FOREWORD INTRODUCTION

3-AMINOPROPYLTRIETHOXYSILANE

CAS N°:919-30-2

SIDS Initial Assessment Report

For

SIAM 17

Arona, Italy, 11-14 November 2003

1.	**Chemical Name:**	3-aminopropyltriethoxysilane
2.	**CAS Number:**	919-30-2
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 Email: Hernandez.oscar@epa.gov
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: Derek Swick SEHSC 703-904-4322 dswick@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 17.

no testing	(X)
testing	( )

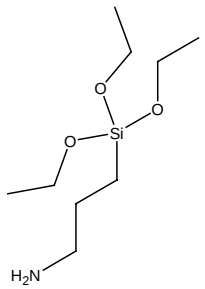
7. Review Process Prior to the SIAM: The U.S. EPA reviewed this case.

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

9. Date of Submission: August 2003

10. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	919-30-2
Chemical Name	3-Aminopropyltriethoxysilane [APTES]
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

3-Aminopropyltriethoxysilane (APTES) has been tested for acute toxicity by the oral, dermal, and inhalation routes of exposure. Acute oral LD_{50}s in rats range from 1570 to 3650 mg/kg bw. The dermal LD_{50} is 4.29 g/kg bw and the 4-hour inhalation LC_{50} of the hydrolysate is greater than 7.35 mg/L. Six hours of exposure to substantially saturated vapor of APTES did not kill any of the 5 male or female rats (LT50 > 6 hours). The kidney is a target organ for toxicity for oral and dermal exposures.
APTES is severely irritating to the skin and eyes. In a Buehler study in guinea pigs, 7/30 animals showed a skin sensitization response. The hydrolysis products of this material do not elicit a sensitization response in a guinea pig maximization test.

Repeated inhalation exposure of rats to 147 mg/m^3 of APTES hydrolysate respirable aerosol for four weeks produced squamous metaplasia and foci of minimal granulomatous laryngitis. No systemic toxicity was observed in rabbits after 9 repeated dermal doses of 17 or 84 mg/kg bw/day or three repeated dermal doses of 126 mg/kg bw/day of APTES; the site of contact NOAEL is less than 17 mg/kg bw/day. The no-observed-adverse-effect level (NOAEL) of APTES in a 90-day oral (gavage) study with rats was 200 mg/kg bw/day.

APTES has been tested in several bacterial reverse mutation/Ames assays, *in vitro* V79 hamster lung cell and Chinese hamster fibroblast chromosome aberration assays, two Chinese hamster ovary cell HGPRT gene mutation assays, and an *in vivo* mouse micronucleus assay. *In vivo* and *in vitro* screening assays have not revealed any evidence of genotoxic potential.

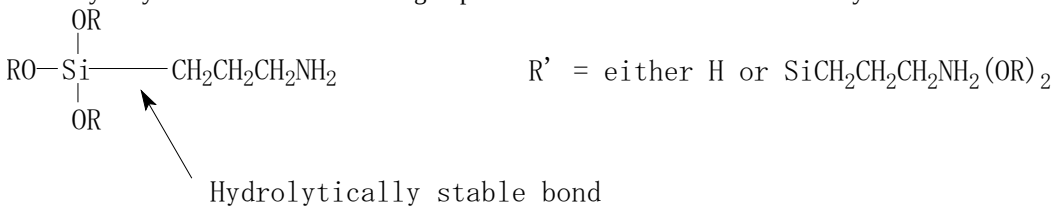
At the highest dose-level (600 mg/kg/day) in a 90 day oral gavage study in rats, no effects were seen on parameters of oestrus cycle and spermatogenesis or reproductive organs. The NOAEL for developmental effects has been identified for APTES following exposure via oral (gavage) in rats, with a value of 100 mg/kg bw/day, the NOAEL for maternal toxicity based on deaths and ulceration of the GI tract is <0.5 mL/kg.

Environment

The estimated partition coefficient Log Kow is 0.31 and the estimated water solubility is $7.6x10^5$ mg/l; these values may not be applicable because the material is hydrolytically unstable. The vapor pressure is 0.02 hPa at 20 °C, the melting point is -70 °C, and the boiling point is 223 °C at 1013 hPa. Photodegradation modeling indicates the half-life in the atmosphere due to the reaction with photochemically induced OH radicals to be approximately 2.4 hours. However, photodegradation as a mode of removal is unlikely and not expected to be a significant degradation process because APTES is hydrolytically unstable.

APTES is hydrolytically unstable ($t_{1/2}$ < 1 hour) over a range of environmentally relevant pH and temperature

conditions, with the exception of pH 7 at 10 or 24.7 °C. At pH 7, the half-life is 56 or 8.4 hours, for 10 or 24.7 °C, respectively. Rapid hydrolysis of this material produces ethanol and trisilanols. The Si-C bond will not further hydrolyze. That bond is hydrolytically stable and the aminopropyl group will not be cleaved. Only the ethoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield:



As a result, aminopropyl-functional resins are generated. The EQC Level III model was used to evaluate the fate, transport and distribution of APTES 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 APTES: air = 0.7%; soil = 91.6%; water = 7.7 %; sediment = 0.00 %. However, APTES is unlikely to be found in the environment, as this material is hydrolytically unstable. APTES is not readily biodegradable. The observed biodegradation is of the hydrolysis products (ethanol and trisilanols). Bioaccumulation is not anticipated since this material is hydrolytically unstable.

In spill conditions, the concentration of the parent silane is very high. The silanols concentration could also be high; however, the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 – 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000 ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. These polymers will not be bioavailable. However, such materials are likely to cause toxicity in aquatic species due to physical effects (encapsulation, blockage of gills). The APTES 96-hr LC_{50} is $\geq$ 934 mg/L for freshwater fish (*Brachydanio rerio*). The 48-hr EC50 for APTES is = 331 mg/L for the water flea (*Daphnia magna*). The 72-hr EbC50 for freshwater green algae (*Scenedesmus subspicatus)* is 603 mg/L. On the basis of cell growth, a 10% suppression of cell growth for the freshwater green algae (*Scenedesmus subspicatus*)was achieved at 72 hour EbC10 = 38 mg/L; on the basis of growth rate, a 10% suppression of cell growth in the same species was achieved at (0-72 hour) ErC10 = 321 mg/L. Since APTES 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 ethanol and trisilanols.

Exposure

The commercial uses of this material are numerous and include various applications as coupling agents and adhesion promoters in fiberglass, adhesives and sealants, foundry resins, and in pre-treatment for coatings. A small percentage of this material may be found in sealants and coatings. 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 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. APTES is transported from the production site as the parent silane to processors/formulators. Generally, APTES is used by the processor/formulator as an adhesion promoter with use levels <1%. In some applications, APTES is used as a crosslinker; these use levels are higher and can approach 3 to 5 %. Once APTES is added to a consumer or industrial product, the parent silane reacts 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 into the polymer matrix and no longer exists and greatly reduces potential for consumer or worker exposure. APTES polymerizes during use. Consumer products will be labeled as containing a sensitizer according to individual member country regulations. Any toxicological effects originating from the alkoxysilane or amine groups of the silane are greatly reduced as a result of this coupling process. The production volume of APTES in the sponsor country was 1992 tonnes in 2002.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

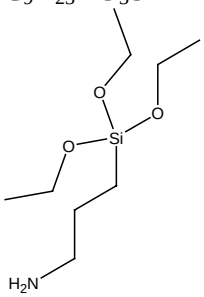
The chemical possesses properties indicating a hazard for human health (skin and eye irritation, and skin sensitization). Based on data presented by the Sponsor country, adequate risk management measures are being applied, exposure to humans and the environment is anticipated to be low, and therefore this chemical is currently a low priority for further work.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 919-30-2
IUPAC Name: 1-Propanamine, 3-(triethoxysilyl)-
Molecular Formula: $C_9H_{23}NO_3Si$
Structural Formula:



Molecular Weight: 221
Synonyms: APTES
(.gamma.-Aminopropyl)triethoxysilane
(3-Aminopropyl)triethoxysilane
1-Propanamine, 3-(triethoxysilyl)-
3-(Triethoxysilyl)-1-propanamine
3-(Triethoxysilyl)propylamine
A-1100
A-1112
AGM 9 (VAN)
NUCA 1100
Propylamine, 3-(triethoxysilyl)-
Silane 1100
Silane, (.gamma.-aminopropyl)triethoxy-
Silane, (3-aminopropyl)triethoxy-
Silicone A-1100
Triethoxy(3-aminopropyl)silane
UC-A 1100

1.2 Purity/Impurities/Additives

Purity: 98% to 100%
Impurities: Ethyl Alcohol (0 – 1 %); 2-Butanone (0-2 %); Dibenzoyl peroxide (0-1 %)

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Comment
Physical state	Liquid	
Melting point	-70°C	
Boiling point	223°C	
Relative density	0.95 @ 25°C	
Vapour pressure	0.02 hPa @ 20°C	
Water solubility	$7.6X10^5$ mg/l @ 25°C	Estimated. This value may not be applicable because the material is hydrolytically unstable
Partition coefficient n-octanol/water (log value)	0.31	Estimated. This value may not be applicable because the material is hydrolytically unstable
Henry's law constant	Not available	

2 GENERAL INFORMATION ON EXPOSURE

Human or environmental exposure to 3-aminopropyltriethoxysilane (APTES) is limited to accidental acute exposures. 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 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. APTES is transported from the production site as the parent silane to processors/formulators. After curing the parent silane is consumed into the polymer matrix and no longer exists and greatly reduces potential for consumer or worker exposure.

Since APTES is sensitive to hydrolysis, which may occur during testing, observed toxicity is likely due to the hydrolysis products ethanol and trisilanols.

2.1 Production Volumes and Use Pattern

Production volume = 1992.221 tonnes in 2002 (in the Sponsor Country). APTES is produced in North America, Europe and Asia.

The commercial uses of this material are numerous and include various applications as coupling agents and adhesion promoters in fiberglass, adhesives and sealants, foundry resins, and in pre-treatment for coatings. A small percentage of this material may be found in sealants and coatings. APTES is transported from the production site as the parent silane to processors/formulators. Generally, APTES is used by the processor/formulator as an adhesion promoter with use levels <1%. In some applications, APTES is used as a crosslinker; these use levels are higher and can approach 3 to 5 %. Once APTES is added to a consumer or industrial product, the parent silane reacts 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 into the polymer matrix and no longer exists and greatly reduces potential for consumer or worker exposure. APTES polymerizes during use.

As coupling agents and adhesion promoters, APTES is intentionally converted by hydrolysis to the trisilanols, which then bond molecularly to inorganic substrates. During hydrolysis, the ethoxy-group is liberated as ethanol. The silane-modified surfaces of these inorganic substrates become incorporated within polymeric resins by a chemical reaction with the amine group. This completes the coupling process. The amino-functional silane is converted and bound within the substrate by polymer coupling. In solvent based coatings, sealants etc., the aminofunctional silane may be present until the curing reactions take place, which is often after application.

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. 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.

2.2.2 Photodegradation

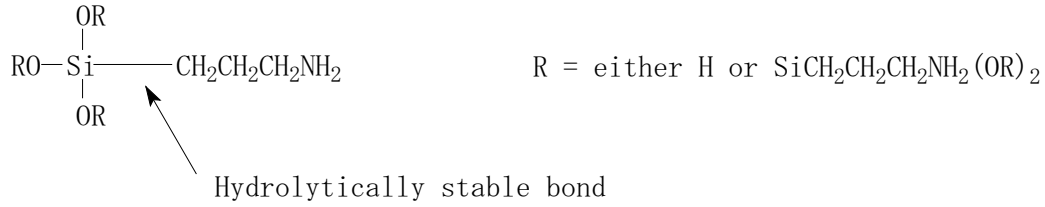
The hydroxyl radical reaction was calculated using EpiWin. The overall OH rate constant is 52 E-12 cm^3/molecule-sec. The half-life is 2.4 hrs, the effective (actual, atmospheric) half-life is even shorter, due to rapid concurrent hydrolysis. However, because of the rapid hydrolysis of this material with moisture in the atmosphere, photolysis in the atmosphere is not predicted to be a significant mode of removal and should be considered secondary to hydrolysis. In addition, the parent silane contains no chromaphors that would absorb visible or UV radiation so no direct photolysis reactions are predicted. The trisilanol resulting from hydrolysis in the atmosphere is similarly not predicted to undergo direct photolysis but could react with hydroxyl radicals or ozone.

2.2.3 Stability in Water

APTES is hydrolytically unstable over a range of environmentally relevant pH and temperature conditions:

	Half life (hours)		
pH	@10 deg C	@24.7 deg C	@37 deg C
4.7	0.97	0.41	0.22
7.0	56	8.4	3.9
9.0	0.78	0.15	0.043

Rapid hydrolysis of this material produces ethanol and trisilanols. The half-lives refer to the reaction to the mono-ol and the mono- and di-ol hydrolyze on a timescale similar to the silane. The Si-C bond will not further hydrolyze. That bond is hydrolytically stable and the aminopropyl group will not by cleaved. Only the ethoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield:



As a result, aminopropyl-functional resins are generated.

2.2.4 Transport between Environmental Compartments

The EQC Level III model (USEPA, 2000) was used to evaluate the fate, transport and distribution of APTES 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: Air = 0.7%; Soil = 91.6%; Water = 7.7 %; Sediment = 0.00 %. However, APTES is unlikely to be found in the environment, as this material is hydrolytically unstable.

2.2.5 Biodegradation

When added to water, APTES rapidly hydrolyzes, generating ethanol and transient silanetriol derivatives, which will crosslink. Note that hydrolysis of this material occurs rapidly, such that the observed biodegradation is of the hydrolysis products (ethanol and trisilanols). Rapid hydrolysis of this material produces ethanol and trisilanols. Available data indicate that APTES is not "readily biodegradable." Degradation of APTES was 67% after 28 days (Huls AG, 1994a). The test material is known to be hydrolytically unstable.

2.2.6 Bioaccumulation

Bioaccumulation is not anticipated since this material is hydrolytically unstable. Rapid hydrolysis of this material produces ethanol and trisilanols. The Si-C bond will not undergo hydrolysis. That bond is hydrolytically stable and the aminopropyl group will not be cleaved. Only the ethoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield:

R-Si(OR')3 type resins where R = CH2CH2CH2NH2 and R' = either H or Si(R)(OR')

As a result, aminopropyl-functional resins are generated.

If the silane is slowly released such that the concentration of the resulting aminopropyl-functional silanetriol is not high enough to result in polymerization, the trisilanol will exist largely as the 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 can not be measured because of the tendency to condense at concentrations greater than 500 ppm. 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.

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 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 open systems. Transport is a source of potential exposure through accidental releases. This material is shipped via road and marine in drums, cans, pails, and returnable intermediate bulk containers (IBCs). Air shipment follows IATA Regulations and is limited to 1 Liter maximum for passenger aircraft and 30 Liter maximum cargo only. Drums and IBCs are not shipped by air.

As for occupational/facility level releases, the exposures will be low due to the rapid hydrolysis of the material. Customers go to great lengths to minimize loss due to the reactive nature of the material, which is necessary in order to ensure accurate formulations. Producers maintain and track the safety record of use of this material at the customer level. In circumstances where an accidental release occurs, the producer often works with the customer to implement additional safety measures. Production and customer use have a long safety history.

A worker may be exposed at the customer level to very low levels (generally <1%) of the silane during the preparation of the coating, sealant, etc. and to a much less extent, during its use in the

final product. The low final percentage in the product (generally 0.1-0.2%) reflects the fact that this material is designed to be reactive and to not survive the application processing at the customer level. Potential routes of exposure for workers include dermal contact, although the MSDS properly warns against contact with the skin. There is no known production process that involves aerosolized material or sprayed material. Customers who manufacture treated fillers may spray the silane onto the filler. In coatings that are applied by spraying, very low levels of free silane may be present (generally 0.1-0.2%). In a spray application (for example, for a coating), the material sprayed is a pre-polymer of a silane at a very low concentration (again, generally 0.1-0.2%). No free parent silane would be available for aerosol inhalation. The vapour pressure of this material is low enough that vapour inhalation is not considered a potential route of exposure.

2.3.2 Consumer Exposure

The use of APTES into the consumer market is limited; it is used in caulks as well as coatings (for example, paint for outdoor furniture). The substance is used at generally <1% in these formulations. Once added to the formulation, the final product will contain generally 0.1-0.2% parent silane; the remainder of the added substance will have reacted with the other components of the formation and is no longer present. After curing the parent silane is consumed into the polymer matrix and no longer exists, eliminating the potential for consumer exposure. In a final consumer product that utilizes an industrial sealant or coating, the inherent retention of the material is extremely low to the dual reactivity (both hydrolysis and curing). The curing time will vary among applications. Dermal exposure is a potential route for consumers. However, after curing the parent silane is consumed into the polymer matrix and no longer exists; this greatly reduces the potential for consumer exposure.

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

APTES has been tested for acute toxicity by the oral, dermal and inhalation routes of exposure.

Studies in Animals

Inhalation

Five rats were exposed for four hours to 7.35 mg/l of a 60% solution of APTES (hydrolyzed APTES). The animals were observed during the following 14 day post exposure period. After exposure, slow righting reflex, labored breathing, hypoactivity, ataxia and discharge from the mouth, nose and eyes were apparent. At 3 days, the animals were fully recovered. All animals gained weight during the study period. There were no other clinical signs. The four-hour LC50 for exposure to aerosolized APTES was determined to be greater than 7.35 mg/l in rats (BRRC, 1983). In a second study, five rats per group were exposed to 5 or 16 ppm undiluted APTES as a vapor for 6 hours. There were no signs of toxicity during or following exposure. There were no remarkable gross pathologic findings. The vapor of this material shows very low acute inhalation toxicity in the rat. Six hours of exposure to substantially saturated vapour generated from APTES did not kill any of the 5 male or 5 female rats. The LT50's with 95% confidence limits were greater than 6 hours for male and female rats (BRRC, 1982).

Dermal

Male and female rabbits were dosed by occlusive dermal route of exposure with 8, 4, 2, and 1 g/kg of APTES for a period of twenty-four hours (BRRC, 1989). The kidney was identified as a target organ in this acute study. Severe local cutaneous effects were observed. The LD50 is 4.29 g/kg bw, indicating the toxicity of this material is very low by the dermal route. A follow-up study was conducted to assess the percutaneous toxicity and nephrotoxic potential of the test article. Single occlusive, cutaneous doses of the test article were given to groups of 6 male rabbits at 3 dose levels (2.0, 4.0, and 6.0 ml/kg) for a period of 24 hours. Single cutaneous applications of 2.0 ml/kg or more of the test article to rabbit skin resulted in kidney and urinary bladder injury. At 2 ml/kg, four animals had no systemic signs of toxicity. Two animals dosed with 2 ml/kg had blood-stained periurogenital discharge, and renal tubular epithelial cell degeneration was observed (1 animal on day 1). On day 2, the one animal sacrificed had microscopic evidence of tubular epithelial cell degeneration and proteinosis involving the kidneys, and one or more lesions involving the bladder. At day 14, there was no evidence of microscopic lesions. These effects appear to develop within one or 2 days after contact and subside thereafter, possibly indicating a capacity for renal repair (BRRC, 1990b).

Oral

APTES was administered by gavage at doses of 4, 2, and 1 g/kg in 5 male rats/group and 2, 1.41 and 1 g/kg in 5 female rats/group. Signs of toxicity included sluggishness, lacrimation, kyphosis, an unkempt appearance, piloerection, staining on the fur, closed eyelids, emaciation, and diarrhea. Survivors recovered at 2 to 9 days. The acute oral toxicity LD50 values were 1570 (females) to

2830 (males) mg/kg (BRRC, 1989). Two rats/sex were administered doses of 2.5, 3.1, 3.9, 4.5 and 5.0 ml/kg APTES. The LD50 was 3650 ml/kg (Degussa-Huls AG, 1978). Salivation, ataxia, and lethargy followed by tonic and clonic convulsions within 1 hour of administration at highest dose level. Survivors at 24 hours exhibited severe diarrhoea and diuresis and further deaths occurred up to 72 hours after administration. The kidney is a target organ for toxicity for oral exposure.

Studies in Humans

No data available.

3.1.3 Irritation

APTES is severely irritating to the skin and eyes, which is consistent with the amino-functionality of this molecule.

Skin Irritation

Studies in Animals

A 4-hour application of 0.5 ml of undiluted APTES to occluded rabbit skin resulted in minor to moderate erythema on 6 of 6 rabbits and minor to severe edema on 6. One hour after the contact period, ecchymosis was apparent on one animal. Necrosis was observed on 3 animals by one day and on another animal by 7 days. There was no erythema or edema evident on any animal at 10 days. At this time ulceration was evident on one animal and alopecia was observed on most. Desquamation, alopecia and ulceration (on one) persisted through 14 days. This material was considered corrosive to the skin by the Department of Transportation (DOT) definition (BRRC, 1989). Four rabbits were administered .5 ml undiluted APTES and observed at 24 and 72 hours. The test material was observed to cause severe skin irritation. Moderate to severe erythema accompanied by edema was observed on all animals after 24 hours exposure. The irritation was more severe on abraded skin and became more pronounced, leading to eschar formation after 72 hours (Dow Corning Corporation (DCC), 1976).

Male and female rabbits were dosed by occlusive dermal route of exposure with 8, 4, 2, and 1 g/kg of APTES for a period of twenty-four hours (BRRC, 1989). Local cutaneous effects were observed consistent with the amine functionality in this molecule (effects included erythema, edema, ecchymosis, necrosis, desquamation, fissuring, ulceration, alopecia and scabs).

The potential skin irritancy of APTES resulting from 9 applications over an 11-day exposure period (BRRC, 1990a) was evaluated. There were 5 rabbits per sex in each group. The test article was administered at a constant volume of 2.0 ml/kg /day in mineral oil (1%, 5% or 7.5% solutions). The animals given 7.5% solutions were treated with the test material at least 6 hours/day for 3 consecutive days and observed for any reversal of the cutaneous irritation for the remainder of the study. APTES is considered to be a significant skin irritant causing dose-dependent cutaneous lesions at doses as low as 1%.

Eye Irritation

Studies in Animals

Following the instillation of 0.005 ml APTES into rabbit eyes, minor to severe corneal injury developed in all rabbits. All 6 rabbits had necrosis of the conjunctivae within one hour. By 48 hours, 5 animals developed a purulent ocular discharge. Three rabbits had an irregularly shaped cornea and vascularization within 7 days; two animals had a normal appearance by 7 days. The other eyes still exhibited substantial injury. This material is a severe eye irritant capable of

producing necrosis (BRRC, 1989). Following the instillation of 0.1 ml APTES into rabbit eyes, severe ocular irritation in all rabbits was observed including those in which the treated eye was washed following instillation (DCC, 1976). Rabbits eyes were dosed with 0.1 ml APTES; the treated eyes of six animals remained unwashed. The treated eyes of three animals were washed for 1 minute, approximately 5 seconds after installation of the test article. The eyes were scored at 24, 48 and 72 hours, and on days 4, 7 and 8-14 after dosing. In both groups severe irritation and necrosis was observed and persisted in at least one animal to day 13 (ToxiGenics, 1981).

Conclusion

APTES is corrosive to the skin and eyes.

3.1.4 Sensitisation

Studies in Animals

Skin

Twenty guinea pigs were tested for skin sensitization in a Buehler assay, [test material hydrolysis was limited by using peanut oil; APTES was shown to be stable in peanut oil in this study] (Pharmakon, 1997). Under the conditions of this study, animals induced with APTES at 20% and challenged at 5% produced a delayed contact hypersensitivity response in 7 of the 20 guinea pigs. In a guinea pig maximization test, animals were induced and challenged with APTES in saline (Pharmakon, 1996). Since the test article readily hydrolyzes in saline, the test was actually conducted on the hydrolysis products of the test material. The hydrolysis products of APTES did not cause a sensitization reaction in guinea pigs. In a guinea pig maximization test, animals were induced and challenged with APTES in water (Dynamit Nobel, 1987). Since the test article readily hydrolyzes in water, the test was actually conducted on the hydrolysis products of the test material. The hydrolysis products of APTES did not cause a sensitization reaction in guinea pigs.

Studies in Humans

No data available.

Conclusion

APTES caused a skin sensitization response in guinea pigs. The hydrolysis products of this material do not elicit a sensitization response.

3.1.5 Repeated Dose Toxicity

Repeated dose toxicity has been investigated by the inhalation, dermal and oral (gavage) routes of exposure.

Studies in Animals

Inhalation

Target concentrations of 0 and 150 mg/m3 of APTES hydrolysate were selected for this repeated exposure inhalation study; 15 male rats per group were exposed for 6 hours per day for a total of 19 exposures over 4 weeks (BRRC, 1991). Five of the fifteen animals in each group were assigned to a satellite group destined for ultrastructural evaluation of the larynx; ten animals of the control and treated groups were subjected to a complete necropsy. Microscopic examinations were conducted on gross lesions, larynx, lungs, trachea, nasal tissues and kidneys. Other organs (brain, spinal cord, and peripheral nerves) were taken from these control animals and processed for light microscopic

evaluation. A 2% hydrolysate solution of APTES was prepared daily and used to generate the aerosol atmosphere in the inhalation chamber. Histological examination showed non-specific irritant, inflammatory, and metaplastic changes within the respiratory tracts of test substance-exposed rats. Laryngeal lesions included squamous metaplasia and foci of minimal granulomatous laryngitis. Other microscopic changes included the presence of cytoplasmic hyalinization (mild to moderate) within the olfactory mucosa, squamous metaplasia (minimal to mild) within the nasal mucosa, cellular hyperplasia within the trachea, alveolar histiocytosis, bronchopneumonia, interstitial pneumonitis and alveolar type II pneumocyte hyperplasia within the lungs. Repeated exposure of rats to 147 mg/m^3 (measured concentration) of APTES hydrolysate respirable aerosol did not produce definitive evidence of the development of laryngeal granulomas, although squamous metaplasia and foci of minimal granulomatous laryngitis were observed.

Dermal

The potential skin irritancy and systemic toxicity of APTES were evaluated in a study involving nine skin applications over 11 days to groups of 5 male and 5 female rabbits (BRRC, 1990a). There were 5 rabbits per sex in each group. The test article was administered at a constant volume of 2.0 ml/kg /day in mineral oil (1%, 5% or 7.5% solutions) and the resulting dose levels corresponded to 17, 84 and 126 mg/kg/day. The animals given 126 mg/kg/day were treated with the test material at least 6 hours/day for 3 consecutive days and observed for any reversal of the cutaneous irritation for the remainder of the study. No systemic toxicity was observed in rabbits after 9 repeated dermal doses of 17 or 84 mg/kg/day or three repeated dermal doses of 126 mg/kg/day of APTES; the site of contact NOAEL is less than 17 mg/kg/day. Nine applications of up to 84 mg/kg/day, or three applications of 126 mg/kg/day, had no effect on survival, growth, haematology, serum chemistry, urine composition, organ weight or the gross appearance of a wide range of organs and tissues. Microscopic examination of a fairly wide range of tissues (including the liver and kidneys) from the control and 84 mg/kg/day groups found no adverse effects.

Oral

The objective of this study was to evaluate the possible toxic effects of APTES when administered orally (gavage) to three groups of 15 rats/sex for a minimum of 90 days (WIL Research, 2001). The test article in the vehicle, peanut oil sparged with nitrogen (in order to reduce hydrolysis of the test article), was administered at dosage levels of 70, 200 and 600 mg/kg/day. These dose levels were chosen based upon the results of the previous 14-day range-finding study (WIL Research, 1999). In this 14-day range-finding study APTES in peanut oil was administered orally by gavage to three groups of rats (five/sex) at levels of 70, 200 and 600 mg/kg/day. Survival was unaffected by APTES administration and no test-article related findings were observed at the macroscopic or microscopic examinations. Organ weights were unaffected by treatment. The only definite test article-related clinical observations were signs of abnormal respiration (rales and/or labored respiration) in the 600 mg/kg/day group. There were no statistically significant differences in body weights, body weight gains, or food consumption. However, there were reductions in body weight gains and food consumption in the 600 mg/kg/day males during weeks 0 to 1 and 1 to 2.

