights at birth and during lactation were unaffected by treatment with the test item No treatment-related effects on sex ratios were noted.

TERMINAL EXAMINATIONS
Parent Animals - Necropsy Findings: No test-item related findings were noted at macroscopic examination of parental males or females.

Parent Animals - Organ Weights:
At 1000 mg/kg bw/d, statistically significant increased mean relative liver and kidney weights were noted for males and females.

Parent Animals - Histopathological Examination:
Liver: In the liver of males, the severity of glycogen deposition was slightly increased at 1000 mg/kg bw/d. This finding was considered in relation with the nutritional state of the animals and of no adverse character.
Kidneys A slightly increased severity of tubular hyaline change occurred in males of Group 4 (1000 mg/kg bw/d) mainly in the outer cortex.The grade was 2.5 versus 2.0 in the controls. Probably this change reflects an increased accumulation of alpha-2-microglobulin which is male rat specific phenomenon of no toxicological relevance for humans.

F1 Pups Necropsy Findings: No test-item related findings were noted at macroscopic examination of pups.

Test condition : This study was designed to investigate the effects of continuous administration of TMSPGE to the rat on reproductive performance, such as gonadal function, estrous cycle, mating behavior, conception, parturition, lactation and weaning.

TMSPGE was administered orally, by gavage, once daily to males for a 70-day pre-pairing period, during the pairing period and until the last litter had reached day 7 post partum. Females received the test item during a 14-day pre-pairing period, and also during the pairing, gestation and lactation periods.

The following dose levels were applied:

Group 1: 0 mg/kg bw/d (vehicle control)
Group 2: 250 mg/kg bw/d
Group 3: 500 mg/kg bw/d
Group 4: 1000 mg/kg bw/d

A standard dose volume of 2 ml/kg body weight with a daily adjustment to the actual body weight was used. Control animals were dosed with the vehicle alone (dried corn oil).

Test substance : Purity = 98.4%

Conclusion : At 1000 mg/kg bw/d, treatment with the test item resulted in signs of discomfort after dosing (noted for P females from early /mid gestation onwards), decreased body weight gain of males, and increased absolute and relative liver and kidney weights in P males and females. Histopathology revealed effects on livers and kidneys of males.

Based on these data a NOAEL for parental animals was established at 500 mg/kg bw/d. A NOAEL for reproductive effects was established at 1000 mg/kg bw/d.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

10.12.2004 (12)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : Test substance exposure occurred during the primary period of organogenesis, i.e., gestation days 6-15.
Frequency of treatm. : Once per day on gestation days 6-15
Duration of test : 3 weeks
Doses : 50, 500 and 1000 mg/kg/day
Control group : yes
NOAEL maternal tox. : >= 1000 mg/kg bw
NOAEL teratogen. : >= 1000 mg/kg bw
Method : OECD Guide-line 414 "Teratogenicity"
Year : 1982
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Methods: Fetal body weights and body measurements, maternal body weights, weights of the maternal livers and uteri and food consumption data were analyzed statistically by a one-way analysis of variance and Dunnett's test (Steel and Torrie, 1960). The Wilcoxon test as modified by Haseman and Hoel (1974) was used to evaluate incidences of fetal resorptions and alterations. Other incidence data were analyzed statistically by the Fischer exact test (Seigel, 1956). The level of significance chosen for all cases was $p < 0.05$.

Remark : As our experience and knowledge associated with the issues surrounding the testing of TMSPGE increased, it has become apparent that it is not stable by the oral route.
Specifically, TMSPGE readily hydrolyzes to methanol and silanols (Note: methanol is included in the EPA HPV Challenge Program). pH has a significant effect on the rate

of hydrolysis, and at pH 4, the hydrolysis is complete within 2.5 minutes. Slight changes in pH affect the rate of hydrolysis, which may result in administration of differing forms of the test article with each dosing. The hydrolysis rate is susceptible to the presence of trace acid and/or base.