In this study, the animals were observed twice daily for mortality and moribundity. Clinical observations were performed on all animals prior to and following dosing and detailed physical examinations were conducted weekly.

Individual body weights were recorded weekly, mean body weight changes were calculated for each week. A final (fasted) body weight was recorded for each animal on the day of scheduled necropsy. Individual food consumption was monitored. Clinical pathology parameters were assessed. A complete necropsy was conducted on all animals. The following tissues from all animals found dead or euthanized in extremis and from all animals in the control and 600

mg/kg/day groups euthanized at the scheduled necropsy, as well as the lungs, liver, and kidneys from all animals in the 70 and 200 mg/kg/day groups were examined microscopically: adrenals, aorta, bone with marrow, bone marrow smear, brain, coagulating gland, eyes with optic nerve, gastrointestinal tract, heart, kidneys, liver, lungs, lymph node, mammary gland (females only), ovaries with oviducts, pancreas, peripheral nerve, pituitary, prostate, salivary glands, seminal vesicles, skeletal muscle, skin, spinal cord, spleen, testis with epididymis and vas deferens, thymus, thyroid, trachea, urinary bladder, uterus with vagina and cervix, and all gross lesions (when possible). In addition, sections of the right testis and epididymis from all males were examined microscopically at the scheduled necropsy.

Test article-related lethality was limited to the 600 mg/kg/day group. One male and eight females in this group were found dead or euthanized in extremis. Just prior (one or two days) to death, many of these animals exhibited labored respiration, gasping, partial closure of the eyes, general paleness, hypothermia, dermal atonia and/or tremors. Additional clinical signs for these animals were generally similar to those in the animals that survived to the scheduled necropsy. All other animals survived to the scheduled necropsy. Test article-related clinical signs were generally limited to the 600 mg/kg/day group males and females. The predominant clinical sign was rales. Body weight gains and food consumption were unaffected by test article administration at all dose levels. No oculopathic changes indicative of a test article-related effect were observed at any dose level. No test article-related changes were present in hematology parameters. At 600 mg/kg/day, test article-related increases were present in mean aspartate aminotransferase values for the males at week 13 and in mean alanine aminotransferase values for the males and females at both evaluations during the study (weeks 4 and 13). Gaseous distention in the intestinal tract (primarily in the cecum) was observed macroscopically at necropsy for most males and females, including those that died prior to the scheduled necropsy. Test article-related organ weight changes were seen in the liver of the 600 mg/kg/day males. In this treatment group, although the mean absolute liver weight was not increased, the mean liver-to-brain weight was increased (not statistically significantly), and the mean liver-to-body weight was statistically increased when compared to controls. Test article-related microscopic changes were limited to the males, and consisted of increased severity of centrilobular to generalized hepatocellular vacuolation. No other test article-related microscopic changes were observed. The no-observed-adverse-effect level (NOAEL) was 200 mg/kg/day.

In a dose-range-finding developmental study 8 rats/dose/sex were administered 0.1, 0.25, 0.5, 1.0, and 1.5 ml/kg/day undiluted APTES on gestation days 6-15. Parameters assessed during study (maternal) included clinical signs; body weight; and necropsy. Deaths and ulceration of the GI tract occurred following gavage at doses of 0.5 to 1.5 mL/kg on days 6-15 of gestation. Hence the NOAEL for essentially non-hydrolysed APTES is <0.5 mL/kg (BRRC, 1994). Microliter dosing was employed in this study such that the accuracy of the dosing remains in question, and limits the comparability of this study to the other studies presented.

Studies in Humans

No data available.

Conclusion

No inhalation data are available for APTES. Repeated inhalation exposure of rats to 147 mg/m^3 of APTES hydrolysate respirable aerosol produced squamous metaplasia and foci of minimal granulomatous laryngitis and hyperplasia was seen throughout the lung; these findings are consistent with administration of an irritating substance. No systemic toxicity was observed in rabbits after 9 repeated dermal doses of 84 mg/kg/day or three repeated dermal doses of 126 mg/kg/day of APTES. The no-observed-adverse-effect level (NOAEL) of APTES in a 90-day oral gavage study with rats was 200 mg/kg/day.

3.1.6 Mutagenicity

In vivo Studies

Five mice/sex/group were dosed once via intraperitoneal injection with 0, 28, 56 or 90 mg/kg APTES. The high dose was equivalent to approximately 80% of the LD50. Blood smears were prepared at 30, 48 and 72 hours post-dosing and peripheral lymphocytes examined. APTES was not clastogenic in an *in vivo* mouse micronucleus assay (BRRC, 1988a).

In vitro Studies

Either in the presence or absence of metabolic activation, APTES was negative in multiple bacterial mutagenicity assays (Hatano Research, 1977, BRRC, 1987, Degussa-Huls AG, 1998a, Kakenkyo Test Institute, 1994a), was negative in *in vitro* mammalian cell gene mutation studies (CHO/HGPRT) (Degussa-Huls, 1998b), lacked significant DNA damaging activity in the Sister Chromatid Exchange Assay (BRRC, 1988b), and was negative in *in vitro* chromosome aberration tests with Chinese Hamster fibroblasts (Degussa-Huls AG, 1999, Kakenkyo Test Institute, 1994b). Note that in two studies (bacterial mutation and in vitro mammalian cell gene mutation), negative responses were observed in assays with exposure to non-hydrolysed APTES, which was maximised by the use of a non-aqueous diluent (DMSO).

Conclusion

An in vivo assay and several in vitro studies examining a range of genetic endpoints have not revealed any evidence of genotoxic potential for APTES.

3.1.7 Carcinogenicity

No data available.

3.1.8 Toxicity for Reproduction

Effects on Fertility

Gavage administration of APTES at 70, 200 or 600 mg/kg/day for 91-92 days, in peanut oil sparged with nitrogen (in order to reduce test article hydrolysis), to groups of 15 male and 15 female rats had no adverse effects on estrous cycle, epididymis and testis weights, or sperm motility, morphology and numbers. The NOAEL for effects on reproductive organs was 600 mg/kg/day (the highest dose level) (WIL Research, 2001) (see Repeated Dose Toxicity section above for additional details). [Note that only the liver effects were observed in this study at 600 mg/kg/day. So, it is appropriate to conclude that NOAEL for reproductive organ toxicity to be greater than 600 mg/kg/day.]

No fertility studies were identified.

Developmental Toxicity

Thirty female rats/group were exposed by gavage from day 6 of gestation through day 20 of gestation to doses of 20, 100 or 600 mg/kg/day of APTES in the vehicle, peanut oil sparged with nitrogen (in order to reduce hydrolysis of the test article) (Breslin, 1998). Extensive monitoring for embryotoxicity, foetal toxicity and foetal malformations was conducted. Increased incidences of mortality and clinical observations, as well as slight decreases in body weight gain and food consumption, were observed at 600 mg/kg/day. The occurrence of maternal toxicity at 600 mg/kg/day was accompanied by slight fetal toxicity, as exhibited by 27 presacral vertebrae and sternebra unossified. No significant maternal or developmental effects were observed at 20 or 100

mg/kg/day. Therefore, the maternal and developmental NOAEL was 100 mg/kg/day. This study was selected as the key study as it is the only definitive developmental toxicity study available.

Several dose range finding studies involving repeated gavage administration to pregnant rats found no adverse effects on foetal development, even at doses that caused maternal toxicity. In a dose-range-finding study 5 or 8 rats/dose/sex were administered 10, 25, 50, 100, 500, 750 or 1000 mg/kg/day APTES in peanut oil on gestation days 6-17. Parameters assessed during study (maternal) included clinical signs, body weight, uterine exam, location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea, gravid uterine weight, and necropsy. Increased incidence of mortality and clinical observations as well as decreased body weight and body weight gain observed at 500 mg/kg and higher. No significant maternal effects at 100 mg/kg. (Breslin, W.J., 1998). In another dose-range-finding study 5 or 8 rats/dose/sex were administered (Part I) 10, 25, 50, 100 and 500 mg/kg/day or (Part II) 500, 750 and 1000 mg/kg/day APTES in peanut oil on gestation days 6-15. Parameters assessed during study (maternal) included clinical signs, body weight, gravid uterine weight, laparohysterectomic exam, location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea, position of the cervix, and necropsy. Mortality was observed at 500, 750 and 1000 mg/kg/day; clinical signs of toxicity (rales, gasping and labored breathing) and necropsy findings (discoloration of lungs) were observed at these levels; decreased body weight and body weight gain was observed at 500 mg/kg/day and higher (MPI Research, 1998). In a third dose-range-finding study 8 rats/dose/sex were administered 0.1, 0.25, 0.5, 1.0, and 1.5 ml/kg/day undiluted APTES on gestation days 6-15. Parameters assessed during study (maternal) included clinical signs; body weight; necropsy; uterus, ovaries, cervix, vagina, and abdominal and thoracic cavities were examined grossly; maternal liver, kidneys, lungs and bladder were weighed and retained in 10% neutral buffered formalin; gravid uterine weight, laparohysterectomic exam, location of viable and nonviable fetuses, early and late resorptions, total number of implantations and corpora lutea; fetal parameters - weight, sex, examined for external variations and malformations including cleft palate. The NOAEL for maternal toxicity was less than .1 ml/kg/day; the NOAEL for teratogenicity was greater than the highest dose tested (1.5 ml/kg/day) BRRC (1994). Microliter dosing was employed in this study such that the accuracy of the dosing remains in question, and limits the comparability of this study to the other dose range finding studies presented here.

Conclusion

NOAEL for reproductive organ toxicity and developmental effects have been identified for APTES, with values greater than 600 mg/kg/day and 100 mg/kg/day, respectively.

3.2 Initial Assessment for Human Health

3-Aminopropyltriethoxysilane (APTES) has been tested for acute toxicity by the oral, dermal, and inhalation routes of exposure. Acute oral LD_{50}s in rats range from 1570 to 3650 mg/kg bw. The dermal LD_{50} is 4.29 g/kg bw and the 4-hour inhalation LC_{50} of the hydrolysate is greater than 7.35 mg/L. Six hours of exposure to substantially saturated vapor of APTES did not kill any of the 5 male or female rats (LT50 > 6 hours). The kidney is a target organ for toxicity for oral and dermal exposures.

APTES is severely irritating to the skin and eyes. In a Buehler study in guinea pigs, 7/30 animals showed a skin sensitization response. The hydrolysis products of this material do not elicit a sensitization response in a guinea pig maximization test.

Repeated inhalation exposure of rats to 147 mg/m^3 of APTES hydrolysate respirable aerosol for four weeks produced squamous metaplasia and foci of minimal granulomatous laryngitis. No

systemic toxicity was observed in rabbits after 9 repeated dermal doses of 17 or 84 mg/kg bw/day or three repeated dermal doses of 126 mg/kg bw/day of APTES; the site of contact NOAEL is less than 17 mg/kg bw/day. The no-observed-adverse-effect level (NOAEL) of APTES in a 90-day oral (gavage) study with rats was 200 mg/kg bw/day.

APTES has been tested in several bacterial reverse mutation/Ames assays, *in vitro* V79 hamster lung cell and Chinese hamster fibroblast chromosome aberration assays, two Chinese hamster ovary cell HGPRT gene mutation assays, and an *in vivo* mouse micronucleus assay. *In vivo* and *in vitro* screening assays have not revealed any evidence of genotoxic potential.

At the highest dose-level (600 mg/kg/day) in a 90 day oral gavage study in rats, no effects were seen on parameters of oestrus cycle and spermatogenesis or reproductive organs. The NOAEL for developmental effects has been identified for APTES following exposure via oral (gavage) in rats, with a value of 100 mg/kg bw/day, the NOAEL for maternal toxicity based on deaths and ulceration of the GI tract is <0.5 mL/kg.

4 HAZARDS TO THE ENVIRONMENT

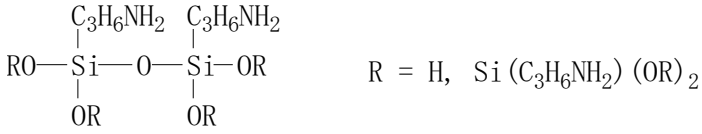
4.1 Aquatic Effects

APTES is sensitive to hydrolysis, which may occur during preparation of the dosing solutions and/or during the testing. Rapid hydrolysis of this material produces ethanol and trisilanols. The Si-C bond will not undergo hydrolysis. That bond is hydrolytically stable and the aminopropyl group will not be cleaved. Only the ethoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield:

R-Si(OR')3 type resins where R = CH2CH2CH2NH2 and R' = either H or Si(R)(OR')

As a result, aminopropyl-functional resins are generated.

In spill conditions, the concentration of the parent silane is very high. The resulting silanol concentration is also high and the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 – 10000. The structure of the resulting resin (assuming pure silane is spilled) is:



As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000 ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer.

Due to the insolubility in water of the higher molecular weight oligomers and polymers, testing of such materials is not anticipated. These polymers will not be bioavailable. Such materials are also likely to cause toxicity due to physical effects (encapsulation, blockage of gills). Ecotoxicity of the silanols may be predicted using modeling programs such as ECOSAR.

Acute Toxicity Test Results

The APTES 96-hr LC_{50} is $\geq$ 934 mg/L to freshwater fish (*Brachydanio rerio*). (Huls AG, 1994b). The 48-hr EC50 for APTES is = 331 mg/L to the water flea (*Daphnia magna;* = 331 mg/L) (Huls AG, 1993). The 72-hr EbC50 to freshwater green algae (*Scenedesmus subspicatus)* is 603 mg/L. On the basis of cell growth, a 10% suppression of cell growth for the freshwater green algae (*Scenedesmus subspicatus*)was achieved at 72 hour EbC10 = 38 mg/L; on the basis of growth rate, a 10% suppression of cell growth in the same species was achieved at (0-72 hour)ErC10 = 321 mg/L (Huls AG, 1994c.)

Chronic Toxicity Test Results

No data available.

4.2 Terrestrial Effects

No data available.

4.3 Other Environmental Effects

No data available.

4.4 Initial Assessment for the Environment

The estimated water solubility of APTES is $7.6X10^5$ mg/l at 25°C and the estimated log Kow of APTES is 0.31. These values may not be applicable because the chemical is hydrolytically unstable. The vapor pressure is 0.02 hPa @ 20^oC. The melting point is -70 °C and the boiling point is 223 °C @ 1013 hPa. Photodegradation modeling indicates the half-life in the atmosphere due to the reaction with photochemically induced OH radicals is estimated to be approximately 2.4 hours. However, photodegradation as a mode of removal is unlikely and not expected to be a significant degradation process because APTES is hydrolytically unstable. Photodegradation of the parent silane is not expected to be a significant degradation process in the aquatic environment due to the rapid rate of hydrolysis.

APTES is hydrolytically unstable ($t_{1/2}$ < 1 day) over a range of environmentally relevant pH and temperature. At pH 7, the half-life is 8.4 hours. Rapid hydrolysis of this material produces ethanol and trisilanols. The Si-C bond will not hydrolyze. That bond is hydrolytically stable and the aminopropyl group will not be cleaved. Only the ethoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield:

R-Si(OR')3 type resins where R = CH2CH2CH2NH2 and R' = either H or Si(R)(OR')

As a result, aminopropyl-functional resins are generated. The EQC Level III model (USEPA, 2000) was used to evaluate the fate, transport and distribution of APTES 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: Air = 0.7%; Soil = 91.6%; Water = 7.7 %; Sediment = 0.00 %. However, APTES is unlikely to be found in the environment, as this material is hydrolytically unstable. APTES is not readily biodegradable. Note that hydrolysis of this material occurs rapidly, such that the observed biodegradation is of the hydrolysis products (ethanol and trisilanols). Bioaccumulation is not anticipated since this material is hydrolytically unstable.

In spill conditions, the concentration of the parent silane is very high. The resulting silanol concentration is also high and the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 – 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. Due to the insolubility in water of the higher molecular weight oligomers and polymers, testing of such materials is not anticipated. These polymers will not be bioavailable. Such materials are also likely to cause toxicity due to physical effects (encapsulation, blockage of gills). Since APTES 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 ethanol and trisilanols. Ecotoxicity of the silanols may be predicted using modeling programs such as ECOSAR. The APTES 96-hr LC_{50} is $\geq$ 934 mg/L to freshwater fish (*Brachydanio rerio*). The 48-hr EC50 for

APTES is = 331 mg/L to the water flea (*Daphnia magna;* = 331 mg/L). The 72-hr EbC50 to freshwater green algae (*Scenedesmus subspicatus)* is 603 mg/L. On the basis of cell growth, a 10% suppression of cell growth for the freshwater green algae (*Scenedesmus subspicatus*)was achieved at 72 hour EbC10 = 38 mg/L; on the basis of growth rate, a 10% suppression of cell growth in the same species was achieved at (0-72 hour)ErC10 = 321 mg/L. Since APTES 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 ethanol and trisilanols.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

The chemical possesses properties indicating a hazard for human health (skin and eye irritation, and skin sensitization). Based on data presented by the Sponsor country, adequate risk management measures are being applied, exposure to humans and the environment is anticipated to be low, and therefore this chemical is currently a low priority for further work.

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I U C L I D

Data Set

Existing Chemical	:	ID: 919-30-2
CAS No.	:	919-30-2
EINECS Name	:	3-aminopropyltriethoxysilane
EC No.	:	213-048-4
Molecular Formula	:	C9H23NO3Si

Producer related part

Company	:	Epona Associates, LLC
Creation date	:	16.06.2003

Substance related part

Company	:	Epona Associates, LLC
Creation date	:	16.06.2003
Status	:	
Memo	:	SEHSC
Printing date	:	08.03.2004
Revision date	:	
Date of last update	:	08.03.2004
Number of pages	:	1
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

30.07.2003

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	**:**	CCO[Si](CCCN)(OCC)OCC
Molecular formula	**:**	C9H23NO3Si
Molecular weight	**:**	221
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	**:**	
Odour	**:**	

26.06.2003

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

(.gamma.-Aminopropyl)triethoxysilane

17.06.2003

(3-Aminopropyl)triethoxysilane

17.06.2003

1-Propanamine, 3-(triethoxysilyl)-

17.06.2003

3-(Triethoxysilyl)-1-propanamine

17.06.2003

3-(Triethoxysilyl)propylamine

17.06.2003

A-1100

17.06.2003

A-1112

17.06.2003

AGM 9 (VAN)

17.06.2003

APTES

07.01.2004

NUCA 1100

17.06.2003

Propylamine, 3-(triethoxysilyl)-

17.06.2003

Silane 1100

17.06.2003

Silane, (.gamma.-aminopropyl)triethoxy-

17.06.2003

Silane, (3-aminopropyl)triethoxy-

17.06.2003

Silicone A-1100

17.06.2003

Triethoxy(3-aminopropyl)silane

17.06.2003

UC-A 1100

17.06.2003

1.3 IMPURITIES

Purity	:	typical for marketed substance
CAS-No	:	78-93-3
EC-No	:	
EINECS-Name	:	2-Butanone
Molecular formula	:	
Value	:	= 0 - 2 % v/v

26.06.2003

Purity	:	typical for marketed substance
CAS-No	:	64-17-5
EC-No	:	200-578-6
EINECS-Name	:	ethanol
Molecular formula	:	
Value	:	= 0 - 1 % v/v

26.06.2003

Purity	:	typical for marketed substance
CAS-No	:	
EC-No	:	
EINECS-Name	:	Dibenzoyl peroxide
Molecular formula	:	
Value	:	= 0 - 1 % v/v

26.06.2003

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity	:	= 1992.221 - tonnes in 2002
Remark	:	The production volume provided reflects the Sponsor countries production and use. APTES is produced in North America, Europe and Asia.
Source	:	Lesser Ketones Manufacturing Association Leesburg, VA
Flag	:	confidential

07.01.2004

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : use
Category :

Remark : The commercial uses of this material are numerous and include various applications as coupling agents and adhesion promoters in fiberglass, adhesives and sealants, foundry resins, and in pre-treatment for coatings. A small percentage of this material may be found in sealants and coatings. Generally, APTES is used by the processor/formulator as an adhesion promoter with use levels <1%. In some applications, APTES is used as a crosslinker; these use levels are higher and can approach 3 to 5 %. Once APTES is added to a consumer or industrial product, the parent silane reacts 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 into the polymer matrix and no longer exists and greatly reduces potential for consumer or worker exposure. APTES polymerizes during use.
07.01.2004

Type of use : industrial
Category : other

Remark :

	Metric Tons	Percent
Use resulting in inclusion into or onto matrix	1835.576	92.14
Nondispersive Use	129.881	6.52
Other (Unknown)	26.764	1.34
Tota		

Source : Lesser Ketones Manufacturing Association Leesburg, VA
Flag : confidential
02.05.2003

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	Percent
Chemical industry: chemicals used in synthesis;	369.019	18.52
Polymers industry;	598.884	30.06
Textile processing industry;	734.846	36.89
Paints, lacquers and varnishes industry;	238.272	11.96
Other (Unknown)	51.200	2.57
Total	1992.221	100.00

Use Category:

Use Category:	Metric Tons	Percent
Adhesive, binding agents;	1828.997	91.81
Intermediates;	100.173	5.03
Surface-active agents;	36.287	1.82
Other (Unknown)	26.764	1.34
Total	1992.221	100.00

Source **:** Lesser Ketones Manufacturing Association Leesburg, VA 07.05.2003

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 of the consumer/bystander
Exposure to the : Substance

Remark : The use of APTES into the consumer market is limited; it is used in caulks as well as coatings (for example, paint for outdoor furniture). The substance is used at generally <1% in these formulations. Once added to the formulation, the final product will contain generally 0.1-0.2% parent silane; the remainder of the added substance will have reacted with the other components of the formation and is no longer present. After curing the parent silane is consumed into the polymer matrix and no longer exists, eliminating the potential for consumer exposure. In a final consumer product that utilizes an industrial sealant or coating, the inherent retention of the material is extremely low to the dual reactivity (both hydrolysis and curing). The curing time will vary among applications. Dermal exposure is a potential route for consumers. However, after curing the parent silane is consumed into the polymer matrix and no longer exists; this greatly reduces the potential for consumer exposure.

07.01.2004

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

Remark : 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 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 open systems. Transport is a source of potential exposure through accidental releases. This material is shipped via road and marine in drums, cans, pails, and returnable intermediate bulk containers (IBCs). Air shipment follows IATA Regulations and is limited to 1 Liter maximum for passenger aircraft and 30 Liter maximum cargo only. Drums and IBCs are not shipped by air.

07.01.2004

Source of exposure : Human: exposure of the operator by intended use
Exposure to the : Substance

Remark : A worker may be exposed at the customer level to very low levels (generally <1%) of the silane during the preparation of the coating, sealant, etc. and to a much less extent, during its use in the final product. The low final percentage in the product (generally 0.1-0.2%) reflects the fact that this material is designed to be reactive and to not survive the application processing at the customer level. Potential routes of exposure for workers include dermal contact, although the MSDS properly warns against contact with the skin. There is no known production process that involves aerosolized material or sprayed material. Customers who manufacture treated fillers may spray the silane onto the filler. In coatings that are applied by spraying, very low levels of free silane may be present (generally 0.1-0.2%). In a spray application (for example, for a coating), the material sprayed is a pre-polymer of a silane at a very low concentration (again, generally 0.1-0.2%). No free parent silane would be available for aerosol inhalation. The vapour pressure of this material is low enough that vapour inhalation is not considered a potential route of exposure.
As for occupational/facility level releases, the exposures will be low due to the rapid hydrolysis of the material. Customers go to great lengths to

minimize loss due to the reactive nature of the material, which is necessary in order to ensure accurate formulations. Producers maintain and track the safety record of use of this material at the customer level. In circumstances where an accidental release occurs, the producer often works with the customer to implement additional safety measures. Production and customer use have a long safety history.

07.01.2004

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.

07.01.2004

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

Remark : The commercial uses of this material are numerous and include various applications as coupling agents and adhesion promoters in fiberglass, adhesives and sealants, foundry resins, and in pre-treatment for coatings. A small percentage of this material may be found in sealants and coatings. 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 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. APTES is transported from the production site as the parent silane to processors/formulators. Generally, APTES is used by the processor/formulator as an adhesion promoter with use levels <1%. In some applications, APTES is used as a crosslinker; these use levels are higher and can approach 3 to 5 %. Once APTES is added to a consumer or industrial product, the parent silane reacts 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 into the polymer matrix and no longer exists and greatly reduces potential for consumer or worker exposure. APTES polymerizes during use.

07.01.2004

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= -70 °C
Sublimation	:	
Method	:	
Year	:	2000
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Test substance	:	Silquest A-1100 silane is Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

07.01.2004 (48)

2.2 BOILING POINT

Value	:	= 223 °C at 1013 hPa
Decomposition	:	ambiguous
Method	:	other
Year	:	1975
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	other calculated
Remark	:	Supporting Data: · Extrapolated boiling point of 220°C @ 101.3 kPa. Ditsent, V.E., I.I. Skorokhodov, N.A. Terent'eva, M.N. Zolotareva, Z.V. Belyakova, and Z.V. Belikova. 1976. Saturated vapor pressure of gamma-aminopropyltriethoxysilane. Zh. Fiz. Khim. 50(7):1905-1906. · Reported boiling point of 217°C @ 101.3 kPa. Dictionary of Organic Compounds, 5th Ed. 1982. Buckingham, J.; Editor. Chapman and Hall, New York, N. Y., USA. 7840 pp. · Reported boiling point of 221°C @ 101.3 kPa. Handbook of Organosilicon Compounds: Advances Since 1961, Vol. 2. 1973. Bazant, V., V. Chvalovsky; and J. Rathousky, Editors. Dekker, New York, N. Y., USA. 619 pp. · Reported boiling point of 220°C @ 101.3 kPa. General Electric, physical properties database.
Result	:	The Antoine vapor pressure correlation coefficients used to calculate the boiling point (equation provided in the abstract) were obtained by regression of measured data. However, the translated abstract does not provide the data used to derive the Antoine coefficients and does not identify the temperature range over which vapor pressures were measured. The table below summarizes the vapor pressure data available in the published literature and compares the measured values to the values calculated using the Antoine vapor pressure correlation.

Temp. (C)	Vapor Pressure (mm Hg) measured	calculated	Deviation (%)	Reference
55.0	1	0	52	Albarino et.al., (1973)

	110.5	10	16	-56	Belyakova et.al. (1972)
	115.0	19	19	-2	Speier et.al. (1971)
	120.5	29	25	14	Klyuchnikov et.al. (1970)
	122.0	28	27	4	Fialova et al. (1973)

Source : Lesser Ketones Manufacturing Association Leesburg, VA
Test condition : This robust summary is based upon a manuscript published in a Russian journal. The English translation of the abstract for the manuscript indicates that the temperature dependence of vapor pressure for the test substance (CAS No. 919-30-2) was determined by isoteniscopic and ebullioscopic methods. Test conditions were not specified.
Test substance : 3-aminopropyl-triethoxysilane (CAS No. 919-30-2)
Conclusion : Vapor pressures calculated using the Antoine equation used to generate the boiling point of the test substance (CAS No. 919-30-2) are generally in good agreement with independently measured data. However, serious error may result if the Antoine vapor pressure correlation is used for extrapolations outside the limits of measured data. Hence, significant error may be associated with the reported boiling point for the test substance (CAS 919-30-2). Nonetheless, the result is comparable to values obtained from the literature and other studies (see Supporting Data).
Reliability : (2) valid with restrictions
This robust summary is based upon an English translation of an abstract for a manuscript published in a Russian journal. The abstract provides the Antoine vapor pressure correlation. However, the vapor pressure data used to generate the Antoine coefficients and the methods used to obtain the data are not provided. Consequently, the reliability of the data or the calculated boiling point are with restriction.

07.01.2004 (1) (3) (4) (28) (39) (53)

2.3 DENSITY

Type : relative density
Value : = .95 at 25 °C
Method :
Year : 2000
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Epona Associates, LLC
Test substance : Silquest A-1100 silane is Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability : (2) valid with restrictions

07.01.2004 (48)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .02 hPa at 20 °C
Decomposition :
Method : other (calculated)
Year : 2003

GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : The relationship between temperature and vapor pressure can be expressed by the equations:

(1) Log P = a + b * Log T + c/T or
(2) Log P = m/T + n

where: a, b, c, m, n are constants derived form measured data.

The above constants for APTES were derived for equation (1) by Ditsent et al (1976) and for equation (2) by Bragin and Karapetyants (1975). However, the translated Russian abstracts from which the information was obtained reported only the constants and did not report the data used to derive the constants. The extrapolated vapor pressures at 20 and 25 ºC for APTES based on these two publications are shown below:

	Ditsent	Bragin
T (ºC)	P (Pa)	P (Pa)
25.0	13	4
20.0	8	2

Vapor pressure of APTES has also been reported over a temperature range of 55-122 ºC. The reported temperatures were entered into the above equations and the resulting estimated values of P compared to the reported measured values of P to determine which equation provided the best estimate. Based on this comparison, equation 2 was identified as the best and vapor pressures of 2 Pa @ 20 deg C of 4 Pa @ 25 deg C as the best values for the fugacity calculations.

Serious error may result if the Antoine vapor pressure correlation is used for extrapolation outside the limits of measured data. Comparison of the extrapolated and measured vapor pressure at 55 ºC (133 Pa; Albarino et. al. 1973) indicates that the extrapolated value may be underestimated by 12 to 52% or more.

Source : Dow Corning Corporation
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
16.01.2004 (4) (22)

Value : = .02 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year : 2003
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Vapor pressure (Pa)= 2.0 (Extrapolated from temperature-vapor pressure correlation.

Vapor pressure of 3-aminopropyltriethoxysilane at 25 °C
was extrapolated from a temperature-vapor pressure relationship that was developed using experimental data measured at temperatures ranging from 55-122 °C.

Source : Epona Associates, LLC
Reliability : (2) valid with restrictions
07.01.2004 (41)

Value : = .02 hPa at 20 °C
Decomposition : ambiguous
Method : other (calculated)
Year : 1975
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : The following table summarizes the vapor pressure data available in the published literature and compares the measured values to values calculated using temperature-vapor pressure correlation provided in the abstract.

Temp. (deg C)	Vapor Pressure (Pa) measured	calculated	Deviation (%)	Reference
55.0	133	118	12	Albarino et. al., (1973)
110.5	1333	2522	-89	Belyakova et al. (1972)
115.0	2533	3091	-22	Speier et al. (1971)
120.5	3866	3932	-2	Klyuchnikov et al. (1970)
122.0	3732	4193	-12	Fialova et al. (1973)

Result : The Antoine vapor pressure correlation coefficients used to calculate the vapor pressure at 20°C (equation provided in the abstract) were obtained by regression of measured data. However, the translated abstract does not provide the data used to derive the Antoine coefficients and does not identify the temperature range over which the vapor pressures were measured. The following table summarizes the vapor pressure data available in the published literature and compares the measured values to values calculated using the Antoine vapor pressure correlation.

Temp. (C)	Vapor Pressure (Pa) measured	calculated	Deviation (%)	Reference
55.0	133	64	52	Albarino et. al., (1973)
110.5	1333	2074	-56	Belyakova et al. (1972)
115.0	2533	2581	-2	Speier et al. (1971)
120.5	3866	3336	14	Klyuchnikov et al. (1970)
122.0	3732	3574	4	Fialova et al. (1973)

Source : Lesser Ketones Manufacturing Association Leesburg, VA
Test condition : This robust summary is based upon a manuscript published in a Russian journal. The English translation of the abstract for the manuscript indicates that the temperature dependence of vapor pressure for the test substance (CAS No. 919-30-2) was determined by isoteniscopic and ebullioscopic methods. Test conditions were not specified.
Test substance : 3-aminopropyl-triethoxysilane (CAS No. 919-30-2)
Conclusion Vapor pressures of the test substance (CAS No. 919-30-2) calculated using the Antoine equation are generally in agreement with independently measured data. However, serious error may result if the Antoine vapor pressure correlation is used for extrapolations outside the limits of measured data. Hence, significant error may be associated with the reported vapor pressure of the test substance (CAS No. 919-30-2) at 20°C. Nonetheless, the result is comparable to values obtained from the literature.
Reliability : (2) valid with restrictions
This robust summary is based upon an English translation of an abstract for a manuscript published in a Russian journal. The abstract provides the Antoine vapor pressure correlation. However, the vapor pressure data used to generate the Antoine coefficients and the methods used to obtain the data are not provided. Consequently, the

reliability of the data or the calculated vapor pressure at 20°C is with restrictions.

07.01.2004 (1) (3) (4) (28) (39) (53)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= .31 at °C
pH value	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Log Kow = 0.31 (Est. value) Log Kow of 3-aminopropyltriethoxysilane at 25 °C was estimated using the SAR Model KOWWIN® (version 1.66). The EQC Level III model (USEPA, 2000) was used to evaluate the fate, transport and distribution of this material between environmental matrices, as recommended by EPA. However, this material is unlikely to be found in the environment as it is hydrolytically unstable.
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

07.01.2004 (5) (41)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= .00008 g/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	no
Deg. product	:	
Method	:	other: estimated
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The EQC Level III model (USEPA, 2000) was used to evaluate the fate, transport and distribution of this material between environmental matrices, as recommended by EPA. However, this material is unlikely to be found in the environment as it is hydrolytically unstable. The water solubility of the triol (hydrolysis product) cannot be measured because at relatively low concentrations (a few hundred ppm), the silanol will start to condense. If a water solubility were estimated from a modelling program, it is likely it would be in the % range. At some concentration it will form a precipitate [resin (condensate)]. Water solubility (g/m3)=7.6x-105 (Est.value) Water solubility of 3-aminopropyltriethoxysilane at 25 °C was estimated using the SAR Model WSKOWWIN® (version 1.40).
Source	:	Epona Associates, LLC

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
07.01.2004 (41)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = 96 °C
Type : closed cup
Method : other: Pensky-Martens closed cup ASTM D 93
Year : 2000
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Epona Associates, LLC
Test substance : Silquest A-1100 silane is Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability : (2) valid with restrictions
07.01.2004 (48)

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
Conc. of substance	:	at 25 °C
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= .2 day(s)
Degradation	:	% after
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	
Conc. of sensitizer	:	
Rate constant	:	= .000000000052881 cm³/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (calculated): EpiWin
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : Atmospheric Oxidation (25 deg C) [AopWin v1.91]

Remark : Photodegradation as a mode of removal is unlikely as APTES is hydrolytically unstable. Photodegradation is not predicted to be a significant degradation process in the aquatic environment due to the rapid rate of hydrolysis. The vapor pressure indicates that APTES resides in the atmosphere and may undergo photodegradation due to ozone and/or hydroxyl radicals. . However, because of the rapid hydrolysis of this material with moisture in the atmosphere, photolysis in the atmosphere is not predicted to take place. The parent silane contains no chromaphors that would absorb visible or UV radiation so no direct photolysis reactions are predicted. The trisilanol resulting from hydrolysis in the atmosphere is similarly not predicted to undergo direct photolysis but could react with hydroxyl radicals or ozone.

Result : Atmospheric Oxidation (25 deg C) [AopWin v1.91]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 52.8810 E-12 cm3/molecule-sec
Half-Life = 0.202 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 2.427 Hrs

Source : Epona Associates, LLC

Reliability : (2) valid with restrictions

05.08.2003 (56)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	= .4 hour(s) at 24.7 °C
t1/2 pH7	:	= 8.4 hour(s) at 24.7 °C
t1/2 pH9	:	= .2 hour(s) at 24.7 °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 835.2130

Remark : APTES is hydrolytically unstable (t1/2 < 1 hour) over a range of environmentally relevant pH and temperature conditions, with the exception of pH7 at 10 or 24.7 deg C. At pH 7, the half-life is 56 or 8.4 hours, for 10 or 24.7 deg C, respectively. Rapid hydrolysis of this material produces ethanol and trisilanols. The Si-C bond will not further hydrolyze. That bond is hydrolytically stable and the aminopropyl group will not be cleaved. Only the ethoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield aminopropyl-functional resins. The study described was not designed to monitor the subsequent condensation reaction involving the silanetriol hydrolysis product. Evidence for this process, including the appearance of additional chromatographic peaks or unexplained changes in analytical response for the silanetriol, was not observed on the timescale of the hydrolysis experiments.

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

pH	4.7	7.0	9.0
t1/2 (hours) @			
10.0 °C:	0.97	56	0.78
24.7 °C:	0.41	8.4	0.15
37.0 °C:	0.22	3.9	0.043

Table 1. Kinetic Constants for Hydronium, Hydroxide, and Solvent (H2O) Catalyzed Hydrolysis Reactions of 3-aminopropyl-triethoxysilane at 24.7 °C.

Constant (units)	1st hydrolysis step	2nd step	3rd step
kH3O+ (M-1 s-1)	23.1	70.3	180
k-OH (M-1 s-1)	127	1130	NA(a)
k0, est. (s-1)	8x10-6	NA(b)	NA(b)

(a) Final hydrolysis reaction step too rapid to measure quantitatively.
(b) Kinetic data not sufficiently precise to yield reliable estimate.

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 ethanol co-product was not considered, but is probably stable under these conditions.

Source : Lesser Ketones Manufacturing Association Leesburg, VA

Test condition : The consecutive hydrolysis reactions 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 : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

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.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
08.01.2004 (45)

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 : 99.8 % (Fugacity Model Level I)
Soil : .2 % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: calculated
Year : 2002

Method : The EQC model (Mackay 1996) 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.

The EQC Level III model (USEPA, 2000) was used to evaluate the fate, transport and distribution of this material between environmental matrices, as recommended by EPA. However, this material is unlikely to be found in the environment as it is hydrolytically unstable.

Result : The EQC Level III model (USEPA, 2000) was used to evaluate the fate, transport and distribution of this material between environmental matrices, as recommended by EPA. Level III Fugacity modeling, using loading rates for Air, Soil, and Water of 1000 kg/h for each media, shows the following percent distribution: Air = 0.7%; Soil = 91.6%; Water = 7.7 %; Sediment = 0.00 %. However, this material is unlikely to be found in the environment as it is hydrolytically unstable.

Results from LEvel II modeling indiacte distribution to air, water and soil of 0, 99.8 and .2%, respectively.

Table 1. Physical and chemical properties of 3-aminopropyltriethoxysilane (CAS No. 919-30-2).

Molecular weight = 221
Data temperature (°C)= 25
Water solubility (g/m3)=7.6x-105 (Est.value Note1) (ref3)
Vapor pressure (Pa)= 2.0 (Extrapolated from temperature-vapor pressure correlation Note2)
Log Kow = 0.31 (Est. value Note3)
Melting point (°C)= -70 (ref4)
Half-life in air (h)=2.4 (Est. value Note4)
Half-life in water (h)= 8.4 (Measured at pH 7.0, 25 °C) (ref5)
Half-life in soil (h)=80 (Est. value Note5)
Half-life in sediment(h)=8.4 (Est. value Note5)

Note1 Water solubility of 3-aminopropyltriethoxysilane at 25 °C was estimated using the SAR Model WSKOWWIN® (version 1.40). The model was used as received from the EPA.
Note2 Vapor pressure of 3-aminopropyltriethoxysilane at 25 °C was extrapolated from a temperature-vapor pressure relationship that was developed using experimental data measured at temperatures ranging from 55-122 °C.
Note3 Log Kow of 3-aminopropyltriethoxysilane at 25 °C was estimated using the SAR Model KOWWIN® (version 1.66). The model was used as received from the EPA.
Note4 The half-life in air of 3-aminopropyltriethoxysilane at 25 °C was estimated using the SAR Model APOWIN® (version 1.90). The model was used as received from the EPA.
Note5 The overall half-life of 3-aminopropyltriethoxysilane 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 4.00), as received from the EPA. The BIOWIN result for ultimate biodegradation timeframe (2.7344; "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.

The measured hydrolysis half-life for 3-aminopropyltriethoxysilane at pH 7.0 is 8.4 hours at 25 °C. As such, 3-aminopropyltriethoxysilane will not exist in the environment, but will rapidly hydrolyze to ethanol and 3-aminopropylsilanetriol. The environmental fate, transport, and distribution of 3-aminopropylsilanetriol were evaluated to provide a more realistic assessment of 3-aminopropyltriethoxysilane. Results from the simulation suggest that >99% of the total steady-state mass of 3-aminopropylsilanetriol will reside in the water and soil compartments, and will not be found in air or sediment. It is expected taht 65-85% of the 3-aminopropylsilanetriol produced by the steady-state hydrolysis of 3-aminopropyltriethoxysilane will degrade in about 20-40 days.

Source : Epona Associates, LLC
Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Upon contact with water or water vapor, 3-aminopropyltriethoxysilane generates ethanol and the

corresponding silanol, 3-aminopropylsilanetriol. Depending upon concentration, 3-aminopropyl-silanetriol will condense to form a highly cross-linked polymeric gel.

Conclusion : If released directly to air, about 40% of the steady-state emission is expected to degrade in air, 50% expected to partition to and degrade in soil, and 6% expected to partition to and degrade in water. When released to soil, 90% of the steady-state emission is expected to degrade in soil, and 10% expected to partition to and degrade in water. When released to water, essentially 100% will degrade in water. Advection from the local environment is expected to be insignificant (£ 1% of the steady-state emission) for all emission scenarios. Global persistence of 3-aminopropyltriethoxysilane in the model system was about 3 days when released directly to air, about 5 days when released to 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 3 days. Based on Level-III modeling, it is expected that > 99% of the total steady-state mass of 3-aminopropyltriethoxysilane will reside in the water and soil compartments and will not be found in air or sediment.

Reliability : (2) valid 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
05.08.2003 (4) (40) (41) (43) (56)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	domestic sewage
Contact time	:	28 day(s)
Degradation	:	= 67 (±) % after 28 day(s)
Result	:	other: not readily biodegradable
Control substance	:	Benzoic acid, sodium salt
Kinetic	:	28 day(s) > 96 % %
Deg. product	:	yes
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

Remark : Note that hydrolysis of this material occurs rapidly, such that the observed biodegradation is of the hydrolysis products (ethanol and trisilanols).

Result	:	Degradation % after time: Duplicates run with test article. Flask 1: Percent degradation after 0, 7, 14, 21, 27 and 28 days was 0, 63, 67, 69, 76, and 68%, respectively. Flask 2: Percent degradation after 0, 7, 14, 21, 27 and 28 days was 0, 64, 65, 67, 82, and 65%, respectively. Results: Mean percent degradation for test article: 0, 63, 66, 68, 79 and 67% after days 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. For the negative control, % degradation was not calculated, but raw data indicates no degradation at any of the time periods measured. Breakdown products (yes/no): Not analytically verified. However, the test material is known to be hydrolytically unstable. When added to water, the test material rapidly hydrolyzes, generating ethanol and transient silanetriol derivatives which will crosslink. Not readily biodegradable
Source	:	Degussa
Test substance	:	3-Aminopropyl-triethoxysilane 919-30-2
Conclusion	:	DYNASYLAN AMEO achieved a breakdown rate of 67%(DOC reduction) within 28 days. Based on these findings, DYNASYLAN AMEO was determined to be "not readily biodegradable". The control substance, sodium benzoate, achieved a breakdown rate of 98% within 10 days and 100% degradation after 28 days demonstrating acceptable activity of the biologic culture.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

07.01.2004 (32)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Elimination	:	
Method	:	other
Year	:	2003
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 ethanol and trisilanols. The Si-C bond will not further hydrolyze. That bond is hydrolytically stable and the aminopropyl group will not by cleaved. Only the ethoxy groups will be hydrolyzed. The transient silanol groups will condense with other silanols to yield: R-Si(OR')3 type resins where R = CH2CH2CH2NH2 and R' = either H or Si(R)(OR')

In other words, aminopropyl-functional resins are generated.

If the silane is slowly released such that the concentration of the resulting aminopropyl-functional silanetriol is not high enough to result in polymerization, the trisilanol will exist largely as the 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 can not be measured because of the tendency to condense at concentrations greater than 500 ppm. 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.

Source **:** Epona Associates, LLC
08.01.2004 (44)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	semistatic
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	>= 934
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	DIN 38412 Part 1; EG Guideline 92/69 C.1; OECD Guideline 203, 1984
Remark	:	In spill conditions, the concentration of the parent silane is very high. The silanols concentration could also be high; however, the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. These polymers will not be bioavailable. However, such materials are likely to cause toxicity in aquatic species due to physical effects (encapsulation, blockage of gills). Since APTES 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 ethanol and trisilanols. This material is sensitive to hydrolysis, which may occur during preparation of the dosing solutions and/or during the testing. Rapid hydrolysis of this material produces ethanol and trisilanols. In spill conditions, the concentration of the parent silane is very high. The resulting silanol concentration is also high and the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000. As the parent silane and the resulting silanol is diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low MW oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. An SEHSC member company has provided these results from an internal study on the equilibrium of methylsilanetriol in water. The methylsilanetriol was formed from methyltrimethoxysilane. It is in equilibrium with the dimer, trimer and other higher oligomers depending on the concentration of the starting methyltrimethoxysilane solution. Based on the equilibrium constants derived from the study, it was calculated that a 1000 ppm solution of methyltrimethoxysilane in water will form an equilibrium solution

of roughly 860 ppm silanol monomer and 140ppm silanol dimer.

Due to the insolubility in water of the higher MW oligomers and polymers, testing of such materials is not anticipated. These polymers will not be bioavailable. Such materials are also likely to cause toxicity due to physical effects (encapsulation, blockage of gills). Ecotoxicity of the silanols may be predicted using modeling programs such as ECOSAR.

In spill conditions, the concentration of the parent silane is very high. The silanols concentration could also be high; however, the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. These polymers will not be bioavailable. However, such materials are likely to cause toxicity in aquatic species due to physical effects (encapsulation, blockage of gills). Since APTES 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 ethanol and trisilanols.

Result **:**
- Biological observations: None reported
- Table showing cumulative mortality: No mortality in treated or control fish
- Lowest test substance concentration causing 100% mortality: NA
- Mortality of controls: 0%
- Abnormal responses: None reported
- Any observations, such as precipitation that might cause a difference between measured and nominal values: When the results are interpreted, one must consider that DYNASYLAN AMEO (99.0 fluid % CAS No. 919-30-2) is sensitive to hydrolysis, and that it hydrolyzes either during preparation of the initial batch or during the testing interval. Measured concentrations: 880 mg/l at 0 hours; 922/947 mg/l at 24 hours; 885 mg/l at 72 hours; average value of 943 mg/l (water filtered initial solution).

Source **:** Degussa

Test condition **:** ·Additional Description of Test Conditions:

Dilution of the test substance included the following: The hard-to-dissolve tested substance was added to tap water to provide a concentration of 1g/l and stirred for 18 hours. The solution was filtered and the TOC content determined. This solution serves as the primary dilution of the test substance. The test began immediately after preparation of the test solution. The nominal test material concentration was 1000 mg/l.

The test included one control and one test chamber in replicate. The pH values ranged from 7.8 to 8.4 units in the controls and 8.2 to 9.3 units in the test chambers. The DO values ranged from 8.0 to 8.9 mg/L in the controls and 7.8 to 9.0 mg/L in the test chambers. All chambers were maintained at 20 to 21o C and water hardness was 18 mg/L as CaCO3. Background TOC was determined to be 6 mg/L.

Analytical control of test substance concentrations was performed using carbon determination on a TOC-500 Infrared Analyzer.

Test substance : DYNALYLAN AMEO 99.0 weight %
Gamma-Aminopropyltriethoxysilane (CAS No. 919-30-2)
Hydrolytically unstable material (half-life in water < 5 hr)

Conclusion : 96 hour LC0 > 934 mg/L (all concentrations are with respect to the material). One must consider that DYNASYLAN AMEO (99.0 fluid % CAS No. 919-30-2) is sensitive to hydrolysis, and that it hydrolyzes either during preparation of the initial batch or during the testing interval.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

19.01.2004 (35)

Type :
Species :
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 48016
Method : other:ECOSAR
Year : 2003
GLP : no
Test substance : other TS:Aliphatic Amines

Method : SMILES : NCCC[Si](O)(O)(O)
CHEM :
CAS Num:
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C3 H11 N1 O3 Si1
MOL WT : 137.21
Log Kow: -2.85 (KowWin estimate)
Melt Pt:
Wat Sol: 5.4E+007 mg/L (calculated)

ECOSAR Class(es) Found

Aliphatic Amines

Remark : Given the rapid hydrolysis of this substance, the available aquatic toxicity tests are likely to reflect the toxicity of the degradation products. The toxicity of the possible trisilanol degradation products was estimated (the alcohol degradation products are unlikely to contribute significantly to the toxicity at the concentrations tested). An estimate of the possible toxicity of a likely trisilanol degradation product for this substance using the ECOSAR program is provided.

There will be a large uncertainty associated with these estimates, but they do show that the hydrolysis product is likely to have a reasonably low toxicity and are reasonably consistent with the actual toxicity data reported for the substance.

Result :

ECOSAR	Organism	Duration	End Pt	Predicted mg/L (ppm)
Aliphatic Amines:	Fish	96-hr	LC50	48016.563

Source : UK Environment (2003) Comments Posted on EDG for 3-

Aminopropyltriethoxysilane CAS No. 919-30-2

Reliability : (2) valid with restrictions
07.01.2004 (27)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= 94
EC50	:	= 331
Analytical monitoring	:	no data
Method	:	OECD Guide-line 202
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : DIN 38412 Part 1; EG Guideline 92/69/EWG

Remark : In spill conditions, the concentration of the parent silane is very high. The silanols concentration could also be high; however, the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. These polymers will not be bioavailable. However, such materials are likely to cause toxicity in aquatic species due to physical effects (encapsulation, blockage of gills). Since APTES 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 ethanol and trisilanols.
This material is sensitive to hydrolysis, which may occur during preparation of the dosing solutions and/or during the testing. Rapid hydrolysis of this material produces ethanol and trisilanols.

In spill conditions, the concentration of the parent silane is very high. The resulting silanol concentration is also high and the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000.

As the parent silane and the resulting silanol is diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low MW oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. An SEHSC member company has provided these results from an internal study on the equilibrium of methylsilanetriol in water. The methylsilanetriol was formed from methyltrimethoxysilane. It is in equilibrium with the dimer, trimer and other higher oligomers depending on the concentration of the starting methyltrimethoxysilane solution. Based on the equilibrium

constants derived from the study, it was calculated that a 1000 ppm solution of methyltrimethoxysilane in water will form an equilibrium solution of roughly 860 ppm silanol monomer and 140ppm silanol dimer.

Due to the insolubility in water of the higher MW oligomers and polymers, testing of such materials is not anticipated. These polymers will not be bioavailable. Such materials are also likely to cause toxicity due to physical effects (encapsulation, blockage of gills). Ecotoxicity of the silanols may be predicted using modeling programs such as ECOSAR.

In spill conditions, the concentration of the parent silane is very high. The silanols concentration could also be high; however, the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. These polymers will not be bioavailable. However, such materials are likely to cause toxicity in aquatic species due to physical effects (encapsulation, blockage of gills). Since APTES 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 ethanol and trisilanols.

Result **:** Biological observations:

· Number immobilized as compared to the number exposed: At concentrations 0, 8.7, 16.4, 28.4, 54.7, 94.0, 174.9, 306.0, 546.5, and 983.7 mg/L, the following % of immobilized individuals was reported at 24 hours: 0, 0, 5, 0, 0, 5, 19, 45, 40, and 62%, respectively, and the following % of immobilized individuals was reported at 48 hours: 0, 0, 5, 0, 0, 0, 10, 19, 50, 60, and 100%.

· Concentration response with 95% confidence limits: 24 hour EC50 values = 592 mg/L (95% confidence limits: 349-1003 mg/L); 48 hour EC50 = 331 mg/L (95% confidence limits: 249-441 mg/L)

· Cumulative immobilization: After 48 hours, the highest concentration for which no immobilization occurred (< 10%) was 94 mg/L. After 48 hours, the lowest concentration for which 100% immobilization occurred was 983.7 mg/L.

· Was control response satisfactory (yes/no/unknown): Yes

When the results are interpreted, one must consider that DYNASYLAN AMEO (99.0 fluid % CAS No. 919-30-2) is sensitive to hydrolysis, and that it hydrolyzes either during preparation of the initial batch or during the testing interval.

Source **:** Degussa

Test condition **:** The hard-to-dissolve tested substance was added to tap water to provide a concentration of 1g/l and stirred for 18 hours. The solution was filtered and the TOC content determined. This solution serves as the primary dilution of the test substance. The test began immediately after preparation of the test solution.

·Additional Description of Test Conditions: The test vessels were glass cylinders graduated to 10 ml. Each concentration had 4 replicate vessels and each vessel contained 5 test organisms. The age of the test organisms was <24 hours and they were not fed during the test.

Vessels were kept in the dark at 20o C and not aerated during the test.

The control pH was 7.5 units and the test vessel pH ranged from 7.5 to 8.7 units. The control DO was 8.4 mg/L and the test vessel DO ranged from 7.8 to 8.7 mg/L. Water hardness was reported as 2.5mmol/L and alkalinity was reported as 0.8 mmol/L. Background TOC was <1 mg/L.

Nominal concentrations in mg/L: 0, 8.7, 16.4, 28.4, 54.7, 94.0, 174.9, 306.0, 546.5, and 983.7 mg/L.

Test substance : DYNALYLAN AMEO: purity 99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : 24 hour EC50 values = 592 mg/L (95% confidence limits: 349-1003 mg/L); 48 hour EC50 = 331 mg/L (95% confidence limits: 249-441 mg/L). All concentrations are with respect to the material.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

19.01.2004 (34)

Type :

Species :

Exposure period : 48 hour(s)

Unit : mg/l

EC50 : = 1896

Method : other: ECOSAR

Year : 2003

GLP : no

Test substance : other TS: Aliphatic Amines

Method : SMILES : NCCC[Si](O)(O)(O)
CHEM :
CAS Num:
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C3 H11 N1 O3 Si1
MOL WT : 137.21
Log Kow: -2.85 (KowWin estimate)
Melt Pt:
Wat Sol: 5.4E+007 mg/L (calculated)

ECOSAR Class(es) Found

Aliphatic Amines

Remark : Given the rapid hydrolysis of this substance, the available aquatic toxicity tests are likely to reflect the toxicity of the degradation products. The toxicity of the possible trisilanol degradation products was estimated (the alcohol degradation products are unlikely to contribute significantly to the toxicity at the concentrations tested). An estimate of the possible toxicity of a likely trisilanol degradation product for this substance using the ECOSAR program is provided.

There will be a large uncertainty associated with these estimates, but they do show that the hydrolysis product is likely to have a reasonably low toxicity and are reasonably consistent with the actual toxicity data reported for the substance.