A non-GLP study was conducted to examine the fate of TMSPGE following oral (gavage) exposure. Five fasted female Sprague-Dawley rats were dosed with 2000 mg/kg TMSPGE mixed with activated charcoal as a tracer. After 20 or 30 minutes the animals were sacrificed, and the stomachs and gastrointestinal tracts examined for presence of test article. The study was also repeated in the absence of the activated charcoal tracer. In all cases, the hydrolysis product(s) of the test article were found in the stomach contents or in the upper gastrointestinal tract, and was observed to have the consistency of a siloxane gel. In cases where the stomach contents included food, small waxy particles of test article were observed. Both the gel-like substance and waxy particle forms of the hydrolysis products of the test article observed in the stomach and upper gastrointestinal tract support the rapid polymerization of TMSPGE under oral (gavage) conditions, as the test article exists as a clear, water like liquid. In either case, little or no absorption of test article appeared to have occurred. In contrast, there was no liquid present in the stomachs of animals gavaged with an equivalent dose of water and sacrificed after 30 minutes.

The lack of clinical signs of toxicity following acute or repeated dosing is likely related to the hydrolysis of TMSPGE and subsequent polymerization of the hydrolysis products, and thus, the lack of bioavailability.
The incidence of malformations and variations in the historical controls is not available. These data were not collected by the laboratory that conducted this study.

Result : There were no test substance-related mortalities. One rat (subsequently replaced) in the 50 mg/kg/day group died as the result of dosing trauma. There were no test substance-related effects on clinical condition, behavior, body weight, body weight gain or food consumption. No effects on liver or gravid uterine weight were observed. No effects on the number of implantation sites or corpora lutea per dam were observed. The incidence of pregnancy was not affected by treatment with the test substance; all rats were confirmed to be pregnant at the gestation day 20 laparohysterectomies. No adverse effects on the number of live fetuses per litter, mean litter size, sex ratio, fetal body weight or crown-rump length were observed. The incidence of fetal resorptions was not altered by test substance administration. No external, visceral or skeletal alterations were observed among test substance-treated rats at an incidence that was statistically different from the control group. When considered collectively, the incidence of total major malformations observed in the external, soft tissue or skeletal examinations was not significantly different among the treated groups as compared to the control group. No major malformations were observed among litters of rats that received either 500 or 1000 mg/kg/day

of the test substance. The sporadic variations and malformations seen occurred at an incidence comparable to a historical control incidence for Sprague-Dawley rats reported in the literature.

Under the conditions of this study, the NOAEL (No Observed Adverse Effect Level) of the test substance for embryotoxicity, developmental toxicity and maternal toxicity was found to be 1000 mg/kg/day or greater when administered orally on gestation days 6-15 to rats.

Source : Dow Corning Corporation

Test condition : The study used timed-pregnant female Sprague-Dawley rats. The supplier performed breeding of the rats. The rats weighed 265 + 44 grams at initiation of dosing.

No vehicle was used; the test substance was administered undiluted.

Observation for mortality and clinical condition was performed daily. Maternal body weights and food consumption were recorded on gestation days 6, 10, 15 and 20. Individual animal doses were adjusted for body weight on gestation days 6, 10 and 15. On gestation day 20, the rats were euthanized and laparohysterectomies were performed. Maternal liver weights and gravid uterine weights (including the ovaries) were recorded. The number and position of live, dead and resorbed fetuses were recorded, as was the number of corpora lutea. All fetuses were weighed, measured (crown-rump length), sexed and examined for external alterations and cleft palate. One-third of the fetuses from each litter were randomly selected for immediate examination by dissection under a stereo microscope for soft tissue alterations (Staples, 1974). The head of each fetus examined for soft tissue alterations was placed in Bouin's fixative and subsequently examined by the razor sectioning technique (Wilson, 1965). All of the fetuses in each litter were eviscerated, placed in 95% ethanol, subsequently cleared with potassium hydroxide and stained with Alizarin red-S (Dawson, 1926) to permit examination for skeletal alterations.