Result :

Predicted

	ECOSAR Organism Duration End Pt mg/L (ppm)	
	==========	
	Aliphatic Amines: Daphnia 48-hr LC50 1895.794	
Source	: UK Environment (2003) Comments Posted on EDG for 3-Aminopropyltriethoxysilane CAS No. 919-30-2	
Reliability	: (2) valid with restrictions	
07.01.2004		(27)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	other
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= 1.3
EC10	:	= 38
EC50	:	= 603
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

Method : OECD 201 and Recommended procedure of the ad-hoc working group of the Federal Environment Bureau for development of ecological and toxicological testing procedures in aquatic systems: Suppression of cell reproduction among green alga Scenedesmus subspicatus.

Remark : For the main test 4, as there is no clear dose-response curve, the results were ecluded from the calculation of the NOEC. The EC10 from the main test 2 is more relevant than the NOEC from the main test 4.
In spill conditions, the concentration of the parent silane is very high. The silanols concentration could also be high; however, the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. These polymers will not be bioavailable. However, such materials are likely to cause toxicity in aquatic species due to physical effects (encapsulation, blockage of gills). Since APTES 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 ethanol and trisilanols.
This material is sensitive to hydrolysis, which may occur during preparation of the dosing solutions and/or during the testing. Rapid hydrolysis of this material produces ethanol and trisilanols.

In spill conditions, the concentration of the parent silane is very high. The resulting silanol concentration is also high and the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The

molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000.

As the parent silane and the resulting silanol is diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low MW oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. An SEHSC member company has provided these results from an internal study on the equilibrium of methylsilanetriol in water. The methylsilanetriol was formed from methyltrimethoxysilane. It is in equilibrium with the dimer, trimer and other higher oligomers depending on the concentration of the starting methyltrimethoxysilane solution. Based on the equilibrium constants derived from the study, it was calculated that a 1000 ppm solution of methyltrimethoxysilane in water will form an equilibrium solution of roughly 860 ppm silanol monomer and 140ppm silanol dimer.

Due to the insolubility in water of the higher MW oligomers and polymers, testing of such materials is not anticipated. These polymers will not be bioavailable. Such materials are also likely to cause toxicity due to physical effects (encapsulation, blockage of gills). Ecotoxicity of the silanols may be predicted using modeling programs such as ECOSAR.

In spill conditions, the concentration of the parent silane is very high. The silanols concentration could also be high; however, the silanol rapidly self-condenses to form water insoluble, resinous oligomers and polymers. The molecular weight of the resulting oligomers and polymers is predicted to be over 1000. Anecdotal evidence suggests the molecular weight of the polymers resulting from spills is 5000 - 10000. As the parent silane and the resulting silanol are diluted, it is predicted that the polymers resulting from condensation will be of lower molecular weight. At sufficiently low silanol concentrations, low molecular weight oligomers are favored. It is calculated that at 1000ppm of a related trialkoxysilane, the equilibrium concentration will be 86% silanol monomer and 14% silanol dimer. At still lower concentrations, the silanol will exist as the uncondensed monomer. These polymers will not be bioavailable. However, such materials are likely to cause toxicity in aquatic species due to physical effects (encapsulation, blockage of gills). Since APTES 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 ethanol and trisilanols.
When the results are interpreted, one must consider that DYNASYLAN AMEO (99.0 fluid % CAS No. 919-30-2) is sensitive to hydrolysis, and that it hydrolyzes either during preparation of the initial batch or during the testing interval.

Result **:** The following effective concentrations were reported:
" 72 hour EbC50 = 603 mg/L (on the basis of cell growth);
" A 10% suppression of cell growth (72 hour EbC10) = 38 mg/L;
" (0-72 hour)ErC10 = 321 mg/L (on the basis of growth rate)
NOEC = 1.3 mg/L (on the basis of cell growth) This value is from Main test 4 since an NOEC value was not established in Main test 2. All concentrations are with respect to the material.

Biological observations:
Cell density at each flask at each measuring point:
Main Test 2

	Cell count (*104 cells/ml)			
Conc.(mg/L)	Test interval (h)			
	0 h	24 h	48 h	72 h

Control	2	7	35	115
33	2	6	27	106
67	2	6	27	111
133	2	6	25	105
278	2	5	20	82
556	2	5	15	51
1000	2	5	16	50

*No median values. All concentrations are with respect to the material. Five each and eight each parallels, respectively, were examined. (After 0 h, the theoretical cell concentration was evaluated).

Main Test 4

	Cell count (*104 cells/ml)			
Conc.(mg/L)	Test interval (h)			
	0 h	24 h	48 h	72 h
Control	2	6	23	97
1.3	2	5	23	89
2.5	2	4	18	85
5.1	2	5	19	87
10.1	2	5	19	88

*No median values. All concentrations are with respect to the material.

Growth curves: The EC values are calculated by regression analysis based on [Probit] transformation of the percentage suppression values. These values then serve as the basis for the subsequent [Probit] analysis in accordance with Cavalli-Sforza (1972). The results are presented below.

Effective Concentrations on the Basis of Cell Growth (EbC)

Parameter	mg/L (substance)
(72 h) EbC50	603
(72 h) EbC10	38
(72 h) EbC90	*

* lies above the highest tested concentration

Effective Concentrations on the Basis of Specific Growth Rate µ(ErC)

Parameter	mg/L (substance)
(72 h) ErC50	*
(72 h) ErC10	321
(72 h) ErC90	*

* lies above the highest tested concentration

Percent biomass/growth rate inhibition per concentration:
Main Test 2
Areas under growth curves, growth rates, corresponding percentage suppression rates,
and pH values with respect to test concentrations. (All concentrations are with respect to the material.)

		(mg/L)						
Method		Blind	33	67	133	278	556	1000
Area Under Growth Curve	Area	94.5	81	83.5	78.5	61	40.5	41
	% suppr.		14.3	11.6	16.9	35.4	57.1	56.6
Growth Rate µ (0-72 h)	µ	1.351	1.323	1.339	1.32	1.238	1.08	1.073
	% suppr.		2.1	0.9	2.3	8.4	20.1	20.6

pH values	After 0 h	7.9	8.3	8.4	8.7	8.9	9.1	9.2
	After 72 h	8.6	8.8	9.1	8.8	8.5	8.3	8.4

Main Test 4
Areas under growth curves, growth rates, corresponding percentage suppression rates,
and pH values with respect to test concentrations. (All concentrations are with respect to the material.)

		(mg/L) Blind	1.3	2.5	5.1	10.1
Area Under Growth	Area	72.5	67.5	59.5	52.5	63
	% suppr.		6.9	17.9	13.8	13.1
Curve Growth Rate μ (0-72 h)	μ	1.294	1.265	1.25	1.258	1.261
	% suppr.		2.2	3.4	2.8	2.6
pH values	After 0 h	7.5	7.8	7.8	7.9	8.1
	After 72h	9.0	8.8	8.7	8.7	8.6

Source : Degussa

Test condition : Nominal concentrations in mg/L in Main test 2: 0, 33, 67, 133, 278, 556, and 1000 mg/L.
Nominal concentrations in mg/L in Main test 4: 1.3, 2.5, 5.1, and 10.1.

·Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): The TOC content was determined in the hydrous, filtered initial solution. The TOC content (mg/L) and the substance content (mg/L) in the hydrous, filtered initial solution in Main Test 2 were reported to be 543 mg/L and 1111 mg/L, respectively. The concentrations used in Main Test 2 were calculated from TOC content and included 33, 67, 133, 278, 556, and 1000 mg/L. The TOC content (mg/L) and the substance content (mg/L) in the hydrous, filtered initial solution in Main Test 4 were reported to be 309 mg/L and 632 mg/L, respectively. The concentrations used in Main Test 4 were calculated from TOC content and included 1.3, 2.5, 5.1, and 10.1 mg/L.

·Additional Description of Test Conditions: Dilution of the test substance included the following: The hard-to-dissolve tested substance was added to synthetic fresh water to provide a concentration of 1g/l and stirred for 18 hours. The solution was filtered and the TOC content determined. This solution serves as the primary dilution of the test substance. Subsamples of the primary dilution was added to the algal medium prior to the introduction of the algal suspension.

Background TOC was <1mg/L and the temperature was 24o C.

Analytical monitoring: The TOC content was determined using a TOC-500 Infrared Analyzer in order to establish the content of the substance in the hydrous, filtered initial solution.

Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : The following effective concentrations were reported: On the basis of cell growth, a median concentration is calculated of 72 hour EbC50 = 603 mg/L and

a 10% suppression of cell growth was achieved at 72 hour EbC10 = 38 mg/L; On the basis of growth rate, a 10% suppression of cell growth was achieved at (0-72 hour)ErC10 = 321 mg/L; The NOEC value was 1.3 mg/L (on the basis of cell growth). All concentrations are with respect to the material.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.01.2004 (33)

Species :
Endpoint :
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 670
Method : other: ECOSAR
Year : 2003
GLP : no
Test substance : other TS: Aliphatic Amines

Remark : Given the rapid hydrolysis of this substance, the available aquatic toxicity tests are likely to reflect the toxicity of the degradation products. The toxicity of the possible trisilanol degradation products was estimated (the alcohol degradation products are unlikely to contribute significantly to the toxicity at the concentrations tested). An estimate of the possible toxicity of a likely trisilanol degradation product for this substance using the ECOSAR program is provided.

There will be a large uncertainty associated with these estimates, but they do show that the hydrolysis product is likely to have a reasonably low toxicity and are reasonably consistent with the actual toxicity data reported for the substance.

Result :

Predicted ECOSAR	Organism	Duration	End Pt	mg/L (ppm)
Aliphatic Amines: Algae		96-hr	LC50	670.334

Source : UK Environment (2003) Comments Posted on EDG for 3-Aminopropyltriethoxysilane CAS No. 919-30-2
Reliability : (2) valid with restrictions
07.01.2004 (27)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

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	:	= 1570 - 2830 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: none
Doses	:	4, 2, and 1 g/kg in males; 2, 1.41 and 1 g/kg in females
Method	:	EPA OTS 798.1175
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : Males (5/dose group) were dosed by peroral intubation with 4, 2, and 1 g/kg; females (5/dose group) were dosed by peroral intubation with 2, 1.41, and 1 g/kg; Post dose observation period: 14 days. No microscopic exam was conducted on animals dosed at 1 ml/kg. Kidneys and urinary bladders from 5 animals dosed at 2 ml/kg, and 2 animals dosed at 4 ml/kg were examined histologically.

Remark : Although no GLP Statement is provided in this report, it is assumed that this study was conducted under GLP. Bushy Run Research Center was a certified GLP laboratory during the conduct of this study. This material is a slight to very low acute peroral toxicant in the rat.

Result : Value [LD50 or LC50] with confidence limits if calculated:
males: LD50 with 95% confidence limits = 2.83 (1.61 to 4.98) g/kg
females: LD50 with 95% confidence limits = 1.57 (1.34 to 1.85) g/kg

·Time of death (provide individual animal time if less than 24 hours after dosing):
Number of deaths at each dose level:

	Dose Level(g/kg)	No. of deaths	Days to death
Males	4	4/5	1,2,2,2
	2	1/5	2
	1	0/5	-
Females	2	5/5	2,3,3,3,4
	1.41	1/5	1
	1	0/5	-

·Description, severity, time of onset and duration of clinical signs at each dose level: Signs of toxicity included sluggishness, lacrimation, kyphosis, an unkempt appearance, piloerection (in one), yellow stains on the perigenital fur (positive for blood by HEMASTIX®), red crust on the perinasal and/or periocular fur, brown stain on the perigenital fur, closed eyelids (in one), emaciation (in one), and diarrhea. Survivors recovered at 2 to 9 days.
. Body weight: Body weights were obtained on the day of dosing, and on days 7 and 14 post-dosing. Body weight gains were as follows:

MALES

Dose (ml/kg)	Mean weight (g) day 0	day 7	day 14
4	244	254	283
2	234	251	302
1	238	278	304

FEMALES

Dose (ml/kg)	Mean weight (g) day 0	day 7	day 14
2	223	-	-
1.41	234	251	302
1	211	231	241

·Necropsy findings, included doses affected, severity and number of animals affected: Victims had dark red or mottled lungs, dark red or white stomachs (glandular portion), yellow intestines, stomachs and intestines filled with gas and/or yellow to brown liquid, discolored kidneys (dark red, brown or mottled) and one mottled dark red spleen. No remarkable gross lesions in survivors. Acute tubular necrosis (involving the cortical tubules) and mineralization of the tubular epithelium evident for males (4 g/kg) and females (2 g/kg). Hyperplasia involving the renal tubule epithelium was apparent in 1 of 2 males examined at 2 g/kg. Focal area of epithelial necrosis in the urinary bladder in one male rat (4 g/kg).
The rats that died following dosing (males at 4 ml.kg and males and females at 2 ml/kg) all has evidence of acute necrosis of the proximal convoluted tubules in the renal cortex. The male rats dosed at 2 ml/kg that survived until 14 days following dosing either had no significant renal lesions (1 of 2) or evidence of tubular hyperplasia indicating a reparative response following necrosis.
·Potential target organs (if identified in the report):
kidney

Source : Epona Associates, LLC
Test substance : Silane A-1100: purity: > 96.1%
Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
08.01.2004 (12)

Type : LD50
Value : = 3.65 ml/kg bw
Species : rat
Strain : Wistar
Sex : male/female
Number of animals : 10
Vehicle : water
Doses : 2.5, 3.1, 3.9, 4.5 and 5.0 ml/kg
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1978
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The acute LD50 value with 95% confidence limits calculated by the method of Litchfield and Wilcoxon (1949), J. Pharm. Exp. Therap. 96:99
Result : · Time of death (provide individual animal time if less than 24 hours after dosing): 50% of deaths occurred within 1 hour

of administration at high dose level.

Number of deaths at each dose level:

· Description, severity, time of onset and duration of clinical signs at each dose level: Salivation, ataxia, and lethargy followed by tonic and clonic convulsions within 1 hour of administration at highest dose level. Survivors at 24 hours exhibited severe diarrhoea and diuresis and further deaths occurred up to 72 hours after administration.

Source : Degussa
Test condition : · Age: Young adult, weight 200 + 2g
· Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): 2.5, 3.1, 3.9, 4.5 and 5.0 ml/kg
· Doses per time period: One administration
· Volume administered: 2.5, 3.1, 3.9, 4.5 and 5.0 ml/kg
· Post dose observation period: 14 days
Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion : LD50 value: 3.65 (3.26 - 4.09) ml/kg
Reliability : (2) valid with restrictions
The study was not conducted according to GLPs.

07.01.2004 (18)

Type : LD50
Value : = 3980 mg/kg bw
Species : rat
Strain : no data
Sex : no data
Number of animals : 2
Vehicle : water
Doses : 3.98 g/kg (20% solution in water)
Method : other
Year : 1958
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : No animals died and the material has a low acute oral toxicity. Extensive liver damage was observed at autopsy.
Source : Dow Corning Corporation
Test condition : I. Age: Not reported
II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): 3.98 g/kg (20% solution in water)
III. Volume administered or concentration: Not reported
IV. Post dose observation period: Not reported
V. Exposure duration (for inhalation studies): N.A.
Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability : (3) invalid
The study was not conducted according to GLPs.

08.01.2004 (24)

Type : LD50
Value : = 3700 mg/kg bw
Species :
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Method : other

Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Value [LD50 or LC50] with confidence limits if calculated: Slightly toxic when ingested on an acute basis. The approximate LD50 = 3.7± 0.2 g/kg of body weight. I. Time of death (provide individual animal time if less than 24 hours after dosing): Not reported II. Description, severity, time of onset and duration of clinical signs at each dose level: Not reported III. Necropsy findings, included doses affected, severity and number of animals affected: Not reported IV. Potential target organs (if identified in the report): Not reported V. If both sexes tested, results should be compared: No information available
Source	:	Dow Corning Corporation
Test condition	:	I. Age: Not reported II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): Not reported III. Doses per time period: N.A. IV. Volume administered or concentration: Not reported V. Post dose observation period: Not reported VI. Exposure duration (for inhalation studies): N.A.
Test substance	:	Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability	:	(3) invalid The study was not conducted according to GLPs.

16.06.2003 (25)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 7.35 mg/l
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	5
Vehicle	:	water
Doses	:	7.35 mg/L
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1983
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Although no GLP Statement is provided in this report, it is assumed that this study was conducted under GLP. Bushy Run Research Center was a certified GLP laboratory during the conduct of this study. The aerosol of this material shows very low acute inhalation toxicity in the rat. Due to the rapid hydrolysis of the test substance, the LC50 reported is representative of the toxicity of the substance and its hydrolysis products.
Result	:	LC50>7.35 mg/L · Time of death (provide individual animal time if less than 24 hours after dosing): Not applicable, there were no deaths.

· Description, severity, time of onset and duration of clinical signs at each dose level: During exposure, a dense fog was present in the animal chamber, preventing observation of the test animals. After exposure, slow righting reflex, labored breathing, hypoactivity, ataxia and discharge from the mouth, nose and eyes were apparent. At 3 days, the animals were fully recovered. All animals gained weight during the study period. There were no other clinical signs.
· Necropsy findings, included doses affected, severity and number of animals affected: No remarkable gross pathologic findings were seen.
· Potential target organs (if identified in the report): None
· If both sexes tested, results should be compared: Responses were consistent between males and females.

Source : Epona Associates, LLC

Test condition :
· Age: Approximately 9 weeks old when exposed. Animals were weighed just before exposure and at 7 and 14 days after exposure. All rats were observed frequently on the day of the test and daily during the subsequent 14-day observation period.
· Doses: Distilled water was used to make a 60% (w/w) solution of the test material. The mixture was stirred for one hour to ensure complete dissolution of the test material. A Solo-Sphere® nebulizer containing the diluted test material was connected to a 120-liter exposure chamber. Dried air was passed into the nebulizer at a pressure of 50 p.s.i. and the resulting aerosol was passed into the exposure chamber. Every 30 minutes during exposure, a sample of chamber atmosphere was drawn through a tared fiberglass filter at the rate of 1.8 l/min. After one minute the filter was removed, dried in a drying oven to a constant weight and the final weight recorded. The change in weight represented the amount of hydrolyzed silane collected and represents approximately 49.77% of the test material. This factor, along with the volume of air sampled, was used to calculate the concentration of test material in the chamber air. The particle size distribution for the test material was determined with a cascade impactor. The ethanol concentration in the exposure chamber, formed from the reaction of the test material with water, was determined five times during the four-hour exposure period by gas chromatographic analysis. Gravimetric chamber analysis indicated that the mean chamber concentration was 7.35 (6.65 to 9.52) mg/liter. This concentration exceeds the limit test for OECD 403 (5 mg/l). The mass mean aerodynamic diameter was 1.6 micrometers with a geometric standard deviation of 2.19.
· Doses per time period: One
· Volume administered or concentration: Not applicable
· Post dose observation period: 14 days
· Exposure duration (for inhalation studies): Four hours using whole body exposure methods.
· Other: The mean ethanol concentration was 3253 (standard deviation of 1621) ppm.

Test substance : A-1100: 99.2% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion :
The four-hour LC50 for exposure to aerosolized test material

was determined to be greater than 7.35 mg/l in rats.

Reliability : (2) valid with restrictions
08.01.2004 (8)

Type : other: LT50
Value :
Species : rat
Strain : Wistar
Sex : male/female
Number of animals : 10
Vehicle :
Doses : 5 or 16 ppm
Exposure time : 6 hour(s)
Method : OECD Guide-line 403 "Acute Inhalation Toxicity"
Year : 1982
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Although no GLP Statement is provided in this report, it is assumed that this study was conducted under GLP. Bushy Run Research Center was a certified GLP laboratory during the conduct of this study. The vapor of this material shows very low acute inhalation toxicity in the rat.

Result :

LT50's with 95% confidence limits:
Males: > 6.0 hours
Females: > 6.0 hours

· Time of death (provide individual animal time if less than 24 hours after dosing): Not applicable; there were no deaths.
· Description, severity, time of onset and duration of clinical signs at each dose level: There were no signs of toxicity during or following exposure.
· Necropsy findings, included doses affected, severity and number of animals affected: No remarkable gross pathologic findings were seen.
· Potential target organs (if identified in the report): None
· If both sexes tested, results should be compared: Responses were consistent between males and females

Source : Epona Associates, LLC

Test condition : · Age: Rats weighing between 200 and 300 g were used. Animals were weighed just before exposure and at 7 and 14 days after exposure. All rats were observed frequently on the day of the test and daily during the subsequent 14-day observation period.
· Doses: Chamber 1 contained female rats and chamber 2 contained male rats. The animals were exposed to a substantially saturated vapor for 6 hours. The vapor was produced by passing air (at 2.5 liters/min) through a sample of the neat test material and then through a 9-liter animal chamber (dynamic conditions) at 25oC. The vapor concentrations of the test material in the two exposure chambers were monitored throughout the 6 hours of exposure by gas chromatography. The concentration in each chamber was determined ten times during the exposure period. The overall means (+ standard deviations) were 16 (+ 5.8) and 5 (+ 2) ppm for chambers 1 and 2, respectively. The reaction of the test material with water and/or water vapor (from respiration and urination) in the exposure chambers produced large quantities of ethanol, which were also

quantitatively monitored by gas chromatography.
· Doses per time period: One
· Post dose observation period: 14 days
· Exposure duration (for inhalation studies): Six hours using whole body exposure methods.
· Other: The mean ethanol concentration in chamber 1 was 490 ppm and was 380 ppm in chamber 2.

Test substance : Silane A-1100 Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : Six hours of exposure to substantially saturated vapor generated from Silane, gamma-aminopropyltriethoxy- (CAS No. 919-30-2) did not kill any of the 5 male or female rats.

Reliability : (2) valid with restrictions
08.01.2004 (7)

Type : other
Value :
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 5
Vehicle : other
Doses :
Exposure time : 6 hour(s)
Method :
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Although no GLP Statement is provided in this report, it is assumed that this study was conducted under GLP. Bushy Run Research Center was a certified GLP laboratory during the conduct of this study. The value of this study is limited, as it was not conducted in conformance with OECD test guidelines.

Result : Exposure to a statically-generated, substantially saturated vapor produced no deaths of male or female rats during or following the 6-hour test. Hypoactivity, ataxia and an alteration of the righting reflex were evident during or following exposure. Animals recovered after one day. Necropsy revealed no remarkable gross lesions.

Source : Epona Associates, LLC

Test condition : Concentrated vapor was produced by enclosing approximately 100 g of the test material in a sealed 100 to 151-liter animal chamber for approximately 18 hours (static conditions). A mixing fan periodically agitated the chamber atmosphere to aid in distribution of the vapor. Oxygen was added as needed for static exposures to maintain the chamber oxygen content at approximately 20%. Animals were weighted at study initiation and on days 7 and 14 (prior to sacrifice). Each animal was subjected to gross pathological evaluation.

Test substance : Silane A-1100: > 99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : The value of this study is limited, as it was not conducted in conformance with OECD test guidelines.

Reliability : (3) invalid
05.08.2003 (12)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	= 4290 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	8, 4, 2, and 1 g/kg
Method	:	EPA OTS 798.1100
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	EPA TSCA Guideline 798-1100
Remark	:	Although no GLP Statement is provided in this report, it is assumed that this study was conducted under GLP. Bushy Run Research Center was a certified GLP laboratory during the conduct of this study.
Result	:	Value [LD50 or LC50] with confidence limits if calculated: · males and females: LD50 with 95% confidence limits = 4.29 (2.90 to 6.34) g/kg. · Time of death (provide individual animal time if less than 24 hours after dosing): Days to death for the five male animals in the 8 g/kg group were 1,1,1,2,2. All other deaths occurred more than 24 hours after dosing. · Description, severity, time of onset and duration of clinical signs at each dose level: Local cutaneous effects included erythema, edema, ecchymosis, necrosis, desquamation, fissuring, ulceration, alopecia and scabs. Blood in rectal and urogenital areas apparent in several animals (especially at 4 g/kg). Hemorrhaging under the skin evident at 4 g/kg. Other signs of toxicity included sluggishness, salivation (in one), unsteady gait (in 2), prostration, and diarrhea (in one). Survivors recovered at 2 to 4 days. · Necropsy findings, included doses affected, severity and number of animals affected: gross pathologic findings included discolored lungs (red, pink, or mottled), lungs of with dark red foci (in one), mottled tan livers, stomachs with dark areas of hemorrhages, stomach with black foci (in one), tan or hemorrhaged kidneys, ureters and urethra with hemorrhages (in one), bladders filled with red liquid (1 with a dark red clot) and the untreated skin of 2 animals stained red. · Potential target organs (if identified in the report): kidney · If both sexes tested, results should be compared: See above.
Source	:	Epona Associates, LLC
Test condition	:	*No significant protocol deviations. *Study conducted under occlusive cover. *Doses: males and females were dosed with 8, 4, 2, and 1 g/kg *Doses per time period: one *Post exposure observation period: 14 days *Duration of exposure: 24 hours *Post-exposure treatment: After the contact period, excess test material is

removed to prevent ingestion.

Test substance : 1-Propanamine, 3-(triethoxysilyl); CAS No. 919-30-2

purity >96.1%

Reliability : (1) valid without restriction
07.01.2004 (12)

Type : other
Value :
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 6
Vehicle :
Doses : 2.0, 4.0, 6.0 ml/kg
Method : other: similar to OECD Guide-line 402
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : An LD50 was not described in the study report.
Result : Two rabbits receiving the highest dose (6.0 ml/kg) developed a moribund appearance and were sacrificed. At 4.0 ml/kg, 2 animals died. There were no deaths from 2.0 ml/kg; four animals had no clinical signs, two dosed at 2 ml/kg had blood stained periurogenital discharge. Renal tubular epithelial cell degeneration was observed in one animal on Day 1. On Day 2, the one animal sacrificed had microscopic evidence of tubular epithelial cell degeneration and proteinosis involving the kidneys, and one or more lesions involving the blader. At Day 14 there was no evidence of microscopic lesions. One control animal became moribund and was sacrificed. Pathologic findings suggested that this animal had enterotoxemia, secondary to constipation (commonly occurring in this species). Each test and control animal that was sacrificed at one or 2 days (scheduled and unscheduled sacrifices) exhibited weight loss. At 5 days all test article-treated rabbits had weight loss which was proportional to the dose received. Each control rabbit had a weight gain compared to initial values, by 5 days. Most surviving test animals demonstrated increases in weight by 14 days and all controls gained considerable weight. Mean weight changes were clearly dose-related. Examination of liver, kidney, lung and heart weights (absolute and relative to body weight) revealed no dose-related effect.

All animals treated with the test article exhibited severe skin irritation. Skin reactions included erythema, edema, necrosis, ecchymoses, desquamation, fissuring, ulceration, scab formation and alopecia. Examination of the skin of control animals revealed no irritation. The most common (and significant) sign of toxicity was the appearance of a discharge of blood within one day after initiation of contact with the test article. Most rabbits from the test article-treated groups had large amounts of blood on the periurogenital fur and under their cages. Rabbits at the highest dose were lethargic and exhibited a loss of coordination. Significant histopathologic findings among all groups treated with the test article included kidney tubule degeneration and proteinosis, urinary bladder hemorrhage, inflammation and necrosis. These lesions were most common in rabbits that died or were sacrificed in a

moribund condition.

Hematologic evaluation revealed a decrease in hematocrit at 2 days. Clinical chemistry results indicated that serum urea nitrogen and creatinine were increased at 2 days; the albumin concentration was decreased at 2 days. Results from urinalysis reveled blood in the urine, with increased bilirubin, urobilinogen and glucose within 2 days. Urine volume was reduced at one day (4.0 ml/kg group) and at 14 days. The pH and glucose levels were elevated at 14 days. Consistent dose-related increases in urine N-acetyl-beta-D-glucosaminidase activity were seen at one and 2 days.

Source : Epona Associates, LLC

Test condition : The purpose of this study was to assess the percutaneous toxicity and nephrotoxic potential of the test article based on clinical signs, clinical pathology and anatomic pathology. Single cutaneous doses of the test article were given to groups of 6 male New Zealand White rabbits at 3 dose levels (2.0, 4.0, and 6.0 ml/kg). The site of application was occluded for a 24-hour contact period. A fourth (control) group of 6 male rabbits was subjected to the 24-hour occlusion procedure but did not receive any test or control substance.

The rabbits weighed 2.2 - 2.5 kilograms at dosing and were four to five months of age. The rabbits were weighed prior to dosing, at 5 days, and at study termination (or death). 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. After 24 hours, the polyethylene sheeting was removed and as much excess test material as possible was removed. One rabbit per dose group was sacrificed at one hour after the termination of the 24-hour contact period. Another was sacrificed 24 hours after the contact period. Rabbits exhibiting a moribund condition were sacrificed. After a 14-day observation period the remaining animals were sacrificed. The animals were observed frequently for signs of toxic effects on the first day of the test and twice daily thereafter for fourteen days (except on weekends). The rabbits were closely observed for the presence of blood in the urine. At death or sacrifice, all animals were subjected to a complete gross pathologic examination. The kidneys, liver, lungs and heart were weighed for each animal. The kidneys, liver and urinary bladder were saved and processed for histologic evaluation. In addition, urine was collected directly from the bladder (using a needle and syringe) and examined for the following: volume, color, turbidity, specific gravity, pH, protein, glucose, ketone, bilirubin, blood, urobilinogen, N-acetyl-beta-D-glucosaminidase, and microscopy. Ear arterial blood was obtained from surviving animals at 2, 5, 9 and 14 days following the beginning of the contact period. Animals that died or that were exhibiting severe signs of toxicity were not used for the blood work. The following parameters were determined: urea nitrogen, creatinine, protein (total), albumin, globulin, bilirubin (total, direct, indirect), aspartate aminotransferase, alanine aminotransferase, creatinine kinase, lactic dehydrogenase, sorbitol dehydrogenase,

sodium, potassium, and chloride.

Test substance	:	Organofunctional Silane A-1100 Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion	:	Single cutaneous applications of 2.0 ml/kg or more of the test article to rabbit skin resulted in kidney and urinary bladder injury. These effects appear to develop within one or 2 days after contact and subside thereafter, possibly indicating a capacity for renal repair.
Reliability	:	(1) valid without restriction

08.01.2004 (14)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	corrosive (causes burns)
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Although no GLP Statement is provided in this report, it is assumed that this study was conducted under GLP. Bushy Run Research Center was a certified GLP laboratory during the conduct of this study.
Result	:	A 4-hour application of 0.5 ml of the test substance to occluded rabbit skin resulted in minor to moderate erythema on 6 of 6 rabbits and minor to severe edema on 6. After 5 hours (one hour after the contact period), ecchymosis was apparent on one animal. Necrosis was observed on 3 animals by one day and on another animal by 7 days. There was no erythema or edema evident on any animal at 10 days. At this time ulceration was evident on one animal and alopecia was observed on most. Desquamation, alopecia and ulceration (on one) persisted through 14 days. This material was considered corrosive to the skin by the Department of Transportation (DOT) definition.
Source	:	Epona Associates, LLC
Test condition	:	Rabbits were dosed with 0.5 ml. The dose was applied to the clipped, intact skin under a gauze patch and was loosely covered with impervious sheeting for a contact period of 4 hours. Excess sample was removed after contact. The skin reactions were scored by the method of Draize at one hour and 1, 2, 3, 7, 10 and 14 days after application.
Test substance	:	Silane A-1100: 99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion	:	This material is considered corrosive to the skin by the Department of Transportation (DOT) definition.
Reliability	:	(1) valid without restriction

08.01.2004 (12)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	no data
Exposure time	:	no data
Number of animals	:	4
Vehicle	:	
PDII	:	6.5
Result	:	highly irritating
Classification	:	irritating
Method	:	other
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Other: FDA Handbook, Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics, FDA (1959) P.47
Result	:	The test material was observed to cause severe skin irritation. Moderate to severe erythema accompanied by edema was observed on all animals after 24 hours exposure. The irritation was more severe on abraded skin and became more pronounced, leading to eschar formation after 72 hours. The Primary Irritation Index was calculated to be 6.5.
Source	:	Dow Corning Corporation
Test condition	:	I. Age: Not specified II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): 0.5 ml III. Volume administered or concentration: 0.5 ml IV. Post dose observation period: 24, 72 hours V. Exposure duration (for inhalation studies): N.A.
Test substance	:	Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2) I. Purity of the test material was not reported
Conclusion	:	The test material was a severe irritant to the skin of rabbits.
Reliability	:	(2) valid with restrictions The study was not conducted according to GLPs.

06.08.2003 (23)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	no data
Exposure time	:	no data
Number of animals	:	1
Vehicle	:	water
PDII	:	
Result	:	corrosive
Classification	:	corrosive (causes burns)
Method	:	other
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	This study was not conducted according to GLPs.
Result	:	A single application of the undiluted test material caused moderate necrosis (24 hours) or a slight hyperemia and edema (7 hours) to the belly (intact or abraded) of a rabbit. Repeated applications caused a moderate irritation to rabbit ear. The 10% aqueous solution of the test material is

slightly irritating to the skin.

Source : Dow Corning Corporation
Test condition : I. Age: Not reported
II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): Not reported
III. Doses per time period: N.A.
IV. Volume administered or concentration: Not reported
V. Post dose observation period: Up to 7 days
VI. Exposure duration (for inhalation studies): N.A.
Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

I. Purity of the test material was not reported
Conclusion : The undiluted test material caused moderate necrosis or burns to the skin of a rabbit.
Reliability : (3) invalid
16.06.2003 (24)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 3
Vehicle :
PDII :
Result :
Classification :
Method : other
Year : 1985
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : A 24-hour application of 0.5 ml of the test substance to occluded rabbit skin resulted in erythema and edema (grades 1 and 2) at the 24 and 72 hour intervals, with the exception of 1 female that had very slight erythema at 96 hours. All erythema and edema cleared by Day 7. Blanching, necrosis, thickening and epidermal scaling were observed in most or all of the animals throughout the observation period.
Source : SEHSC
Test condition : Rabbits were dosed with 0.5 ml. The dose was applied to two test sites: one site defined as clipped, intact skin, the second site abraded with minor incisions. Both sites were covered with a gauze patch and impervious sheeting for a contact period of 24 hours. Excess sample was removed after contact. The skin reactions were scored by the method of Draize at 24, 72 and 96 hours and 7 days after application.
Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability : (2) valid with restrictions
This study did not follow current guidelines and it was not possible to determine if the study was conducted under GLP.
08.01.2004 (31)

Species : other
Concentration : no data
Exposure : no data
Exposure time : no data
Number of animals :
Vehicle :
PDII :
Result : slightly irritating
Classification :

Method	:	other
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	A single short-term skin contact with undiluted test material produced a slight reddening of the skin. Repeated and or prolonged skin contact produced moderate amount of tissue destruction and the formation of a permanent scar.
Source	:	Dow Corning Corporation
Test condition	:	I. Age: Not reported II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): Not reported III. Doses per time period: N.A. IV. Volume administered or concentration: Not reported V. Post dose observation period: Not reported VI. Exposure duration (for inhalation studies): N.A.
Test substance	:	Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2) I. Purity of the test material was not reported
Conclusion	:	Single short-term contact with skin produced slight irritation. Repeated and/or prolonged contact produced moderate irritation and formation of a permanent scar.
Reliability	:	(3) invalid The study was not conducted according to GLPs.

16.06.2003 (25)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	unspecified
Comment	:	no data
Number of animals	:	6
Vehicle	:	none
Result	:	highly irritating
Classification	:	irritating
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Although no GLP Statement is provided in this report, it is assumed that this study was conducted under GLP. Bushy Run Research Center was a certified GLP laboratory during the conduct of this study.
Result	:	Instillation of 0.1 ml into rabbit eyes resulted in severe corneal injury, iritis and severe conjunctival irritation. Within one hour each rabbit developed necrosis of the conjunctivae. By 48 hours, 6 of 6 animals had a purulent ocular discharge. All rabbits exhibited irregularly shaped corneas (characterized by surface bulges) and 4 animals had corneal vascularization by 7 days. Because of the severe, possibly irreversible irritation noted on each rabbit at 7 days, all rabbits were sacrificed. Following the instillation of 0.005 ml into rabbit eyes, minor to severe corneal injury developed in 6 of 6 rabbits.

All rabbits had necrosis of the conjunctivae within one hour. By 48 hours, 5 animals developed a purulent ocular discharge. Three rabbits had an irregularly shaped cornea and vascularization within 7 days. Two animals had a normal appearance by 7 days. One of the animals died at 20 days. There was no evidence that this death was related to the treatment. A total of 3 of the remaining 5 eyes were completely healed by 21 days. The other eyes still exhibited substantial injury.

Source : Epona Associates, LLC
Test condition : Rabbits were dosed with volumes of 0.1 ml and 0.005 ml. The dose is instilled into the lower conjunctival sac of one eye per animal. The eyelids are held together for one second. The eyes were scored at one and five hours, and at 1, 2, 3, 7 and 14 days after dosing.
Test substance : Silane A-1100:>99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion : This material is a severe eye irritant capable of producing necrosis.
Reliability : (1) valid without restriction
08.01.2004 (12)

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : unspecified
Comment : rinsed after (see exposure time)
Number of animals : 6
Vehicle : none
Result : highly irritating
Classification : irritating
Method : other
Year : 1976
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Modified method that laid down in the FDA Handbook, Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics, FDA (1959) P.49
Result : The test material produced severe ocular irritation in all rabbits including those in which the treated eye was washed following instillation. Maximum scores were recorded for all parameters and in view of the severity of these reactions and the obvious permanent damage which would result from this insult, all animals were sacrificed after 24 hours.
Source : Dow Corning Corporation
Test condition : I. Age: Not reported
II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): 0.1 ml
III. Doses per time period:
IV. Volume administered or concentration: 0.1 ml
V. Post dose observation period: 1, 2, 3, 4 and 7 days.
Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

I. Purity of the test material was not reported.
Conclusion : The test material was found to be extremely irritant to the eyes of rabbits.
Reliability : (2) valid with restrictions
06.08.2003 (23)

Species : rabbit

Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	unspecified
Comment	:	other
Number of animals	:	9
Vehicle	:	none
Result	:	highly irritating
Classification	:	irritating
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Unwashed group: Corneal opacities were observed in two animals beginning at 48 hours, and were observed in all animals on days 7-14. Corneal necrosis was observed for all animals at 24 hours to day 4, and persisted in three animals on days 13 and 14. Iritis, redness and chemosis was observed in most or all animals by 24 hours, and persisted in at least one animal by day 13. Blistering of the conjunctivae and/or nictitating membrane as well as discoloration of the nictitating membrane was observed for all animals at 24 and 48 hours. Washed group: Corneal opacities were observed in one animal beginning at 48 hours, and for all animals from 72 hours until day 14. Corneal necrosis was observed for all animals at 24 hours to day 7, and persisted in two animals on days 8 to 10. Iritis, redness and chemosis was observed in all animals by 24 to 48 hours, and persisted in at least one animal by day 13. Blistering of the conjunctivae and/or nictitating membrane was observed for all animals at 24 and 48 hours. Discoloration of the nictitating membrane was observed in one animal at 24 and 48 hours.
Source	:	Lesser Ketones Manufacturing Association Leesburg, VA
Test condition	:	Rabbits were dosed with 0.1 ml. The dose was instilled into the lower conjunctival sac of one eye per animal. The other eye served as the untreated control. The treated eyelids were held together for one second. The treated eyes of six animals remained unwashed. The treated eyes of three animals were washed for 1 minute approximately 5 seconds after installation of the test article. The eyes were scored at 24, 48 and 72 hours, and on days 4, 7 and 8-14 after dosing. The test article was given a descriptive rating using the method of Kay and Calandra.
Test substance	:	X-59381 Aminoalkyl Silane: Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion	:	This material is an extremely irritating to the eye.
Reliability	:	(2) valid with restrictions

06.08.2003 (55)

Species	:	rabbit
Concentration	:	other
Dose	:	other
Exposure time	:	unspecified
Comment	:	no data
Number of animals	:	1
Vehicle	:	water
Result	:	highly irritating
Classification	:	risk of serious damage to eyes
Method	:	other

Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	In the undiluted form, the material is extremely irritating to the eyes and produced extensive pain, swelling and conjunctivitis accompanied by corneal damage which likely would result in permanent loss of vision. The 10% aqueous solution is slightly irritating to the eyes which subsided in 24 hours.
Source	:	Dow Corning Corporation
Test condition	:	I. Age: Not reported II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): Not reported III. Doses per time period: N.A. IV. Volume administered or concentration: Not reported V. Post dose observation period: Not reported VI. Exposure duration (for inhalation studies): N.A.
Test substance	:	Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2) I. Purity of the test material was not reported
Conclusion	:	The test material was extremely irritating with extensive pain to the washed and unwashed eyes of a rabbit. It reacts very rapidly with cornea causing deep burn with probable permanent eye injury.
Reliability	:	(3) invalid The study was not conducted according to GLPs.

16.06.2003 (24)

Species	:	other
Concentration	:	no data
Dose	:	other
Exposure time	:	unspecified
Comment	:	no data
Number of animals	:	
Vehicle	:	none
Result	:	highly irritating
Classification	:	risk of serious damage to eyes
Method	:	other
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Direct eye contact with the test material produced serious injury to ocular tissue, including severe burns persisting for more than one week which may result in permanent impairment of vision.
Source	:	Dow Corning Corporation
Test condition	:	I. Age: Not reported II. Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail): Not reported III. Doses per time period: N.A. IV. Volume administered or concentration: Not reported V. Post dose observation period: Not reported VI. Exposure duration (for inhalation studies): N.A. Species not reported.
Test substance	:	Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2) I. Purity of test material was not reported
Conclusion	:	The test material produced severe ocular irritation,

including burns which may result in permanent impairment of vision.

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

16.06.2003 (25)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	1st: Induction .25 % intracutaneous 2nd: Induction 70 % occlusive epicutaneous 3rd: Challenge 70 % occlusive epicutaneous
Number of animals	:	10
Vehicle	:	physiol. saline
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1995
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	All animals gained weight and survived to study termination. No positive responses were observed at 24 hours or 48 hours in the test group receiving test article at a 70% concentration in saline. No responses were observed at any vehicle treated site. The positive control animals induced and challenged with DNCB exhibited the anticipated responses at challenge, indicating a reliable and valid test.
Source	:	Epona Associates, LLC
Test condition	:	Test Animals Age at initiation: four to six weeks; Weight at initiation: 300 - 372 grams. Study Design Dose Range-Finding Studies: An intradermal dose range-finding study and a topical dose range-finding study were conducted to determine the intradermal and topical irritation potential of the test article. In the intradermal dose range-finding study, guinea pigs were intradermally injected with concentrations of 0.5, 1.5, 3 and 5% of the test article in saline. Twenty-four hours after injection, the sites were graded on a scale of 0 (no reaction) to 4 (severe erythema and edema; skin damage). Due to the severity of the irritation observed (necrosis), additional animals were intradermally injected with concentrations of 0.01, 0.05, 0.10, and 0.25% test article in saline and graded. Based on the results of these dose-range finding studies, the dose chosen for the intradermal induction portion of the definitive test was 0.25% test article in saline, which is associated with no irritation to slight patchy mild redness. In the topical dose range-finding study, animals were topically exposed to concentrations of 1.0, 10 and 50% test article in saline as well as neat test article. The treatment area was wrapped occlusively for 24 hours, and graded for irritation on a scale of 0 to 4. Due to the lack of irritation observed, two additional animals were

topically exposed to concentrations of 60, 70, 80 and 90% of test article in saline and graded. Based on the results of these dose range-finding studies, the dose chosen for the topical induction and challenge portion of the definitive study was 70%, which is associated with no sign of irritation. Scoring of the sites dosed with 80% and 90% were prohibited in one animal due to mechanical damage.

Definitive Test: The guinea pigs in the definitive sensitization maximization test undergo an intradermal induction stage, followed by a topical induction stage, and a subsequent challenge period. During the intradermal induction stage, the test article, vehicle, and positive control, respectively, with or without Freund's complete adjuvant (FCA), were injected intradermally. Seven days after the intradermal injections, a patch, saturated with 70% test article in saline, vehicle control or positive control was applied to the injection area, and covered with an occlusive dressing for 48 hours. Fourteen days after topical induction, the animals were challenged with test article in saline, vehicle control or positive control under occluded patches for 24 hours (distal from the injection sites). Twenty-four hours after dosing, the occlusive cover was removed. Twenty-four hours following unwrapping, the sites were scored for irritation. The sites were re-examined 24 hours following the first scoring.

Test substance : Silquest A-1100: 99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Since the test article readily hydrolyzes in saline, the test was actually conducted on the hydrolysis products of the test material.

Conclusion : Appropriate concurrent negative and positive compliance controls were included and the expected responses were observed. Under the conditions of this study, the hydrolysis products of gamma-aminopropyltriethoxysilane did not elicit a delayed contact hypersensitivity response in guinea pigs.

Reliability : (1) valid without restriction
06.08.2003 (49)

Type : Buehler Test
Species : guinea pig
Concentration : 1st: Induction 20 % occlusive epicutaneous
2nd: Challenge 5 % occlusive epicutaneous
3rd:
Number of animals : 44
Vehicle : peanut oil
Result : sensitizing
Classification : sensitizing
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : There were no signs of systemic toxicity during the study. All animals gained weight during the study and there were no significant test-article related differences in vehicle and test group mean body weight.

No positive responses were observed in the peanut oil control animals at either the vehicle or test article sites at the 24-hour grading. In the peanut oil control animals at the 48-hour grading one animal exhibited a positive response at the test article site, a grade of one (1). Of the twenty animals induced with the test article at 20% and challenged at 5%, three animals were observed with a positive response of one (1) at the 24-hour grading, and three exhibited a positive response of one (1) and four exhibited a positive response of two (2) at the 48 hour grading. The positive control animals induced and challenged with DNCB exhibited the anticipated responses at challenge, indicating a reliable and valid test.

Source : Epona Associates, LLC

Test condition : Age at initiation: four weeks; Weight at initiation: 308 - 400 grams.

Study Design
Dose Range-Finding Study: Prior to initiation of the definitive study, the irritation potential of the test article was determined. Four animals were each exposed to three concentrations (40, 60 and 80%) of the test article in peanut oil and the neat material. The treatment material was applied beneath a Hill Top Chamber® and held in place for six hours. The treated sites were examined approximately 24 hours after the end of exposure and graded according to a 0-to-3 severity scale. Due to excessive irritation (grades of 1 to 3) observed in the primary irritation screen, a secondary irritation screen was performed. Four unexposed animals were each exposed to four concentrations (5, 10, 20 and 30%) of the test article in peanut oil. Based on these results, the concentration chosen for induction, 20%, was the highest dose to cause mild irritation. The highest non-irritating concentration, 5%, was chosen for challenge.

Definitive Study: A group of 5 male and 5 female guinea pigs was induced using the procedure described above with three six-hour occluded dermal applications of peanut oil with 7 days between applications. A test article group consisting of 10 males and 10 females was treated in a similar manner with 20% test article. A positive control group of 3 male and 3 female guinea pigs was induced with a known dermal sensitizer, 1-chloro-2,4-dinitrobenzene (DNCB). Fourteen days after the last induction, all animals were dermally challenged with an occluded application on naive test site(s). The vehicle control animals were challenged with peanut oil and test article at 5%. The test group was treated with the test article at 5%. The positive control animals were challenged with DNCB @ 0.02 and 0.2% in acetone. All animals were observed for local (dermal) and systemic effects. Eighteen to 22 hours after removal of challenge patches, all test sites were depilated and graded at 24-hours and 48-hours using the 0-to-3 grading scale. The initial and final body weights of the animals were recorded. Grades of 1 or greater in the test group would indicate sensitization, provided grades of less than 1 are seen in the vehicle control animals.

Test substance : Silquest A-1100: 99.5% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : Appropriate concurrent negative and positive compliance

controls were included and the expected responses were observed. Under the conditions of this study, induction with gamma-aminopropyltriethoxysilane at 20% did elicit a delayed contact hypersensitivity response in guinea pigs when challenged with gamma-aminopropyltriethoxysilane at 5% and compared to the irritation observed in the vehicle group treated with gamma-aminopropyltriethoxysilane at the same concentration.

Reliability : (1) valid without restriction
06.08.2003 (50)

Type : Guinea pig maximization test
Species : guinea pig
Concentration : 1st: Induction .5 % intracutaneous
2nd: Induction 50 % open epicutaneous
3rd: Challenge 50 % open epicutaneous
Number of animals : 30
Vehicle : water
Result : not sensitizing
Classification : not sensitizing
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : No adverse skin reactions were noted at the test material or vehicle control sites of the test or control animlas at the 24 or 48 hour observations.
Source : Epona Associates, LLC
Test condition : 20 test and 10 control animals were used for the main study. Based on preliminary studies, the following concentrations were used for induction and challenge: Intradermal induction: .5% (w/v); Topical Induction: 50% (w/v); Tpoical challenge: 50% (w/v).
Conclusion : The test substance produced a 0% (0/20) sensitisation rate and was classified as a non sensitizer to guinea pig skin.
Reliability : (1) valid without restriction
15.01.2004 (26)

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : other: Crl:CD (SD)BR
Route of admin. : gavage
Exposure period : 91 or 92 consecutive days
Frequency of treatm. : Daily
Post exposure period : Not applicable. All animals were euthanized and necropsied upon completion of the treatment period; no recovery or other satellite groups were included.
Doses : 0, 70, 200, and 600 mg/kg/day
Control group : yes
NOAEL : = 200 mg/kg bw
Method : other: in general compliance with USEPA OPPTS Guideline 870.3100 (August 1998) and OECD Guidelines for Testing of Chemicals, Section 408 (September 1998).
Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : OECD Guideline 408

Statistical Method: All analyses were conducted using two-tailed tests for minimum significance levels of 1% and 5% comparing the test article-treated groups to the control group by sex. All means were presented with standard deviations (S.D.) and the number of sampling units (N) used to calculate the means. Statistical analyses were not conducted if the number of animals was two or less. All statistical tests were performed using appropriate computing devices or programs. Body weight, body weight change, food consumption, clinical pathology, absolute and relative organ weight data and epididymal and testicular sperm numbers and sperm production rates were subjected to a one-way analysis of variance (ANOVA), followed by Dunnett's test if the ANOVA revealed statistical significance ($p<0.05$). The percentage of motile spermatozoa and the percentage of sperm with normal morphology were analyzed by the Kruskal-Wallis nonparametric ANOVA test to determine intergrouup differences, followed by the Mann-Whitney U-Test comparing the control and test article-treated groups if the ANOVA revealed statistical significance ($p<0.05$). Clinical laboratory values for leukocytes that occur at a low incidence (i.e., monocytes, eosinophils and basophils) were not subjected to statistical analysis.

Remark : The dosing solutions were shown to be stable (test substance in peanut oil sparged with nitrogen).

Result : One control group male (day 28), one 200 mg/kg/day group female (day 65) and two 600 mg/kg/day groups males (day 18) were found dead. Clinical signs for these animals were similar to those discussed below. Macroscopic and/or microscopic findings indicated that none of these deaths was treatment related; these deaths were attributed to dsoing error.
Test article-related lethality was limited to the 600 mg/kg/day group. One male and eight females in this group were found dead or euthanized in extremis. Just prior (one or two days) to death, many of these animals exhibited labored respiration, gasping, partial closure of the eyes, general paleness, hypothermia, dermal atonia and/or tremors. Additional clinical signs for these animals were generally similar to those in the animals that survived to the scheduled necropsy. These are discussed below.
All other animals survived to the scheduled necropsy (days 91 or 92). Test article-related clinical signs were generally limited to the 600 mg/kg/day group males and females. The predominant clinical sign was rales. Sporadic occurrences of rales for individual animals were noted as early as the first week of dosing, with as many as one-half of the animals having sporadic observations of rales noted by the third week of dosing, and continuing at a similar incidence at the observations prior to and following dosing through the end of the study. Additional treatment-related clinical signs in the 600 mg/kg/day group included wet and/or dried material (red, yellow, brown and/or clear) on various body surfaces and abnormal excreta (feces smaller than normal, soft and/or mucoid feces and decreased defecation). These additional clinical signs also occurred at the lower dose levels; however, the incidence was generally sporadic. No other treatment-related clinical signs were noted. All other findings occurred similarly in the control group, were limited in incidence (typically

single occurrences in one or two animals/group) and/or were common findings in laboratory rats.
Body weight gains and food consumption were unaffected by test article administration at all dose levels. No oculopathic changes indicative of a test article-related effect were observed at any dose level. No test article-related changes were present in hematology parameters, estrous cycle data or spermatogenic endpoints.
At 600 mg/kg/day, test article-related increases were present in mean aspartate aminotransferase values for the males at week 13 and in mean alanine aminotransferase values for the males and females at both evaluations during the study (weeks 4 and 13). Gaseous distention in the intestinal tract (primarily in the cecum) was observed macroscopically at necropsy for most males and females, including those that died prior to the scheduled necropsy.
Test article-related organ weight changes were seen in the liver of the 600 mg/kg/day males. In this treatment group, although the mean absolute liver weight was not increased, the mean liver-to-brain weight was increased (not statistically significantly), and the mean liver-to-body weight was statistically increased when compared to controls. Test article-related microscopic changes were limited to the males, and consisted of increased severity of centrilobular to generalized hepatocellular vacuolation. No other test article-related microscopic changes were observed.

Source : Epona Associates, LLC

Test condition : The objective of this study was to evaluate the possible toxic effects of gamma-aminopropyltriethoxysilane when administered orally (gavage) to rats for a minimum of 90 days. In a range-finding study, gamma-aminopropyltriethoxysilane was administered in peanut oil orally (by gavage) to three groups of rats (five/sex) for rats were administered gamma-aminopropyltriethoxysilane in peanut oil at dosage levels of 70, 200 and 600 mg/kg/day. A concurrent control group received the vehicle on a comparable regimen. All animals were dosed at a volume of 10 mL/kg. The animals were observed twice daily for mortality and moribundity. Clinical exams were performed daily and detailed physical examinations were performed weekly. Individual body weights and food consumption were recorded weekly. Complete necropsies were performed on all animals and selected organs were weighed. Selected tissues were examined microscopically from all animals. Survival was unaffected by gamma-aminopropyltriethoxysilane administration. No test-article related findings were observed at the macroscopic or microscopic examinations. Organ weights were unaffected by treatment. Clinical signs included one or more instances of rales and/or labored respiration in the 600 mg/kg/day group. These findings were noted in two males and two females during the last three days of dosing prior to necropsy. There were no statistically significant differences in body weights, body weight gains, or food consumption. However, there were reductions in body weight gains and food consumption in the 600 mg/kg/day males during weeks 0 to 1 and 1 to 2. The no-observed-adverse-effect level (NOAEL) for gamma-aminopropyltriethoxysilane in rats following a 14-day repeated treatment via gavage was 200 mg/kg/day. Dose levels of 70, 200 and 600 mg/kg/day were selected for the

90-day oral (gavage) toxicity study of gamma-aminopropyltriethoxysilane in rats.