Test substance : 3-Glycidoxypropyltrimethoxysilane (CAS No. 2530-83-8)

Conclusion : The test substance exhibited no adverse effects on the maternal animals or the developing unborn. The NOAEL for maternal and developmental toxicity exceeds current OECD and EPA maximum dose level requirements for studies of this type.

Reliability : (1) valid without restriction
Based on a review of the report, the study was judged to be scientifically defensible.

Flag : Critical study for SIDS endpoint

14.07.2004 (37)

Species : rat

Sex : female

Strain : Fischer 344

Route of admin. : gavage

Exposure period : Test substance exposure occurred during the primary period of organogenesis, i.e., gestation days 6-15.

Frequency of treatm. : Once per day on gestation days 6-15

Duration of test : The overall duration of the test was approximately three weeks.

Doses	:	500, 1500 and 3000 mg/kg/day
Control group	:	yes
NOAEL maternal tox.	:	= 1500 mg/kg bw
NOAEL teratogen.	:	= 1500 mg/kg bw
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The unit of comparison was the pregnant female or the litter (Weil, 1970). Results of the quantitative continuous variables (e.g., maternal body weights, organ weights, etc.) were intercompared for the three test article-exposed groups and the vehicle control group by use of Levene's test for equal variances (Levene, 1960), analysis of variance (ANOVA), and t-tests with Bonferroni probabilities for pairwise comparisons. When Levene's test indicated homogeneous variances and the ANOVA was significant, the pooled t-test was used. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances (Brown and Forsythe, 1974) followed, when necessary, by the separate variance t-test. Nonparametric data obtained following laparohysterectomy were statistically treated using the Kruskal-Wallis test (Sokal and Rohlf, 1969) followed by the Mann-Whitney U test (Sokal and Rohlf, 1969) when appropriate. Incidence data were compared using Fisher's Exact Test (Sokal and Rohlf, 1969). For all statistical tests, the fiducial limit of 0.05 (two-tailed) was used as the criterion for significance.

Result : There were no treatment-related maternal deaths. No dams aborted. One female each at 0 and 500 mg/kg/day delivered early and was removed from study. 17-23 litters were examined in each dose group. There were no statistically significant differences among groups for maternal gestational body weights. Gestational weight gain was significantly reduced at 3000 mg/kg/day for gd 6-12 and 6-15 (the treatment period), and food consumption was significantly reduced at 3000 mg/kg/day for gd 9-12. Treatment-related (but not statistically significant) clinical signs, observed only at 3000 mg/kg/day, included hypoactivity, audible respiration and unkempt appearance (one to two dams each). At the gd 21 sacrifice there were no effects of treatment on maternal body weight or gestational weight gain (absolute or corrected, on gravid uterine weight or on liver weight (absolute and relative). Gestational parameters, including number of ovarian corpora lutea, total, viable and nonviable implantations per litter, and sex ratio were unaffected by treatment. Fetal body weights per litter (all fetuses, males or females) were equivalent across dose groups.

There was no significant increase in the incidence of malformations (individual, pooled external, visceral, skeletal or total) in any treatment group relative to controls. There were no treatment-related differences among groups for individual external variations, for pooled external, visceral or skeletal variations or for total variations. One skeletal variation, unossified anterior arch of the atlas, exhibited a significantly increased

incidence at 3000 mg/kg/day, indicating minimal fetotoxicity. Otherwise, there were no indications of variations.

Under the conditions of this study, dosing Fischer 344 rats with the test substance by gavage during organogenesis resulted in evidence of maternal toxicity at 3000 mg/kg/day and evidence of developmental delay at 3000 mg/kg/day. No r teratogenicity was observed at any dosage employed, including that which produced maternal toxicity. The NOAEL (No Observed Adverse Effect Level) of the test substance for embryotoxicity, developmental toxicity and maternal toxicity was found to be 1500 mg/kg/day when administered orally on gestation days 6-15 to rats.

Test condition : The study used timed-pregnant female Fischer 344 rats. The laboratory performed breeding of the rats.

Certified corn oil was used as the vehicle. The dose volume employed was 5.0 ml/kg.