There were 15 rats per sex in each group. Young adult rats were approximately seven weeks old at the initiation of dosing and body weight values ranged from 213 to 279 grams for the males and from 150 to 207 grams for the females. Ocular examinations were conducted on all animals prior to the initiation of dosing (week -1) and during week 12. All ocular examinations were conducted using an indirect ophthalmoscope, preceded by pupillary dilation with an appropriate mydriatic agent. The test article in the vehicle, peanut oil sparged with nitrogen, was administered orally by gavage to three groups (15/sex/group) of Crl:CDÒ(SD)BR rats for 91 or 92 consecutive days at dosage levels of 70, 200 and 600 mg/kg/day. These dose levels were chosen based upon the results of the previous 14-day range-finding study. A concurrent control group received the vehicle on a comparable regimen. The animals were observed twice daily, once in the morning and once in the afternoon, for mortality and moribundity. Clinical observations were performed on all animals prior to and approximately 1-2 hours following dosing. All significant findings were recorded. Detailed physical examinations were conducted weekly during the study period and just prior to the scheduled necropsy. Animals were routinely observed in their home cages and while being handled and weighed. Individual body weights were recorded weekly beginning one week prior to randomization (week -1). Mean body weight changes were calculated for each week. A final (fasted) body weight was recorded for each animal on the day of scheduled necropsy. Individual food consumption was measured weekly beginning one week prior to randomization (week 1). Food intake was calculated as g/animal/day for the corresponding body weight intervals. When food consumption could not be measured for a given interval (due to spillage, weighing error, etc.), the appropriate interval was footnoted as "NA" (Not Applicable) on the individual tables. Clinical pathology parameters (hematology and serum chemistry) were evaluated on all animals during week 4 and at study termination (week 13). The animals were fasted overnight prior to the collection of blood samples. Blood samples for general clinical pathology evaluations were collected from a lateral tail vein at both time points. Blood samples for assessment of coagulation parameters were collected from the vena cava at the time of necropsy. The following hematology parameters were evaluated: total leukocyte count (white cell), erythrocyte count (red cells), hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, prothrombin time, activated partial thromboplastin time (APTT; terminal evaluation only), reticulocyte count (percent and absolute), differential leukocyte count (percent and absolute: neutrophil, lymphocyte, monocyte, eosinophil and basophil). The following serum chemistry parameters were evaluated: alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, blood urea nitrogen, total protein, total bilirubin, creatinine, Ca, Na, K, Cl, P, glucose, albumin, globulin, albumin/globulin ratio, and total cholesterol. Urine samples were collected

via metabolism chambers following the eighth exposure of female rats and following the seventh exposure of male rats. Urine volume was measured using calibrated test tubes, and urine color and turbidity were visually assessed. Urinalysis parameters were urine osmolality, pH, protein, glucose, ketone, bilirubin, blood and urobilinogen. Vaginal smears for determination of the stage of estrus were obtained from all surviving females once daily beginning 21 days prior to the scheduled necropsy. The average cycle length was calculated for complete estrous cycles (i.e., the total number of returns to metestrus [M] or diestrus [D] from estrus [E] or proestrus [P]) beginning 21 days prior to the scheduled necropsy. The final vaginal smear for each female was collected on the day of necropsy. A complete necropsy was conducted on all animals. Animals euthanized in extremis or at the scheduled necropsy were euthanized by carbon dioxide asphyxiation followed by exsanguinations. The necropsy included, but was not limited to, examination of the external surface, all orifices and the cranial, abdominal and pelvic cavities and their viscera. At the time of necropsy, the following tissues and organs were collected and preserved in 10% neutral buffered formalin: adrenals (2), aorta, bone with marrow (femur, sternebrae), bone marrow smear (from femur), brain (forebrain, midbrain, hindbrain), coagulating gland, eyes with optic nerve (2; preserved in Davidson's solution), gastrointestinal tract (esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum), heart, kidneys (2), liver (sections of two lobes), lungs (including bronchi, fixed by inflation with fixation), lymph node (mesenteric, submandibular), mammary gland (females only), ovaries with oviducts (2), pancreas, peripheral nerve (sciatic), pituitary, prostate, salivary glands (submaxillary, 2), seminal vesicles (2), skeletal muscle (vastus medialis), skin, spinal cord (cervical, midthoracic, lumbar), spleen, testis with epididymis (1) and vas deferens, thymus, thyroid (with parathyroids if present (2)), trachea, urinary bladder, uterus with vagina and cervix, and all gross lesions (when possible). Bone marrow smears were obtained from all animals not found dead, but were not placed in 10% neutral buffered formalin. The right testis/epididymis from all males at the scheduled necropsy and both testes/epididymides from those males found dead were preserved in Bouin's solution and prepared for microscopic examination using PAS/hematoxylin staining. The left testis/epididymis from all males euthanized at the scheduled necropsy were prepared for sperm analysis as described below. The following organs from animals euthanized at the scheduled necropsy were weighed: adrenals, brain, epididymides (weighed separately; total and cauda), kidneys, liver, ovaries (with oviducts), pituitary, prostate, seminal vesicles with coagulating glands (with accessory fluids), testes (weighed separately), and thyroid (fixed weight). Organ to final body weight and organ to brain weight ratios were calculated. After fixation, specified tissues were trimmed according to standard operating procedures. Trimmed tissues were processed into paraffin blocks, sectioned at five to eight microns, mounted on clean glass microscope slides and stained with hematoxylin and eosin. The tissues noted above from all animals found dead or euthanized in extremis and from all animals in the control and 600 mg/kg/day groups euthanized

at the scheduled necropsy, as well as the lungs, liver, and kidneys from all animals in the 70 and 200 mg/kg/day groups were examined microscopically. In addition, PAS/hematoxylin-stained sections of the right testis and epididymis from all males were examined microscopically at the scheduled necropsy. Spermatogenic analysis was conducted according to the following protocol. For motility/viability assessment, immediately following euthanasia, the reproductive tract of each male was exposed via a ventral mid-line incision. The right epididymis was excised and weighed separately. An incision was made in the distal region of the cauda epididymis. The cauda was then placed in Dulbecco's phosphate-buffered saline (maintained at approximately 37oC) with 10 mg/ml Bovine Serum Albumin (BSA). A sample of the diluted sperm was then loaded into a 100 µm cannula for determination of motility. As sperm motility can be affected by temperature shock, all cannulas, diluents and slides were pre-warmed and maintained at approximately 37oC. Motility determinations were performed under constant temperature using the Hamilton-Thorne HTM-IVOS Version 10 computer-assisted sperm analysis (CASA) system. At least 200 (if possible) motile and nonmotile spermatozoa/animal were analyzed. A sample of sperm for morphology assessment was obtained from the right cauda epididymis of each male. Sperm morphology was evaluated using a modification of the wet-mount technique described by Linder et al., 1992. Abnormal forms of sperm (double heads, double tails, micro- or megacephalic, etc.) were recorded from a differential count of 200 spermatozoa/animal. For enumeration of epididymal and testicular sperm numbers and sperm production rates, the left testis and epididymis from each male at the scheduled necropsy were weighed and frozen, then homogenized and evaluated for sperm production rate using the method described by Blazak et al., 1985. Analyses were performed using the Hamilton-Thorne CASA system.

Test substance : A-1100: Purity: 98.99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : Although several of these test article-related findings (clinical signs, gaseous intestinal distension, hepatocellular vacuolation) also occurred at 0, 70 and/or 200 mg/kg/day, all were limited or sporadic in incidence. Based upon the results of this study, a no-observed-effect level (NOEL) was not determined. However, the no-observed-adverse-effect level (NOAEL) was 200 mg/kg/day.

Reliability : (1) valid without restriction

08.01.2004 (57) (58)

Type : Sub-acute
Species : rat
Sex : male/female
Strain : other
Route of admin. : gavage
Exposure period : 14 consecutive days
Frequency of treatm. : Daily
Post exposure period : Not applicable
Doses : 0, 70, 200, and 600 mg/kg/day
Control group : yes
Method : OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year : 1998
GLP : yes

Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Statistical Methods: All analyses were conducted using two-tailed tests for minimum significance levels of 1% and 5% comparing the test article-treated groups to the control group by sex. All means were presented with standard deviations (S.D.) and the number of sampling units (N) used to calculate the means. Statistical analyses were not conducted if the number of animals was two or less. All statistical tests were performed by a Digital® MicroVAX® 3400 computer with appropriate programming. Body weight, body weight change, food consumption, clinical pathology, and absolute and relative organ weight data were subjected to a one-way analysis of variance (ANOVA), followed by Dunnett's test.
Result	:	Survival was unaffected by gamma-aminopropyltriethoxysilane administration. No test-article related findings were observed at the macroscopic or microscopic examinations. Organ weights were unaffected by treatment. The only definite test article-related clinical observations were signs of abnormal respiration (rales and/or labored respiration) in the 600 mg/kg/day group. These findings were noted in two males and two females during the last three days of dosing and/or prior to necropsy. Another female in the 600 mg/kg/day group had rales on one occasion during this period. There were no statistically significant differences in body weights, body weight gains, or food consumption. However, there were reductions in body weight gains and food consumption in the 600 mg/kg/day males during weeks 0 to 1 and 1 to 2.
Source	:	Epona Associates, LLC
Test condition	:	The objective of this study was to evaluate the possible toxic effects of gamma-aminopropyltriethoxy-silane when administered orally (gavage) to rats for 14 days and to establish dose levels for a subchronic toxicity study. The test article in the vehicle, peanut oil, was administered orally by gavage to three groups of rats (five/sex) for 14 consecutive days at dosage levels of 70, 200 and 600 mg/kg/day. A concurrent control group received the vehicle on a comparable regimen. All animals were dosed at a volume of 10 mL/kg. Young adult rats were approximately six weeks old at the initiation of dosing and body weight values ranged from 164 to 229 grams for the males and from 139 to 179 grams for the females. The animals were observed twice daily, once in the morning and once in the afternoon, for mortality and moribundity. Clinical observations were performed on all animals prior to and approximately 1-2 hours following dosing. All significant findings were recorded. Detailed physical examinations were conducted weekly during the study period and just prior to the scheduled necropsy. Individual body weights were recorded weekly beginning one week prior to randomization (week -1). Mean body weight changes were calculated for each week and mean body weight changes were calculated for each corresponding interval. A final (fasted) body weight was recorded for each animal on the day of scheduled necropsy. Individual food consumption was measured weekly beginning one week prior to randomization (week ?1). Food intake was calculated as g/animal/day for the corresponding body weight intervals. A complete necropsy was conducted on all animals. The necropsy included, but was not limited to,

examination of the external surface, all orifices and the cranial, abdominal and pelvic cavities and their viscera. At the time of necropsy, the following tissues and organs were collected and preserved in 10% neutral buffered formalin: adrenals (2), aorta, bone with marrow (femur, sternebrae), bone marrow smear (from femur), brain (forebrain, midbrain, hindbrain), eyes with optic nerve (2) preserved in Davidson's solution), gastrointestinal tract (esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum), heart, kidneys (2), liver (sections of two lobes), lungs (including bronchi, fixed by inflation with fixation), lymph node (mesenteric, submandibular), mammary gland (females only), ovaries with oviducts (2), pancreas, peripheral nerve (sciatic), pituitary, prostate, salivary glands (submaxillary, 2), seminal vesicles (2), skeletal muscle (vastus medialis), skin, spinal cord (cervical, midthoracic, lumbar), spleen, testes with epididymis (2) packed in Bouin's solution, thymus, thyroid (with parathyroids if present (2)), trachea, urinary bladder, uterus with vagina, and all gross lesions (when possible). The following organs from animals euthanized at the scheduled necropsy were weighed: adrenals, brain, kidneys, liver, ovaries (with oviducts), and testes. Paired organs were weighed together. Organ to final body weight ratios were calculated. After fixation, specified tissues were trimmed according to standard operating procedures. Trimmed tissues were processed into paraffin blocks, sectioned at five to eight microns, mounted on clean glass microscope slides and stained with hematoxylin and eosin. The liver, kidneys, lungs, testes and gross lesions suspected of being related to treatment were examined microscopically from all animals in the control and 600 mg/kg/day groups. The stomach was examined microscopically from all animals in all groups.

Test substance : A-1100: 98.99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : Based on the results of this range-finding study, dose levels of 70, 200 and 600 mg/kg/day were selected for the 90-day oral (gavage) toxicity study of gamma-aminopropyltriethoxysilane in rats.

Reliability : (1) valid without restriction

06.08.2003 (57)

Type : Sub-acute
Species : rat
Sex : male
Strain : Fischer 344
Route of admin. : inhalation: aerosol
Exposure period : 6 hours per day for a total of 19 exposures over 4 weeks
Frequency of treatm. : Five days/week for three weeks and four consecutive days during the fourth week
Post exposure period : Not applicable. The rats were observed daily during exposure and observations were recorded on a group basis. Preceding and following each exposure and on weekends, observations were recorded for animals exhibiting overt clinical signs.
Doses : 0 and 147 mg/m3
Control group : yes
Method : other: similar to OECD Guide-line 412
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Methods: 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 BMDP 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 test substance hydrolysate gravimetric concentration of 147 mg/m3 was obtained. The mass median aerodynamic diameter was 2.92 microns with a geometric standard deviation of 1.74. The daily mean chamber temperature and relative humidity ranged from 19-20oC and 73-94%, respectively. No mortality or exposure-related clinical signs were observed during the study. A depression in body weight gain was observed for the test substance-exposed animals during the first week of the study. At necropsy, focal/multifocal color changes of the lungs were noted in ninety percent of the animals of the test substance-exposed group. Histological examination showed nonspecific irritant, inflammatory, and metaplastic changes within the respiratory tracts of test substance-exposed rats. Laryngeal lesions included squamous metaplasia and foci of minimal granulomatous laryngitis. Other microscopic changes included the presence of cytoplasmic hyalinization (mild to moderate) within the olfactory mucosa, squamous metaplasia (minimal to mild) within the nasal mucosa, cellular hyperplasia within the trachea, alveolar histiocytosis, bronchopneumonia, interstitial pneumonitis and alveolar type II pneumocyte hyperplasia within the lungs.

Source : Epona Associates, LLC

Test condition : The inhalation chambers used in the study were constructed of stainless steel with glass windows for animal observations. Chamber volume was 1330 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. The animals were acclimated to the chamber (air-only exposure) for 2 days prior to the initiation of the exposure regimen. The position of the cages was rotated daily within each chamber.

Target concentrations of 0 and 150 mg/m3 were selected for this study. A 2% test substance hydrolysate solution was prepared daily and used to generate the aerosol atmosphere in the inhalation chamber. Chamber concentrations of test substance hydrolysate were determined by gravimetric methods. 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 once a day for the first 16 exposure days of the study. The data collected were analyzed by probit analysis (Finney, 1964) to obtain the mass median aerodynamic diameter (MMAD) and the geometric

standard deviation.

There were 15 rats per group. Five of the fifteen animals in each group were assigned to a satellite group destined for ultrastructural evaluation of the larynx. The male rats weighed 101 to 153 grams at initiation of exposure. Observation for mortality and clinical condition were performed daily. All animals were weighed prior to study initiation, weekly during the study, and immediately prior to study termination. Ten animals of the control and treated groups were subjected to a complete necropsy and the following tissues were fixed in 10% neutral buffered formalin for histologic evaluation: gross lesions, larynx, lungs, trachea, nasal turbinates and kidneys. For the satellite groups, the larynges of three control animals and five test substance-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 fomaldehyde. The larynges from these two rats were then further immersion-fixed in 2% glutaraldehyde. Other organs (brain, spinal cord, and peripheral nerves) were taken from these control animals and processed for light microscopic evaluation.

Test substance : A-1100: 99% Silane, gamma-aminopropyltriethoxysilane (CAS Number 919-30-2)

A 2% hydrolysate solution of the test substance was used to generate a respirable aerosol for inhalation.

Conclusion : Repeated exposure of rats to 147 mg/m3 of test substance hydrolysate respirable aerosol did not produce definitive evidence of the development of laryngeal granulomas, although squamous metaplasia and foci of minimal granulomatous laryngitis were observed.

Reliability : (2) valid with restrictions
08.01.2004 (15)

Type : Sub-acute
Species : rabbit
Sex : male/female
Strain : New Zealand white
Route of admin. : dermal
Exposure period : 6 hours/day
Frequency of treatm. : Animals in the 0, 17, and 84 mg/kg/day groups were treated for five consecutive days in the first week, followed by two days without treatment, and subsequently four consecutive days of treatment in the second week for a total of nine appli
Post exposure period : Not applicable. All animals were euthanized and necropsied upon completion of the treatment period; no recovery or other satellite groups were included.
Doses : 0, 17, 84, and 126 mg/kg/day
Control group : yes
Method : other
Year : 1988
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Method: Levene's test was done to test for variance homogeneity. In the case of heterogeneity of variance at $p < 0.05$, transformations were used to stabilize

the variance. Analysis of variance (ANOVA) was done on the homogeneous or ranked data. If the ANOVA was significant, Dunnett's t-test was used for pairwise comparison between groups. When no transformation established variance homogeneity at $p < 0.001$, the data were also examined by nonparametric techniques. These statistics include the Kruskal-Wallis H-test ANOVA and, if this test was significant, the Nemenyi-Kruskal-Wallis test for multiple comparisons or the Wilcoxon-Mann-Whitney two-sample rank test. Standard one-way ANOVA was used to analyze initial body weights, food consumptions, clinical chemistry and hematology values (except red blood cell morphology), organ weights, organ-to-body weight percentages, and organ-to-body weight ratios. Standard one-way analysis of covariance (ANCOVA) was used to analyze body weight, with initial body weight as the covariate. Although Levene's test for variance homogeneity was done, no transformations were used because covariance adjustment removed extraneous heterogeneity. If the ANCOVA was significant, Dunnett's t-test was used for pairwise comparisons between groups.

Result : No mortality occurred during the study. No treatment-related effects in body weights, food consumption, hematology, clinical chemistry, urinalysis, or organ weights occurred. Mild erythema and desquamation resulted from treatment with mineral oil alone (control group) and in the low dose group. The lesions occurred earlier in the animals in the 17 mg/kg/day group. Moderate to severe erythema, edema, desquamation, atonia, and fissuring developed progressively in both sexes treated with 84 mg/kg/day. Moderate to severe lesions were observed in the high dose group animals following the second treatment, and dosing was terminated after the third treatment. A slight improvement in erythema, edema, and atonia occurred following termination of the dosing, but desquamation and fissuring showed no significant improvement by the end of the study. Observations related to the test article at necropsy were restricted to cutaneous lesions at the treatment site. Microscopically, the test material resulted in moderately severe local skin changes characterized by crusting, acanthosis/hyperkeratosis, and ulcerative dermatitis primarily in the mid and high dose groups. Other tissues showed no microscopic changes related to test material treatment. Based on results from previous studies, kidneys from all animals were examined microscopically, but no lesions were observed in the treated animals.

The site of contact NOAEL was less than 17 mg/kg/day.

Source : Epona Associates, LLC

Test condition : The objective of this study was to evaluate the potential skin irritancy and systemic toxicity of the test article resulting from 9 applications over an 11-day exposure period.

There were 5 rabbits per sex in each group. Rabbits were approximately 18 weeks old at the initiation of dosing and body weight values ranged from 2976 to 3388 grams for the males and from 2885 to 3484 grams for the females. The test article was administered at a constant volume of 2.0 ml/kg /day in mineral oil (1%, 5% or 7.5% solutions) and the resulting dose levels corresponded to 17, 84 and 126 mg/kg/day. These dose levels were chosen based upon the

results of a four-day probe with the test material diluted to 1, 5, 7.5 and 10% in mineral oil. The control group was treated with mineral oil only, at the same volume. The doses were applied using the treatment regimen identified above. The animals given 126 mg/kg/day were treated with the test material at least 6 hours/day for 3 consecutive days and observed for any reversal of the cutaneous irritation for the remainder of the study. Prior to dosing and subsequently as required, the fur was clipped from the dorsal area of the trunk of each animal. The clipped area was covered with a gauze patch and the test solution was applied to the gauze patch. Each animal was then wrapped and returned to its cage for a period of 6 hours. At the end of the exposure period, the wrappings were removed and the exposure area was wiped with a dry cloth to remove any remaining test material.

The animals were observed twice daily for mortality and once daily for signs of local and systemic toxicity. Individual body weights were recorded on the first day of treatment (Day 1) and on Days 8 and 12. Food consumption was measured daily. Cutaneous irritation was scored daily for all animals immediately before each application of the test material, on the days when no test material was applied, and on the day of necropsy using a Draize scoring procedure. Clinical pathology parameters (hematology and serum chemistry) were evaluated on all animals at study termination (day 12). Blood samples were collected from the marginal ear vein and urine was collected from the urinary bladder following anesthesia. The following hematology parameters were evaluated: red blood cell count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, white blood cell count, and differential white blood cell count and blood cell morphology (relative and absolute: corrected white blood cell count, segmented neutrophils count, band neutrophils count, lymphocyte count, monocyte count, eosinophil count and basophil count). The following serum chemistry parameters were evaluated: alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, creatinine kinase, lactate dehydrogenase, sorbitol dehydrogenase, blood urea nitrogen, total protein, total bilirubin, direct bilirubin, indirect bilirubin, serum hemoglobin, creatinine, Ca, Na, K, Cl, P, glucose, albumin, and globulin. Urinalysis parameters included physical appearance, specific gravity, pH, protein, glucose, ketone, bilirubin, blood, urobilinogen, microscopic examination of sediment, and color. A complete necropsy was conducted on all animals.

The necropsy included, but was not limited to, examination of the external surface, all orifices and the cranial, thoracic, abdominal and pelvic cavities and their viscera, the external surfaces of the brain and spinal cord, and the nasal cavity and paranasal sinuses. At the time of necropsy, the following tissues and organs were collected and preserved in 10% neutral buffered formalin: adrenals (2), aorta, bone with marrow (sternum), brain (pons/cerebellar cortex; thalamus/cerebral cortex/hippocampus; caudate nucleus/cerebral cortex, eyes

preserved in Zenker's solution), gastrointestinal tract (esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum), heart, kidneys, liver, gallbladder, lungs (sections of right and left lobe and mainstem bronchi), lymph node (mesenteric and nonmesenteric), mammary gland (females only), ovaries, pancreas, peripheral nerve (sciatic), pituitary, prostate, salivary glands (submandibular), muscle (thigh), skin (treated and untreated), spinal cord (cervical, midthoracic, lumbar), spleen, sternum and bone marrow, testes, thymus, thyroid (with parathyroids if present), trachea, urinary bladder, uterus (corpus and cervix), vagina, and all gross lesions. The adrenals, brain, epididymides, heart, kidneys, lesions, liver, lungs, lymph nodes, ovaries, pituitary, spleen, sternum and bone marrow, testes, thymus, thyroid, and uterus were examined microscopically for all animals in the control and 84 mg/kg/day groups. Treated and untreated skin and kidneys were examined for all animals in the study.

Test substance : Organofunctional Silane A-1100: 99% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : Based on the results of this study, the test article is considered to be a significant skin irritant causing dose-dependent cutaneous lesions at doses as low as 17 mg/kg/day. However, the test article caused no systemic toxicity in rabbits after 9 repeated doses of 84 mg/kg/day or three repeated doses of 126 mg/kg/day.

Reliability : (1) valid without restriction

08.01.2004 (13)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Mammalian cell gene mutation assay
System of testing : Non-bacterial
Test concentration : 200, 600, 1800, 3000, 5000 ug/ml
Cycotoxic concentr. : >5000 ug/ml
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 476
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Methods: Two-sample t-test analysis
Result : Cytotoxicity test: Concentrations in the range of 50-5000 ug/ml were tested for induction of cytotoxicity. There was no effect of the test substance on cloning efficiency of the CHO cells in the presence or absence of metabolic activation at any concentration tested.

·Frequency of reversions/mutations/aberrations, polyploidy as appropriate: The frequency of mutations was low in all groups. In the absence of metabolic activation mutant frequencies of test substance treated cells were within the range of historical negative controls (i.e., 0-21 mutants per 10 (6) viable cells. The test substance did not produce a significant mutant frequency at any concentration tested in the absence of metabolic activation. In the presence of metabolic activation, the test substance did induce significant increases of the mutant frequencies at the concentration of 600 ug/ml. The observed mutant frequencies were with the range of the historical negative control (0-23 mutants per 10(6) viable cells) and did not show a dose response

relationship, the statistical significance is the result of normal assay variation rather than indicative of a mutagenic effect of the test substance.
·Precipitation concentration, if applicable: Not applicable
·Mitotic index: Not applicable

Source : Degussa

Test condition : Species/Strain or cell type and or cell line: Chinese Hamster ovary K-cells, HPRT locus

Metabolic activation:
·Species and cell type: Wistar rats, liver
·Quantity: Not reported
·Induced or not induced: Yes, with Phenobarbital and beta-Napthoflavone

·Test Design:
Ø Number of replicates: Two
Ø Frequency of dosing: One 4-hr exposure
Ø Positive and negative control groups and treatment: Ethyl methane sulfonate, 300 ug/ml, and 3-(20)-Methylcholantherene, 10 ug/ml, were used as positive controls. Ham's F12 medium with 2 mM L-Glutamine, 100 IU/ml Penicillin, and 100 ug/ml Streptomycin were used as negative control.
Ø Number of metaphases analyzed: Not applicable
·Solvent: Cell culture medium
·Description of follow up repeat study: No follow up repeat study was performed.
·Criteria for evaluating results (e.g. cell evaluated per dose group): The test compound was reported as positive if it caused a statistically significant, dose related increase in mutant frequency at test concentrations of the test substance resulting in greater than 20% cell survival. Also, a positive result was recorded only if the mean mutant frequency in treated cultures reached a value above the maximum spontaneous mutant frequency (of approximately 20/106 viable cells).

Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Reliability : (1) valid without restriction

16.01.2004 (20)

Type : Chromosomal aberration test
System of testing : V79 Chinese hamster lung cells
Test concentration : 50, 100, 200, 400, 600, 1000, 1800, 3000, 5000 ug/plate
Cycotoxic concentr. : >5000 ug/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 473
Year : 1999
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Methods: Chi-square test

Result : Cytotoxicity determination:Nine concentrations of the test substance (50-5000 ug/ml) in the presence and absence of metabolic activation were used to determine cytotoxicity and to set doses for the chromosme aberration study. Only after 18 hours exposure without metabolic activation was cytotoxicity observed.

The following test substance concentrations were scored for chromosomal aberrations:

0, 600, 3000, 5000 ug/ml: +/- S9 mix, 20 hours exposure; test#1
0, 600, 3000, 500 ug/ml: +/- S9 mix, 20 hours exposure; test#2

Frequency of aberrations, polyploidy
as appropriate: Without metabolic activation the cells treated with the test material revealed chromosomal aberrations frequencies excluding gaps of 0.0 to 2.0 % and with S9 mix was 1.0 to 3.5%. The frequency of polyploid cells in both parts of the experiment was within the expected range (<10%) of historical controls.

Source : Degussa

Test condition : Species/Strain or cell type and or cell line: V79 Chinese hamster lung cells
Metabolic activation: Yes
I.Species and cell type: S9
II.Quantity:
III.Induced with phenonobarbital/B-Napthoflavone

I.Test Design:
A.Number of replicates: Per experimental point, at least 2,000 cells (1,000 per slide) were scored.
B.Frequency of dosing: Single dose; 3 or 18 hours
C.Positive and negative control groups and treatment:
Positive controls were Mitomycin C (MMC) without metabolic activation andCyclophosphamide (CP) with metabolic activation. MEM4 served as negative control without activation and MEMO plus S9 mix was used for the assay with metabolic activation.
D.Number of metaphases analyzed: 2,000 cells (1,000 per slide.
II.Solvent: cell culture medium
III.Description of follow up repeat study:
IV.Criteria for evaluating results (e.g. cell evaluated per dose group): The test chemical is to be considered clastogenic in this assay if 1. it induces chromosomal aberrations (excl. gaps) in statistically significant manner in one or more concentrations 2. the induced proportion of aberrant cells at such test substance concentrations exceeds the normal range of the test system (i.e.>>5%) 3. positive results can be verified in an independent experiment.

Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

I. Provided by Sivento Chemie GmbH and >99% pure by GC

Conclusion : According to the author, in the in vitro cytogenetic assay, 3-aminopropyl-triethoxysilane did not induce statistically and biologically significant increases in the chromosomal aberration frequency of V79 Chinese hamster cells and is therefore judged to be not clastogenic in vitro.

Reliability : (1) valid without restriction
16.01.2004 (2) (21) (29) (36) (47) (51) (52) (54)

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium strains TA 97, TA 98, TA 100, TA1535, TA1537, and TA1536
Test concentration : Without S9: 0.01, 0.03, 0.1, 0.3, and 1.0 mg/plate

With S9: 0.3, 1.0, 3.0, 10.0, and 20.0 mg/plate
Cycotoxic concentr. : > or = 3 mg/plate
Metabolic activation : with and without
Result : negative
Method : other

Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	EPA Health Effect Test Guidelines EPA Report No. 560/6-84-002 (October, 1984) Statistical Methods: Responses (number of revertants) to the test substance were compared to concurrent negative and positive controls, as well as to historical data.
Result	:	Mutagenic activity was not observed with any of the five bacterial strains tested with or without the presence of an Aroclor 1254-induced rat liver S9 metabolic activation system. No cytotoxicity was observed with any of the dose levels tested without S9 activation. However, the highest two dose levels tested in the presence of S9 showed evidence of treatment related cytotoxicity with all five strains as either sparse growth or a total absence of growth of the background lawn of bacteria. Strain TA 1537 also showed signs of toxicity at the 3-mg/kg dose level.
Source	:	Epona Associates, LLC
Test condition	:	Species/Strain or cell type and or cell line, bacterial or non-bacterial: Salmonella typhimurium: TA 98, TA 100, TA 1535, TA 1537 and TA 1538 Metabolic activation: Species and cell type: Rat liver Quantity: 0.5 ml of a 9000 x g supernatant of rat liver homogenate per ml of reaction mixture Induced or not induced: Yes: Aroclor 1254 The control and test substance were administered once. The solvent (negative control) for all treatments/strains was dimethylsulfoxide (DMSO).
Test substance	:	Organofunctional Silane A-1100: 99.4% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion	:	Appropriate concurrent negative and positive controls were included, and the expected responses were observed. The test substance, gamma-aminopropyltriethoxysilane, did not demonstrate genetic activity in any of the tests conducted in this evaluation, both with and without metabolic activation. The results indicate that the test substance was not considered mutagenic under these test conditions.
Reliability	:	(1) valid without restriction
06.08.2003		(9)
Type	:	Mammalian cell gene mutation assay
System of testing	:	CHO-K1-BH4 (Subclone D1), HGPRT locus
Test concentration	:	Without activation: 0.3, 0.6, 1.0, 2.0, and 2.5 mg/ml With activation: 0.3, 0.6, 1.0, 2.0, 3.0, and 4.0 mg/ml
Cycotoxic concentr.	:	3 mg/ml without activation; 5.0 with activation
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : EPA Health Effects Test Guidelines, EPA report no. 560/6-83-001 (October 1983); HG-DNA-Sister Chrom. In Vitro Fed. Reg. 50 (#188) Sept. 27, 1985, amend Fed. Reg. 51 9# 9) January 14, 1986.

Statistical Methods: The data were analyzed in comparison to concurrent control values after transformation of the mutation frequencies (MF) values according to the conversion method of Box and Cox (1964). This procedure for CHO data follows procedures described by Snee and Irr: (MF + 1)0.15 (1981). For CHO mutation studies with a concurrent control frequency of zero mutants, the variance of recent historical controls was used for the statistical analyses. Positive controls for the CHO mutation test were run concurrently to assess the sensitivity of the assays in comparison to historical experiment with the test system. Data for positive control agents were not compared statistically whenever differences were at least 5 times the concurrent negative control value and results were within the historical positive control range. All statistical tests were performed to determine whether the treatment with the test agent produced a response statistically different from the value(s) obtained with the concurrent solvent control.

Result : Quantitative cytotoxicity data were determined in a preliminary cytotoxicity test and the results were as follows:

Conc Test Subst. (mg/ml)	% Relative to solvent control Without S-9	With S-9
0.001	101.9	92.1
0.003	87.2	95.9
0.01	90.2	91.2
0.03	82.2	91.6
0.1	89.7	96.9
0.3	83.9	89.0
1	62.1	80.7
3	cytotoxic	19.9
5	cytotoxic	cytotoxic

The test material did not produce any dose-related increases in the incidence of mutations of CHO cells at concentrations between 0.3 to 2.5 mg/ml in tests without an S9 metabolic activation system. However, mutation values were outside of acceptable historical control limits for one of the two solvent control cultures and for most cultures treated with the test material. Because of similar instability with CHO cells in other recent tests at BRRC, the reproducibility of these increases was determined in a second, independent test using a freshly thawed culture of CHO cells. No indication of positive genotoxic increases was evident either in the repeat test without S9 activation or in the mutation test conducted with S9 activation.

Source : Epona Associates, LLC

Test condition : Species/Strain or cell type and or cell line, bacterial or non-bacterial: CHO-K1-BH4 (Subclone D1); HGPRT locus.
Metabolic Activation: Yes, both with and without
Species and cell type: Rat liver
Quantity: 50 µl of a 9000 x g supernatant of rat liver homogenate per ml of reaction mixture
Induced or not induced: Yes

Selection of test concentrations: In a preliminary study, CHO cells were exposed for five hours to a range of concentrations from 0.001 to 5.0 mg/ml of the test material to determine relative cytotoxicity and an appropriate range of test doses. Dimethylsulfoxide (DMSO) was used as the solvent for dilutions. All dilutions were prepared immediately prior to testing. The cytotoxicity of the various concentrations, tested both in the presence and absence of an S9 metabolic activation system, was determined by measuring the relative growth of treated and controls cells incubated overnight following removal of the test chemical. The test material was highly cytotoxic and a concentration of 3 mg/ml or higher in the test without S9 activation produced complete lysis of CHO cells tested. In the test with S9 activation, slightly less cytotoxicity was observed at 3 mg/ml but 5 mg/ml was lethal to CHO cells. Based on these results, a concentration range between 0.06 to 2.5 mg/ml was tested in the mutagenicity test without S9 while concentrations between 0.3 to 4.0 mg/ml were tested in the presence of S9. A repeat test conducted without S9 activation tested concentrations between 0.3 to 2.5 mg/ml.

Definitive test: Duplicate cultures of CHO cells were exposed for 5 hours to a minimum of five concentrations of the test material in test both without and without the addition of a rat-liver S9 metabolic activation system. Various dose levels of the test material were attained by direct addition of various aliquots of the diluted test agent into the cell culture medium. DMSO was used as the diluent. All dilutions were freshly prepared prior to testing. The surviving fraction was determined at 18 to 24 hours after the removal of the test material using 4 plates/culture and 100 cells/plate. The mutant fraction was determined after a 9 to 12 day sub-culturing period to allow "expression" of the mutant phenotype. The mutant fraction was assessed in selective medium with 2 x 105 cells/plate in 5 plates/dosed culture (i.e. 1 x 106 total cells/dosed culture). The plating efficiency of these cells was assessed in non-selective medium using 4 plates/dosed culture with 100 cells/plate. The mutagenicity/survival/plating efficiency data from at least the top five concentrations that allowed sufficient cell survival for assessment of survival and quantification of mutants were recorded. The percentage of cells surviving the treatment, the numbers of mutant colonies, the percentage of clonable cells and the calculated number of mutants/106 clonable cells were calculated.

Test substance : Organofunctional Silane A-1100: 99.4% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

Conclusion : Silane, gamma-aminopropyltriethoxy- (CAS No. 919-30-2) was concluded to lack significant genotoxic potential under conditions of the CHO mutation test system.

Appropriate concurrent negative and positive controls were included and the expected responses were observed. The test substance, gamma-aminopropyltriethoxysilane (CAS No. 919-30-2), did not demonstrate genetic activity in this evaluation, both with and without metabolic activation. The results indicate that the test substance was not considered mutagenic under these test conditions.

Reliability : (1) valid without restriction
08.01.2004 (11)

Type : Salmonella typhimurium reverse mutation assay
System of testing : Salmonella typhimurium strains TA 98, TA 100, TA 1535, and TA 1537
Test concentration : 0, 50, 160, 500, 1600 and 5000 ug/plate
Cycotoxic concentr. : >5000 ug/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Method: None. A doubling of the mean revertants per plate accompanied by a dose response constituted a positive response.
Result : I. Frequency of reversions/mutations/aberrations, polyploidy as appropriate: The frequency of reversions was low in all groups.
II. Precipitation concentration, if applicable: Not applicable
III. Mitotic index: Not applicable
Source : Degussa
Test condition : Species/Strain or cell type and or cell line, bacterial or non-bacterial: Salmonella typhimurium strains TA 98, TA 100, TA 1535, and TA 1537

Metabolic activation:
I. Species and cell type: Wistar rats, liver
II. Quantity: 0.5 ml
III. Induced or not induced: Induced, with Phenobarbital
and beta-naphthoflavone

I. Test Design:
A. Number of replicates: Three
B. Frequency of dosing: Once
C. Positive and negative control groups and treatment: 2-aminoanthracene, 2.5 ug/plate, and 2-nitrofluorine, 2.5 micrograms/plate were used as positive controls. DMSO was used as a negative control.
D. Number of metaphases analyzed: Not applicable
II. Solvent: DMSO
III. Description of follow up repeat study: A preincubation period test was followed by a plate incorporation test.
IV. Criteria for evaluating results (e.g. cell evaluated per dose group): A doubling of the mean revertants per place accompanied by a dose response constituted a positive response.
Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion : Not genotoxic
Reliability : (1) valid without restriction
06.08.2003 (19)

Type : Salmonella typhimurium reverse mutation assay
System of testing : Salmonella typhimurium strains TA 97, TA 98, and TA 100
Test concentration : 0, 8, 40, 200, 1000, and 5000 ug/plate
Cycotoxic concentr. : >5000 ug/plate
Metabolic activation : with and without
Result : negative

Method : OECD Guide-line 471
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Analysis of variance (F-test) and regression analysis
Result : · Frequency of reversions/mutations/aberrations, polyploidy as appropriate: The treatment did not cause a two fold increase in mean revertant numbers compared with the solvent control, with any tester strain either in the absence or presence of S-9.
· Precipitation concentration, if applicable: Not applicable
· Mitotic index: Not applicable
Source : Degussa
Test condition : Species/Strain or cell type and or cell line, bacterial or non-bacterial: Salmonella typhimurium strains TA 97, TA 98, and TA 100
Metabolic activation:
· Species and cell type: Wistar rat, liver
· Quantity: 1.0 ml
· Induced or not induced: Induced with Aroclor-1254

· Test Design:
Ø Number of replicates: One
Ø Frequency of dosing: Once
Ø Positive 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 ethyl glycol dimethyl either (EGDME).
Ø Number 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 : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Reliability : (1) valid without restriction
21.06.2003 (17)

Type : Ames test
System of testing : Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Test concentration : unknown
Cycotoxic concentr. : With metabolic activation: Bacterial toxicity was observed at 100ug/plate in any of the strains with or metabolic activation; Without metabolic activation: Bacterial toxicity was observed at 100ug/plate in any of the strains without
Metabolic activation : with and without
Result : negative
Method : other
Year : 1977
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Method unknown
Remark : The above information is from a 1-page summary and therefore contains many unknowns. The original report exists only in

Japanese.

Result : I. Frequency of reversions/mutations/aberrations, polyploidy as appropriate: No increase in the number of the revertant colonies was observed at 0.1 to 10ug/plate in any of the strains tested with or without metabolic activation.
II. Precipitation concentration, if applicable:
III. Mitotic index:

Source : Lesser Ketones Manufacturing Association Leesburg, VA

Test condition : I. Test Design:
A. Number of replicates: Unknown
B. Frequency of dosing: Unknown
C. Positive and negative control groups and treatment: Unknown
D. Number of metaphases analyzed: Unknown
II. Solvent: Unknown
III. Description of follow up repeat study:
IV. Criteria for evaluating results (e.g. cell evaluated per dose group):

Test substance : 1-Propanamine, 3-(triethoxysilyl)-CAS# 919-30-2 Synonym-3-Aminopropyl triethoxy silane

Conclusion : The summary page stated " the test material was judged to be non-mutagenic to the bacteria in the test conditions.

Reliability : (4) not assignable

06.08.2003 (30)

Type : Ames test

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

Test concentration : Unknown

Cycotoxic concentr. : see result

Metabolic activation : with and without

Result : negative

Method : other

Year : 1994

GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Method : EPA Health Effect Test Guidelines EPA Report No. 560/6-84-002 (October, 1984).

Statistical Methods: Responses (number of revertants) to the test substance were compared to concurrent negative and positive controls, as well as to historical data.

Remark : The above information is from a 1-page summary and therefore contains many unknowns. The original report exists only in Japanese.

Result : I. Frequency of reversions/mutations/aberrations, polyploidy as appropriate: No increase in the number of the revertant colonies in comparison with the solvent control was observed in any concentration from 313 to 5000 ug/plate of the substance in any strain with or without metabolic activation.
II. Precipitation concentration, if applicable:
III. Mitotic index:

Source : Lesser Ketones Manufacturing Association Leesburg, VA

Test condition : Species/Strain or cell type and or cell line, bacterial or non-bacterial: Salmonella typhimurium: TA 98, TA 100, TA 1535, TA 1537 and TA 1538
Metabolic activation: Yes, both with and without

Species and cell type: Rat liver

Quantity: 0.5 ml of a 9000 x g supernatant of rat liver homogenate per ml of reaction mixture

Induced or not induced: Yes: Aroclor 1254

I. Test Design:
A. Number of replicates: Unknown
B. Frequency of dosing: Unknown
C. Positive and negative control groups and treatment: Unknown except for solvent control.
D. Number of metaphases analyzed: Unknown
II. Solvent: DMSO
III. Description of follow up repeat study:
IV. Criteria for evaluating results (e.g. cell evaluated per dose group):

Test substance : Organofunctional Silane A-1100: 99.4%
Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

I. No information provided with regard to test substance, see general remarks.

Conclusion : The summary page stated "It was concluded that the test material is non-mutagenic in the bacteria in the test conditions.

Reliability : (4) not assignable
06.08.2003 (37)

Type : Chromosomal aberration test
System of testing : Fibroblast cells of CHinese hamster (CHL/IU)
Test concentration : 575, 1150 and 2300 ug/ml
Cycotoxic concentr. : not reported
Metabolic activation : with and without
Result : negative
Method : other
Year : 1994
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Based on the Japanese guidelines for the testing of chemicals.
Remark : The above information is from a 2-page summary and therefore contains many unknowns. The original report exists only in Japanese. The year of testing was not reported.
Result : I. Frequency of reversions/mutations/aberrations, polyploidy as appropriate: No increase in the number of the revertant colonies was observed at 0.1 to 10ug/plate in any of the strains tested with or without metabolic activation.
II. Precipitation concentration, if applicable:
III. Mitotic index: Mitotic indices were nearly 100% at 2300 micrograms/ml in 24 hr treatment in the direct method, and in the absence of S9mix and in the presence of S9mix in the metabolic activation method.
The test results revealed the incidence of cells with chromosome aberration, structural or numerical, was lower than 5%, while those with the positive controls MMC and CPA exceeded 50% and 20%, respectively.
Source : Lesser Ketones Manufacturing Association Leesburg, VA
Test condition : Species/Strain or cell type and or cell line, bacterial or non-bacterial: Fibroblast cells of Chinese hamster (CHL/IU)
Metabolic activation:
I. Species and cell type: S9
II. Quantity: Unknown

III. Induced or not induced: unknown

I. Test Design:
A. Number of replicates: Unknown
B. Frequency of dosing: Unknown
C. Positive and negative control groups and treatment: Unknown
D. Number of metaphases analyzed: Unknown
II. Solvent: DMSO
III. Description of follow up repeat study:
IV. Criteria for evaluating results (e.g. cell evaluated per dose group):

Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)

I. No information provided with regard to test substance, see general remarks.

Conclusion : The summary page stated " the test material was decided not to induce any chromosome aberration in the test conditions.

Reliability : (4) not assignable

06.08.2003 (38)

Type : Sister chromatid exchange assay
System of testing : CHO-K1-BH4 (Subclone D1)
Test concentration : 0.06 to 2.50 mg/ml (without S-9)
0.3 to 4 mg/ml (with S-9)

Cycotoxic concentr. : 3 mg/ml
Metabolic activation : with and without
Result : negative
Method : other: EPA Health Effects Test Guidelines, EPA report no. 560/6-83-001 (October 1983); HG-DNA-Sister Chrom. In Vitro Fed. Reg. 50 (#188) Sept. 27, 1985, amend Fed. Reg. 51 9# 9) January 14, 1986.
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The data were analyzed in comparison to concurrent control values after transformation of the SCE values according to the conversion method of Box and Cox (1964). This procedure for CHO data follows procedures described by Snee and Irr: (MF + 1)0.15 (1981). For SCE data, statistical analyses of historical data at BRRC indicated that an exponent of 0.15 is the appropriate value for transformation of SCE values. All statistical tests were performed to determine whether the treatment with the test agent produced a response statistically different from the value(s) obtained with the concurrent solvent control.

Result : The test material did not produce dose-related or statistically significant increases in the incidences of SCEs in CHO cells in tests both with and without the incorporation of an S9 metabolic activation system. No remarkable effects upon the progression of the cells through the mitotic cycle were evident in determinations of numbers of cells at the first vs. second stage of mitosis. The expected responses were observed with the positive controls, confirming the sensitivity of the assay.

Source : Epona Associates, LLC

Test condition : Dose selection: Selection of a suitable range of doses for testing was based upon preliminary experiments to determine relative cytotoxicity of the test chemical. In these tests, a concentration of 3 mg/ml produced 80.1% inhibition of growth when tested with an S9 metabolic activation system. The 3 mg/ml dose tested without metabolic activation produced excessive cytotoxicity and lysed or detached the CHO cells in the culture dish which prevented counting. For the definitive tests to determine potential effects upon SCEs, a range of doses was tested both with and

without addition of an S9 metabolic activation system. The highest three doses which allowed a sufficient number of mitotic cells were scored for SCEs.

Definitive test: For determination of direct genotoxic action, CHO cells were exposed to the test substance and appropriate controls for 5 hours without S9 activation. Indirect activity, requiring metabolic activation by liver S9 homogenate, was studied with a 2-hour exposure period. Bromodeoxyuridine (BrdU) was present at a concentration of 3 µg/ml in the growth medium during treatment and during the culture period following exposure. A total of twenty-five cells/concentration was examined for SCE frequencies using duplicate cultures. At least 5 dose levels were tested both with and without metabolic activation. SCE production was determined for the highest 3 doses which did not produce excessive cytotoxic inhibition of cell division. The number of SCEs/cell, mean number of SCEs/chromosome and the level of statistical significance of the increases above the concurrent solvent control values were calculated.

Test substance : Silane, gamma-aminopropyltriethoxy- (CAS No. 919-30-2)
Purity 99.4 %

Conclusion : Silane, gamma-aminopropyltriethoxy- (CAS No. 919-30-2) was concluded to lack significant DNA damage activity under conditions of the SCE test system.

Reliability : (1) valid without restriction
08.01.2004 (11)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : Swiss Webster
Route of admin. : i.p.
Exposure period : single dose
Doses : 160, 128 and 102 mg/kg; micronucleus study: 90, 56 and 28 mg/kg.
Result : negative
Method : other
Year : 1988
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : EPA Health Effects Test Guidelines, EPA Report 560/6-83-001; Schlegel and MacGregor, Mutation Research 104 (367-369) 1982.

Statistical Methods: LD50 calculated using the probit method; Fisher's Exact test used to compare for significant differences from vehicle control micronuclei frequencies

Result : Effect on mitotic index or PCE/NCE ratio by dose level by sex: Toxicity study: the PCE/NCE ratio of the vehicle control and the highest dose level with more than 3 survivors was quantified and compared to determine possible bone marrow toxicity at 48 hours. The PCE/NCE ratio was not reduced in male or female mice in comparison to control values. It was not necessary to assess bone marrow toxicity at 72 hours post-dosing. Micronucleus study: No statistically significant decreases in the PCE/NCE ratio relative to the control values were observed at any of the three sample periods. Female mice sampled at the 48-hour period had moderate decrease in the PCE/NCE ratio relative

to control value. Analysis of Variance testing showed that these decreases were not significantly different.

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal): negative

Mortality at each dose level by sex:

Dose (mg/kg)	Sex	No. Dead	% Mortality
65	M	0/5	0
82	M	0/5	0
102	M	0/5	0
128	M	3/5	60
160	M	5/5	100
65	F	0/5	0
82	F	0/5	0
102	F	3/5	60
128	F	5/5	100
160	F	5/5	100
Control	M	0/5	0
Control	F	0/5	0

Mutant/aberration/mPCE/polyploidy frequency, as appropriate:

Toxicity Test

Dose (mg/kg)	Sex	Mean PCE/1000 NCE +/- (S.D.)	%Control
102	M	32.6 (12.1)	111.6%
Control	M	29.2 (5.1)	
82	F	44.2 (11.2)	120.8%
Control	F	36.6 (6.7)	

Micronucleus Test (30 hour sample)

Dose (mg/kg)	Sex	#PCE Observed	#mPCE	%mPCE
control	combined	10,000	18	0.18
28	combined	10,000	29	0.29
56	combined	10,000	19	0.19
90	combined	10,000	17	0.17
+ control	combined	10,000	245	2.45 (a)

Micronucleus Test (48 hour sample)

Dose (mg/kg)	Sex	#PCE Observed	#mPCE	%mPCE
control	M	5000	15	0.30
control	F	5000	3	0.06
28	M	5000	23	0.46
28	F	5000	10	0.20(b)
56	M	5000	13	0.26
56	F	5000	11	0.22(b)
90	M	5000	15	0.30
90	F	5000	10	0.20(b)

Micronucleus test (72 hour sample)

Dose (mg/kg)	Sex	#PCE Observed	#mPCE	%mPCE
control	M	5000	15	0.30
control	F	5000	8	0.16
28	M	5000	14	0.28
28	F	5000	1	0.02
56	M	5000	6	0.12
56	F	5000	3	0.06
90	M	5000	12	0.24
90	F	5000	5	0.10

(a) = statistically significant increase above control, p< 0.001
(b) = statistically significant increase above control, 0.05>p> 0.01

Source : Epona Associates, LLC

Test condition :
- Age at study initiation: 5 weeks old
- No. of animals per dose: 5/sex
- Vehicle: corn oil
- Duration of test: single dose, blood smears prepared at 30, 48 and 72 hours post-dosing.
- Frequency of treatment: single dose
- Sampling times and number of samples: blood smears prepared at 30, 48 and 72 hours post-dosing.
- Control groups and treatment: 5/sex, blood smears prepared at 30 hours post-dosing.
- Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): Chromosome damage was measured by quantifying the incidence of micronuclei in peripheral blood polychromatic erythrocytes (PCE). A minimum of 1000 PCEs was examined microscopically for each animal/sample time, unless cytotoxicity prevented this goal. The PCE: normochromatic erythrocyte (NCE) ratio for approximately 1000 total cells was calculated as an estimate of cytotoxicity.
- Criteria for selection of M.T.D.: Three dose levels of approximately 80, 50 and 25% of the LD50 value were evaluated for effects on the incidence of micronuclei.

Test substance : 1-Propanamine, 3-(triethoxysilyl); CAS No. 919-30-2

Purity: 99.4%

Conclusion : CAS No. 919-30-2 was not an active agent in producing treatment related increases in numbers of micronuclei in PCEs in Swiss-Webster mice. Relatively high dose levels of CAS No. 919-30-2 were tested up to 80% of the LD50 with no indication of a positive induction of micronuclei. CAS No. 919-30-2 was considered to be inactive as a clastogenic agent under the statistical criteria used.

Reliability : (1) valid without restriction
Statistically significant increases were observed with the female mice sampled at the 48 hour sample period. However, these statistical increases were the result of the unusually low spontaneous incidence of the concurrent vehicle control group. There was no evidence of a treatment related increase in the micronucleus frequency and the micronucleus responses for the treated mice were within the histroical range of variability for this test system. The statistically significant increases observed for the female mice at the 48 hour sample period were not considered biologically significant.

Flag : Critical study for SIDS endpoint

06.08.2003 (10)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type : other:90 day study with reproductive endpoints

Species : rat

Sex : male/female

Strain	:	other: Crl:CD (SD)BR
Route of admin.	:	gavage
Exposure period	:	91 or 92 days
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	70, 200 and 600 mg/kg/day
Control group	:	yes
other: NOAEL systemic	:	= 200 mg/kg bw
other: NOAEL reproductive	:	>= 600 mg/kg bw
Result	:	no effect on fertility
Method	:	other: in general compliance with USEPA OPPTS Guideline 870.3100 (August 1998) and OECD Guidelines for Testing of Chemicals, Section 408 (September 1998).
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	OECD Guideline 408 Statistical Method: All analyses were conducted using two-tailed tests for minimum significance levels of 1% and 5% comparing the test article-treated groups to the control group by sex. All means were presented with standard deviations (S.D.) and the number of sampling units (N) used to calculate the means. Statistical analyses were not conducted if the number of animals was two or less. All statistical tests were performed using appropriate computing devices or programs. Body weight, body weight change, food consumption, clinical pathology, absolute and relative organ weight data and epididymal and testicular sperm numbers and sperm production rates were subjected to a one-way analysis of variance (ANOVA), followed by Dunnett's test if the ANOVA revealed statistical significance ($p<0.05$). The percentage of motile spermatozoa and the percentage of sperm with normal morphology were analyzed by the Kruskal-Wallis nonparametric ANOVA test to determine intergrouup differences, followed by the Mann-Whitney U-Test comparing the control and test article-treated groups if the ANOVA revealed statistical significance ($p<0.05$). Clinical laboratory values for leukocytes that occur at a low incidence (i.e., monocytes, eosinophils and basophils) were not subjected to statistical analysis.
Remark	:	600 mg/kg/day was the highest dose tested; at this dose no effects were seen on parameters of oestrous cysle and spermatogenesis or reproductive organs. The true NOAEL for reproductive organ toxicity may be much higher.
Result	:	90-Day Oral Gavage Toxicity Study: Reproductive Organ Toxicity: There were no effects of treatment on estrous cycle data or spermatogenic endpoints. No other test article-related reproductive organ microscopic changes were observed. The NOAEL for reproductive endpoints is 600 mg/kg/day. The NOAEL for systemic toxicity is 200 mg/kg/day. Dose-range-finding study: gamma-aminopropyltriethoxysilane was administered in peanut oil orally (by gavage) to three groups of rats

(five/sex) for rats were administered gamma-aminopropyltriethoxysilane in peanut oil at dosage levels of 70, 200 and 600 mg/kg/day. A concurrent control group received the vehicle on a comparable regimen. Survival was unaffected by gamma-aminopropyltriethoxysilane administration. No test-article related findings were observed at the macroscopic or microscopic examinations. Organ weights were unaffected by treatment. Clinical signs included one or more instances of rales and/or labored respiration in the 600 mg/kg/day group. These findings were noted in two males and two females during the last three days of dosing prior to necropsy. There were no statistically significant differences in body weights, body weight gains, or food consumption. However, there were reductions in body weight gains and food consumption in the 600 mg/kg/day males during weeks 0 to 1 and 1 to 2. The no-observed-adverse-effect level (NOAEL) for gamma-aminopropyltriethoxysilane in rats following a 14-day repeated treatment via gavage was 200 mg/kg/day.