Observations for mortality and clinical condition were performed daily. Maternal body weights were measured on gestational days 0, 6, 12, 15, 18 and 21. Food consumption was measured in three-day intervals throughout gestation. Individual animal doses were based on the weight of each female on gd 6. At the scheduled sacrifice on gd 21, the rats were euthanized and laparohysterectomies were performed. Maternal liver weights and gravid uterine weights (including the ovaries) were recorded. Ovarian corpora lutea of pregnancy were counted. The status of implantation sites (i.e. resorptions, dead fetuses, live fetuses) was recorded. Live fetuses were dissected from the uterus, counted, weighed, sexed and examined for external abnormalities and cleft palate. Approximately one-half of the live fetuses in each litter were examined for visceral malformations and variations (Staples, 1974). The head of these fetuses were fixed in Bouin's solution and examined for soft tissue craniofacial malformations and variations (Wilson, 1965, 1973). The remaining (intact) fetuses in each litter were eviscerated, fixed in alcohol, stained with Alizarin red S (Crary, 1962; Peltzer and Schardein, 1966) and examined for skeletal malformations and variations.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Purity > 99%

Conclusion : The test substance exhibited maternal toxicity at 3000 mg/kg/day and evidence of developmental delay at 3000 mg/kg/day. The NOAEL for maternal and developmental toxicity exceeds current OECD and EPA maximum dose level requirements for studies of this type.

Reliability : (1) valid without restriction

10.12.2004 (15)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : gavage

Exposure period	:	Test substance exposure occurred during the primary period of organogenesis, i.e., gestation days 6-18.
Frequency of treatm.	:	Once per day on gestation days 6-18
Duration of test	:	The overall duration of the test was approximately three weeks.
Doses	:	50, 200 and 400 mg/kg/day
Control group	:	yes
NOAEL maternal tox.	:	= 200 mg/kg bw
NOAEL teratogen.	:	>= 400 - mg/kg bw
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1991
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The unit of comparison was the pregnant female or the litter. Data collected for nonpregnant females were not included in the statistical analyses. Results of the quantitative continuous variables (e.g., maternal body weights, organ weights, etc.) were intercompared for the three exposed groups and the vehicle control group by use of Levene's test for equal variances (Levene, 1960), analysis of variance (ANOVA), and t-tests with Bonferroni probabilities for pairwise comparisons. The t-tests were used when the F value from the ANOVA was significant. When Levene's test indicated homogeneous variances and the ANOVA was significant, the pooled t-test was used. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances (Brown and Forsythe, 1974) followed, when necessary, by the separate variance t-test. Nonparametric data obtained following laparohysterectomy were statistically treated using the Kruskal-Wallis test (Sokal and Rohlf, 1969) followed by the Mann-Whitney U test (Sokal and Rohlf, 1969) when appropriate. Incidence data were compared using Fisher's Exact Test (Sokal and Rohlf, 1969). For all statistical tests, the fiducial limit of 0.05 (two-tailed) was used as the criterion for significance.

Result : The pregnancy rate was equivalent for all groups . One of 19 pregnant does at 400 mg/kg/day exhibited characteristic signs of gasping, labored and audible respiration, and was found dead on the morning of scheduled sacrifice, gd 29. No additional signs of maternal toxicity were observed in the 400 mg/kg/day group. There was no evidence of maternal toxicity at 200 or 50 mg/kg/day.

Fetal examination indicated no evidence of embryotoxicity or malformations in any of the treatment groups. There were no effects on mean fetal body weight and no treatment-related differences in the incidences of external, visceral or skeletal variations.

Under the conditions of this study, dosing New Zealand white rabbits with the test substance by gavage during organogenesis resulted in 5.3% maternal mortality at 400 mg/kg/day. No developmental toxicity was observed in this study. The NOEL (No Observed Effect Level) of the test substance for maternal effects was 200 mg/kg/day. The NOEL for developmental toxicity was at least 400 mg/kg/day.

Test condition : The study used timed-pregnant female New Zealand white rabbits. The laboratory performed breeding of the rabbits.

Certified corn oil was used as the vehicle. The dose volume employed was 2.0 ml/kg/day.

Observations for mortality and clinical condition were performed daily (twice daily during the dosing period). Maternal body weights were measured on gestational days 0, 6, 12, 15, 18 and 29. Food consumption was measured daily throughout gestation (gd 0-29). Individual animal doses were based on the weight of each female on gd 6. At the scheduled sacrifice on gd 29, the rats were necropsied and examined for thoracoabdominal and pelvic gross pathology, pregnancy status (i.e. resorptions, dead fetuses, live fetuses), and measurement of body, liver and gravid uterine weight. Uteri from females that appeared nongravid were placed in a 10% ammonium sulfide solution for detection of early resorptions (Salewski, 1964). All fetuses in each litter were weighed and examined for external malformations, cleft palate and variations. Approximately one-half of the live fetuses in each litter were examined for visceral malformations and variations (Staples, 1974); the sexes of all fetuses were determined internally. The head of these fetuses were fixed in Bouin's solution and examined for soft tissue craniofacial malformations and variations (van Julsingha and Bennett, 1977). All live fetuses (50% intact, 50% decapitated) in each litter were eviscerated, fixed in alcohol, and processed for skeletal staining with Alizarin red S (Crary, 1962; Peltzer and Schardein, 1966). Intact fetuses (not decapitated) were examined for skeletal malformations and variations. All fetal skeletal preparations were retained.

Test substance : 3-Glycidoxypropyltrimethoxysilane (TMSPGE, CAS No. 2530-83-8)

Purity > 98%

Conclusion : The test substance exhibited maternal toxicity at 400 mg/kg/day, but there was no evidence of developmental toxicity at doses up to 400 mg/kg/day.

Reliability : (1) valid without restriction
09.12.2004 (17)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience : other: Monitoring study

Result : More than 50 air samples, collected during production handling at ambient temperature in production plants, have shown no detectable TMSPGE. The detection limit ranged from 0.05 to 1 ppm, depending upon the volume of air sampled.

Reliability : (1) valid without restriction
09.12.2004 (19)

5.11 ADDITIONAL REMARKS

Type : other

Remark : As our experience and knowledge associated with the issues surrounding the testing of TMSPGE increased, it has become apparent that it is not stable by the oral route. Specifically, TMSPGE readily hydrolyzes to methanol and silanols. pH has a significant effect on the rate of hydrolysis, and at pH 4, the hydrolysis is complete within 2.5 minutes. Slight changes in pH affect the rate of hydrolysis, which may result in administration of differing forms of the test article with each dosing. The hydrolysis rate is susceptible to the presence of trace acid and/or base.

A non-GLP study was conducted to examine the fate of TMSPGE following oral (gavage) exposure. Five fasted female Sprague-Dawley rats were dosed with 2000 mg/kg TMSPGE mixed with activated charcoal as a tracer. After 20 or 30 minutes the animals were sacrificed, and the stomachs and gastrointestinal tracts examined for presence of test article. The study was also repeated in the absence of the activated charcoal tracer. In all cases, the hydrolysis product(s) of the test article were found in the stomach contents or in the upper gastrointestinal tract, and was observed to have the consistency of a siloxane gel. In cases where the stomach contents included food, small waxy particles of test article were observed. Both the gel-like substance and waxy particle forms of the hydrolysis products of the test article observed in the stomach and upper gastrointestinal tract support the rapid polymerization of TMSPGE under oral (gavage) conditions, as the test article exists as a clear, water like liquid. In either case, little or no absorption of test article appeared to have occurred. In contrast, there was no liquid present in the stomachs of animals gavaged with an equivalent dose of water and sacrificed after 30 minutes.

The lack of clinical signs of toxicity following acute or repeated dosing is likely related to the hydrolysis of TMSPGE and subsequent polymerization of the hydrolysis products, and thus, the lack of bioavailability.

Reliability : (2) valid with restrictions
Not GLP

10.12.2004 (56) (70) (75)

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