Source : Epona Associates, LLC

Test condition : The objective of this study was to evaluate the possible toxic effects of gamma-aminopropyltriethoxysilane when administered orally (gavage) to rats for a minimum of 90 days.
Dose-range finding study: gamma-aminopropyltriethoxysilane was administered in peanut oil orally (by gavage) to three groups of rats (five/sex) for rats were administered gamma-aminopropyltriethoxysilane in peanut oil at dosage levels of 70, 200 and 600 mg/kg/day. A concurrent control group received the vehicle on a comparable regimen. All animals were dosed at a volume of 10 mL/kg. The animals were observed twice daily for mortality and moribundity. Clinical exams were performed daily and detailed physical examinations were performed weekly. Individual body weights and food consumption were recorded weekly. Complete necropsies were performed on all animals and selected organs were weighed. Selected tissues were examined microscopically from all animals.

90-Day Oral gavage Toxicity Study: Dose levels of 70, 200 and 600 mg/kg/day were selected for the 90-day oral (gavage) toxicity study of gamma-aminopropyltriethoxysilane in rats. There were 15 rats per sex in each group. Young adult rats were approximately seven weeks old at the initiation of dosing and body weight values ranged from 213 to 279 grams for the males and from 150 to 207 grams for the females. Ocular examinations were conducted on all animals prior to the initiation of dosing (week -1) and during week 12. All ocular examinations were conducted using an indirect ophthalmoscope, preceded by pupillary dilation with an appropriate mydriatic agent. The test article in the vehicle, peanut oil sparged with nitrogen, was administered orally by gavage to three groups (15/sex/group) of Crl:CDÒ(SD)BR rats for 91 or 92 consecutive days at dosage levels of 70, 200 and 600 mg/kg/day. These dose levels were chosen based upon the results of the previous 14-day range-finding study. A concurrent control group received the vehicle on a comparable regimen. The animals were observed twice daily, once in the morning and once in the afternoon, for mortality and moribundity. Clinical observations were performed on all animals prior to and approximately 1-2 hours following dosing. All significant findings were recorded. Detailed physical examinations were conducted weekly during the study period and just prior to the scheduled necropsy. Animals were routinely observed in their home cages and while being handled and weighed. Individual body weights were recorded weekly beginning one week prior to randomization (week -1). Mean body weight changes were calculated for each week. A final (fasted) body weight was recorded for each animal on the day of scheduled necropsy. Individual food consumption was measured weekly beginning one week prior to randomization (week ?1). Food intake was calculated as g/animal/day for the corresponding body weight intervals. When food consumption could not be measured for a given interval (due to spillage,

weighing error, etc.), the appropriate interval was footnoted as "NA" (Not Applicable) on the individual tables. Clinical pathology parameters (hematology and serum chemistry) were evaluated on all animals during week 4 and at study termination (week 13). The animals were fasted overnight prior to the collection of blood samples. Blood samples for general clinical pathology evaluations were collected from a lateral tail vein at both time points. Blood samples for assessment of coagulation parameters were collected from the vena cava at the time of necropsy. The following hematology parameters were evaluated: total leukocyte count (white cell), erythrocyte count (red cells), hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, prothrombin time, activated partial thromboplastin time (APTT; terminal evaluation only), reticulocyte count (percent and absolute), differential leukocyte count (percent and absolute: neutrophil, lymphocyte, monocyte, eosinophil and basophil). The following serum chemistry parameters were evaluated: alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, blood urea nitrogen, total protein, total bilirubin, creatinine, Ca, Na, K, Cl, P, glucose, albumin, globulin, albumin/globulin ratio, and total cholesterol. Urine samples were collected via metabolism chambers following the eighth exposure of female rats and following the seventh exposure of male rats. Urine volume was measured using calibrated test tubes, and urine color and turbidity were visually assessed. Urinalysis parameters were urine osmolality, pH, protein, glucose, ketone, bilirubin, blood and urobilinogen. Vaginal smears for determination of the stage of estrus were obtained from all surviving females once daily beginning 21 days prior to the scheduled necropsy. The average cycle length was calculated for complete estrous cycles (i.e., the total number of returns to metestrus [M] or diestrus [D] from estrus [E] or proestrus [P]) beginning 21 days prior to the scheduled necropsy. The final vaginal smear for each female was collected on the day of necropsy. A complete necropsy was conducted on all animals. Animals euthanized in extremis or at the scheduled necropsy were euthanized by carbon dioxide asphyxiation followed by exsanguinations. The necropsy included, but was not limited to, examination of the external surface, all orifices and the cranial, abdominal and pelvic cavities and their viscera. At the time of necropsy, the following tissues and organs were collected and preserved in 10% neutral buffered formalin: adrenals (2), aorta, bone with marrow (femur, sternebrae), bone marrow smear (from femur), brain (forebrain, midbrain, hindbrain), coagulating gland, eyes with optic nerve (2; preserved in Davidson's solution), gastrointestinal tract (esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum), heart, kidneys (2), liver (sections of two lobes), lungs (including bronchi, fixed by inflation with fixation), lymph node (mesenteric, submandibular), mammary gland (females only), ovaries with oviducts (2), pancreas, peripheral nerve (sciatic), pituitary, prostate, salivary glands (submaxillary, 2), seminal vesicles (2), skeletal muscle (vastus medialis), skin, spinal cord (cervical, midthoracic, lumbar), spleen, testis with epididymis (1) and vas deferens, thymus, thyroid (with parathyroids if present (2)), trachea, urinary bladder, uterus with vagina and cervix, and all gross lesions (when possible). Bone marrow smears were obtained from all animals not found dead, but were not placed in 10% neutral buffered formalin. The right testis/epididymis from all males at the scheduled necropsy and both testes/epididymides from those males found dead were preserved in Bouin's solution and prepared for microscopic examination using PAS/hematoxylin staining. The left testis/epididymis from all males euthanized at the scheduled necropsy were prepared for sperm analysis as described below. The following organs from animals euthanized at the scheduled necropsy were weighed: adrenals, brain, epididymides (weighed separately; total and cauda), kidneys, liver, ovaries (with oviducts), pituitary, prostate, seminal vesicles with coagulating glands (with accessory fluids), testes (weighed

separately), and thyroid (fixed weight). Organ to final body weight and organ to brain weight ratios were calculated. After fixation, specified tissues were trimmed according to standard operating procedures. Trimmed tissues were processed into paraffin blocks, sectioned at five to eight microns, mounted on clean glass microscope slides and stained with hematoxylin and eosin. The tissues noted above from all animals found dead or euthanized in extremis and from all animals in the control and 600 mg/kg/day groups euthanized at the scheduled necropsy, as well as the lungs, liver, and kidneys from all animals in the 70 and 200 mg/kg/day groups were examined microscopically. In addition, PAS/hematoxylin-stained sections of the right testis and epididymis from all males were examined microscopically at the scheduled necropsy. Spermatogenic analysis was conducted according to the following protocol. For motility/viability assessment, immediately following euthanasia, the reproductive tract of each male was exposed via a ventral mid-line incision. The right epididymis was excised and weighed separately. An incision was made in the distal region of the cauda epididymis. The cauda was then placed in Dulbecco's phosphate-buffered saline (maintained at approximately 37oC) with 10 mg/ml Bovine Serum Albumin (BSA). A sample of the diluted sperm was then loaded into a 100 µm cannula for determination of motility. As sperm motility can be affected by temperature shock, all cannulas, diluents and slides were pre-warmed and maintained at approximately 37oC. Motility determinations were performed under constant temperature using the Hamilton-Thorne HTM-IVOS Version 10 computer-assisted sperm analysis (CASA) system. At least 200 (if possible) motile and nonmotile spermatozoa/animal were analyzed. A sample of sperm for morphology assessment was obtained from the right cauda epididymis of each male. Sperm morphology was evaluated using a modification of the wet-mount technique described by Linder et al., 1992. Abnormal forms of sperm (double heads, double tails, micro- or megacephalic, etc.) were recorded from a differential count of 200 spermatozoa/animal. For enumeration of epididymal and testicular sperm numbers and sperm production rates, the left testis and epididymis from each male at the scheduled necropsy were weighed and frozen, then homogenized and evaluated for sperm production rate using the method described by Blazak et al., 1985. Analyses were performed using the Hamilton-Thorne CASA system.

Conclusion : Although several of these test article-related findings (clinical signs, gaseous intestinal distension, hepatocellular vacuolation) also occurred at 0, 70 and/or 200 mg/kg/day, all were limited or sporadic in incidence. Based upon the results of this study, a no-observed-effect level (NOEL) was not determined. However, the no-observed-adverse-effect level (NOAEL) was 200 mg/kg/day.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

08.01.2004 (58)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	other
Route of admin.	:	gavage
Exposure period	:	day 6 of gestation through day 20 of gestation
Frequency of treatm.	:	once per day
Duration of test	:	Through day 20 of gestation
Doses	:	20, 100 or 600 mg/kg/day
Control group	:	yes
NOAEL maternal tox.	:	= 100 mg/kg bw

NOAEL teratogen. : = 100 mg/kg bw
LOAEL Maternal Toxicity : = 600 mg/kg bw
Method : EPA OTS 798.4900
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Health Effects Testing Guidelines (TSCA) September 1985

Statistical Methods: One-way analysis of variance (ANOVA) was used to analyze mean maternal gestation body weights, body weight changes, and food consumption, mean number of corpora lutea, implantation sites, live fetuses(male and female), postimplantation losses, resorptions (early and late), mean fetal weights (male and female), gravid uterine weights, carcass weights, and net weight change from day 0. If the ANOVA was significant, pairwise comparisons to the vehicle control were performed using Dunnett's test. A Kruskal-Wallis test was used to analyze mean percent preimplantation losses and live fetuses (male and female) per animal, mean percent postimplantation losses, dead fetuses, and resorptions (early and late) expressed as percentages of implantations per animal, mean percent affected fetuses per litter for external, visceral, and skeletal malformations and developmental variations, and mean percent affected fetuses per liter for external, visceral, and skeletal malformations and developmental variations. If the Kruskal-Wallis test was significant, pairwise comparisons to the vehicle control were made using a Mann-Whitney U test. A Pearson chi-square test was used to analyze fetal and litter incidence of fetal external, visceral and skeletal malformations and developmental variations, as well as litter incidence of total fetal external, visceral and skeletal malformations and developmental variations. If the chi-square test was significant, pairwise comparisons to the vehicle control were performed using a Fischer's exact test.

Result : - Mortality and day of death:

Dose (mg/kg/day)	No. Dead	Day of Death (gestation day)
0	0/30	-
20	0/30	-
100	0/30	-
600	5/30	7,7,13, 15,17

- Number pregnant per dose level:

Dose (mg/kg/day)	No. Pregnant
0	29/30
20	25/30
100	26/30
600	22/30

- Number aborting: none
- Number of resorptions, early/late if available:

Dose (mg/kg/day)	No. Resorptions (early + late)
0	34
20	25
100	38
600	25

- Number of implantations:

Dose (mg/kg/day)	No. Implantations
0	437
20	368
100	361
600	358

- Pre and post implantation loss:

Dose (mg/kg/day)	Preimplantation loss	Postimplantation loss
0	50	34
20	67	25
100	74	38
600	60	25

- Number of corpora lutea:

Dose (mg/kg/day)	No. Corpora lutea
0	487
20	435
100	435
600	418

- Duration of Pregnancy: 20 days
- Body weight: No significant body weight effects at any dose level. Slight decrease in body weight gain observed gd 6 through 9 at 600 mg/kg/day considered treatment related. This decrease was not statistically significant but was consistent with significant decreases in food consumption.

Dose (mg/kg/day)	Mean body weight, grams (gd 20)
0	404.7
20	405.1
100	390.4
600	407.4

- Food/water consumption: A statistically significant decrease in food consumption was observed gd 6 through 9 at 600 mg/kg/day. No other significant treatment related effects on food consumption observed at any dose level during the treatment period.
- Description, severity, time of onset and duration of clinical signs: An increased incidence of the following clinical signs were observed in the 600 mg/kg/day group: decreased activity, cold to touch, body surface stained, and material around the nose and eye. Respiratory signs including labored breathing, gasping, and rales observed in the 600 mg/kg/day group. Most of these signs were observed in moribund animals.
- Hematological findings incidence and severity
- Clinical biochemistry findings incidence and severity
- Gross pathology incidence and severity: No significant findings at any dose level.
- Organ weight changes, particularly effects on total uterine weight: No significant effect on gravid uterine weights at any dose level.
- Histopathology incidence and severity: No significant findings at any dose level.
- Fetal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen:
· Litter size and weights: No significant treatment related effect at any dose level.
· Number viable (number alive and number dead): No significant treatment related effect at any dose level.
· Sex ratio: No significant treatment related effect at any dose level.

· Postnatal growth (depending on protocol)
· Postnatal survival (depending on protocol)
· Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: No significant effects on fetal external or visceral malformations or developmental variations at any dose level. Statistically significant increases in the incidences of the variations 27 presacral vertebrae and sternebra unossified were observed at 600 mg/kg/day were attributed to treatment and considered manifestations of slight fetal toxicity.

NOAEL (NOEL) and LOAEL (LOEL) maternal toxicity: NOAEL 100 mg/kg/day; LOAEL 600 mg/kg/day
NOAEL (NOEL) and LOAEL (LOEL) developmental toxicity: NOAEL 100 mg/kg/day; LOAEL 600 mg/kg/day

Increased incidence of mortality and clinical observations as well as slight decreases in body weight gain and food consumption observed at 600 mg/kg/day. No significant maternal effects at 100 or 20 mg/kg/day.

403, 343, 323, and 333 fetuses were examined for the 0, 20, 100 and 600 mg/kg/day dose groups, respectively. No significant treatment related effects were observed on the following uterine parameters at any dose level: mean number of corpora lutea, implantations and live fetuses; percent pre-implantation losses, resorptions, and post-implantation losses; percent male or female fetuses; or fetal weights. A statistically significant increase in the mean number of corpora lutea at the 600 mg/kg/day dose level was not considered test article related as ovulation and copora lutea formation occured prior to exposure.

Slight fetal toxicity, as exhibited by a statistically significant increase in the incidences of minor skeletal variations, 27 presacral vertebrae and sternebra unossified at 600 mg/kg/day. No significant developmental effects at 100 or 20 mg/kg/day.

Fetal effects exhibited as a statistically significant increase in the incidences of minor skeletal variations, 27 presacral vertebrae and sternebra unossified at 600 mg/kg/day. No statistically significant developmental effects at 100 or 20 mg/kg/day.

Source : Epona Associates, LLC

Test condition : ·Number of animals per dose per sex: 30
·Vehicle: peanut oil
·Clinical observations performed and frequency: cageside observations performed twice per day; detailed clinical observations daily.
·Mating procedures: One male and one female per cage; proof of pregnancy was an in situ copulatory plug or vaginal smear for sperm.
·Parameters assessed during study (maternal and fetal): maternal parameters - clinical signs, body weight, food consumption, laparohysterectomic exam, location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea, necropsy; fetal parameters - weight, sex, external malformations and variations, soft-tissue defects, skeletal exam. Gross pathology was performed. Hematology was not evaluated.

Test substance : 1-Propanamine, 3-(triethoxysilyl); CAS No. 919-30-2

Purity: 99.5%

Conclusion : Increased incidences of mortality and clinical observations, as well as slight decreases in body weight gain and food consumption were observed at 600 mg/kg/day. The occurrence of maternal toxicity at 600 mg/kg/day was accompanied by

slight fetal toxicity, as exhibited by 27 presacral vertebrae and sternebra unossified. No significant maternal or developmental effects were observed at 20 or 100 mg/kg/day. Therefore, the maternal and developmental NOAEL was 100 mg/kg/day.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
08.01.2004 (6)

Species : rat
Sex : female
Strain : other
Route of admin. : gavage
Exposure period : day 6 of gestation through day 17 of gestation
Frequency of treatm. : once per day
Duration of test : Through day 20 of gestation
Doses : 10, 25, 50, 100, 500, 750 or 1000 mg/kg/day
Control group : yes
NOAEL maternal tox. : = 100 mg/kg bw
NOAEL teratogen. : = 100 mg/kg bw
LOAEL Maternal Toxicity : = 500 mg/kg bw
Method : EPA OTS 798.4900
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Health Effects Testing Guidelines (40CFR Part 798.4900) September 1985.

No statistical analysis conducted

Result : Increased incidence of mortality and clinical observations as well as decreased body weight and body weight gain observed at 500 mg/kg bw and higher. No significant maternal effects at 100 mg/kg bw.
Source : Epona Associates, LLC
Test condition : Dose-Range-Finding Study:
·Number of animals per dose per sex: 5 or 8
·Vehicle: peanut oil
·Clinical observations performed and frequency: cageside observations performed twice per day; detailed clinical observations daily from day 6 of gestation through day 20 of gestation.
·Mating procedures: One male and one female per cage; proof of pregnancy was an in situ copulatory plug or vaginal smear for sperm.
·Parameters assessed during study (maternal): clinical signs, body weight, uterine exam, location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea, gravid uterine weight, necropsy.
Test substance : 1-Propanamine, 3-(triethoxysilyl); CAS No. 919-30-2
Conclusion : Based on the results of this study, the dose levels chosen for the definitive study were 20, 100 or 600 mg/kg/day.
Reliability : (1) valid without restriction
08.01.2004 (6)

Species : rat
Sex : female
Strain : other
Route of admin. : gavage
Exposure period : day 6 of gestation through day 17 of gestation

Frequency of treatm.	:	Once per day
Duration of test	:	Through day 20 of gestation
Doses	:	Part I: 10, 25, 50, 100 and 500 mg/kg/day Part II: 500, 750 and 1000 mg/kg/day
Control group	:	yes
NOAEL maternal tox.	:	= 100 mg/kg bw
NOAEL teratogen.	:	= 100 mg/kg bw
Method	:	EPA OTS 798.4900
Year	:	1997
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Statistical Method: Statistical analysis was not conducted. All means are accompanied by standard deviations.
Result	:	Mortality at 500, 750 and 1000 mg/kg/day; clinical signs of toxicity (rales, gasping and labored breathing) and necropsy findings (discoloration of lungs) observed at these levels; decreased body weight and body weight gain at 500 mg/kg/day and higher.
Source	:	Epona Associates, LLC
Test condition	:	The objective of this study was to establish dosage levels of the test article for a developmental toxicity study in rats. This study was conducted in two parts, Part I and Part II. All procedures performed in the two parts were identical, with the exception that gravid uterine weights were not recorded for the second set of animals. · Number of animals per dose per sex: 5 in Part I and 8 in Part II · Vehicle: peanut oil · Clinical observations performed and frequency: cageside observations performed twice per day; detailed clinical observations daily. · Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): One male and one female per cage; proof of pregnancy was an in situ copulatory plug or vaginal smear for sperm. · Parameters assessed during study (maternal and fetal): maternal parameters - clinical signs, body weight (on GD 0, 6, 9, 12, 15, 18 and 20), gravid uterine weight, laparohysterectomic exam, location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea, position of the cervix, necropsy
Test substance	:	A-1100: 99.5% Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2)
Conclusion	:	Based on the results of this study, the maternal no-observed-adverse-effect-level (NOAEL) was determined to be 100 mg/kg/day; the developmental NOAEL was 100 mg/kg/day.
Reliability	:	(1) valid without restriction

08.03.2004 (46)

Species	:	rat
Sex	:	female
Strain	:	other
Route of admin.	:	gavage
Exposure period	:	day 6 of gestation through day 15 of gestation
Frequency of treatm.	:	Once per day
Duration of test	:	Through day 21 of gestation
Doses	:	0.1, 0.25, 0.5, 1.0, and 1.5 ml/kg/day
Control group	:	yes
NOAEL maternal tox.	:	< .1 ml/kg bw
NOAEL teratogen.	:	= 1.5 - ml/kg bw

Method : EPA OTS 798.4900
Year : 1993
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Statistical Methods: The unit of comparison was the pregnant dam or the litter. The data for quantitative, continuous variables were intercompared for the 5 treatment groups and the control group by use of Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. The t-tests were used when the F value from the ANOVA was significant. When Levene's test indicated similar variances, and the ANOVA was significant, a pooled t-test was used for pairwise comparisons. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances followed, when necessary, by a separate variance t-test for pairwise comparisons. Nonparmaetric data were statistically evaluated using the Kruskal-Wallis test followed by the Mann-Whitney-U test when appropriate. Incidence data were compared using the Fisher's Exact Test. For all statistical tests, the probability value of < 0.05 (two-tailed) was used as the critical level of significance.

Result : · Duration of Pregnancy: 21 days

· Body weight: Effects on Mean maternal body weights for the 1.0 ml/kg/day group were reduced throughout the treatment period (gd 9, 12, and 15) and subsequent to treatment on gd 18. Maternal body weights were reduced in the 0.25 mg/kg/day group on gd 9. Body weight gains were reduced for the 3 mid dose (0.25, 0.5 and 1.0 ml/kg/day) groups during the first 3 days of treatment. Although not statistically significant, reduced body weight gain was also demonstrated in the 0.1 ml/kg/day group for gd 6 to 9. Body weight gains appeared to be reduced in the 1.0 ml/kg/day group subsequent to treatment on gd 15 to 18 and 18 to 21. However, the apparent reductions in weight gain during the post treatment period could not be ascribed to test substance treatment, particularly since the 1.0 ml/kg/day group had a smaller average litter size (and therefore less expected weight gain) relative to the control group.

Dose ml/kg/day	Mean body weight (grams) GD 2
0	422
0.1	420
0.25	402
0.5	428
1.0	364
1.5	427

· Food/water consumption: Reductions in food consumption were consistent with reduced body weight gains. That is, food consumption was reduced for the first 3 days of treatment in the 1.0, 0.5, and 0.25 ml/kg/day groups and for the entire treatment interval for the 1.0 ml/kg/day group. In addition, although not statistically significant, food consumption valued for gd 6 to 9 were reduced by approximately 18% in the 0.1 ml/kg/day group.

· Description, severity, time of onset and duration of clinical signs: Pertinent clinical findings observed in the

high dose group included hypoactivity, unkempt appearance, urine stains, cold extremities, urogenital discharge, labored/audible respiration, lacrimation, perinasal/periocular encrustation, perioral wetness and salivation. Most of these signs were also observed in the 1.0 ml/kg/day group. In the 0.5 and 0.25 ml/kg/day groups, urine stains and/or urogenital area wetness, unkempt appearance, gasping and/or audible respiration, perinasal encrustation, perioral wetness/encrustation and salivation were observed. Audible respiration (and/or gasping) was observed in all dams from the low dose group as well. In addition, urine stains, urogenital area wetness, unkempt appearance, and perinasal/perioral encrustation were observed in a single dam from the low dose group.

· Gross pathology incidence and severity: Pertinent treatment-related necropsy findings for dams which were found dead included ulcerations of the glandular and nonglandular portions of the stomach and/or duodenum, and color changes in the kidneys. There were no pertinent treatment-related findings in dams which were necropsied on gd 21. Color changes in the lungs were considered to be associated with postmortem changes or an artifact following carbon dioxide asphyxiation.

· Organ weight changes, particularly effects on total uterine weight: There were no differences in gravid uterine weight, and no differences in absolute or relative liver or kidney weights.

· Histopathology incidence and severity: NA.

· Fetal data, provide at a minimum qualitative descriptions of responses where dose related
effects were seen: There were no effects of treatment on fetal body weights/litter or on the sex or incidences of malformations and variations.

· Mortality and day of death:

Dose ml/kg/day - Part I	No. Dead	Day of Death (gestation day)
0	0/8	-
0.1	0/8	-
0.25	0/8	-
0.5	1/8	7
1.0	2/8	11, 12
1.5	6/8	6-10

Maternal mortality was observed at dose levels of 1.5, 1.0, and 0.5 ml/kg/day; mortality was dose-dependent and ranged from 67% at the high dose level to 29% at 1.0 ml/kg/day and 14% at 0.5 ml/kg/day.

There were no effects of treatment on gestational parameters including the number of ovarian corpora lutea, percentage of pre-implantation loss, and the number of total, viable or nonviable implantations/litter. (The statistically significantly increased percent Preimplantation loss in the 1.0 mg/kg/day group was not considered to be related to treatment but rather to the inclusion of a single dam bearing a litter of 1 early resorption in this dose group). There were no effects of treatment on the percentage of males (sex ratio)/litter.

Number pregnant per dose level:

Dose ml/kg/day	No. Pregnant
0	7/8
0.1	8/8
0.25	7/8
0.5	6/7
1.0	5/6
1.5	2/2

· Duration of Pregnancy: 21 days

· Body weight: Effects on Mean maternal body weights for the 1.0 ml/kg/day group were reduced throughout the treatment period (gd 9, 12, and 15) and subsequent to treatment on gd 18. Maternal body weights were reduced in the 0.25 mg/kg/day group on gd 9. Body weight gains were reduced for the 3 mid dose (0.25, 0.5 and 1.0 ml/kg/day) groups during the first 3 days of treatment. Although not statistically significant, reduced body weight gain was also demonstrated in the 0.1 ml/kg/day group for gd 6 to 9. Body weight gains appeared to be reduced in the 1.0 ml/kg/day group subsequent to treatment on gd 15 to 18 and 18 to 21. However, the apparent reductions in weight gain during the post treatment period could not be ascribed to test substance treatment, particularly since the 1.0 ml/kg/day group had a smaller average litter size (and therefore less expected weight gain) relative to the control group.

Dose ml/kg/day	Mean body weight (grams) GD 2
0	422
0.1	420
0.25	402
0.5	428
1.0	364
1.5	427

· Food/water consumption: Reductions in food consumption were consistent with reduced body weight gains. That is, food consumption was reduced for the first 3 days of treatment in the 1.0, 0.5, and 0.25 ml/kg/day groups and for the entire treatment interval for the 1.0 ml/kg/day group. In addition, although not statistically significant, food consumption valued for gd 6 to 9 were reduced by approximately 18% in the 0.1 ml/kg/day group.

· Description, severity, time of onset and duration of clinical signs: Pertinent clinical findings observed in the high dose group included hypoactivity, unkempt appearance, urine stains, cold extremities, urogenital discharge, labored/audible respiration, lacrimation, perinasal/periocular encrustation, perioral wetness and salivation. Most of these signs were also observed in the 1.0 ml/kg/day group. In the 0.5 and 0.25 ml/kg/day groups, urine stains and/or urogenital area wetness, unkempt appearance, gasping and/or audible respiration, perinasal encrustation, perioral wetness/encrustation and salivation were observed. Audible respiration (and/or gasping) was observed in all dams from the low dose group as well. In addition, urine stains, urogenital area wetness, unkempt appearance, and perinasal/perioral encrustation were

observed in a single dam from the low dose group.

· Gross pathology incidence and severity: Pertinent treatment-related necropsy findings for dams which were found dead included ulcerations of the glandular and nonglandular portions of the stomach and/or duodenum, and color changes in the kidneys. There were no pertinent treatment-related findings in dams which were necropsied on gd 21. Color changes in the lungs were considered to be associated with postmortem changes or an artifact following carbon dioxide asphyxiation.

· Organ weight changes, particularly effects on total uterine weight: There were no differences in gravid uterine weight, and no differences in absolute or relative liver or kidney weights.

· Histopathology incidence and severity: NA.

· Fetal data, provide at a minimum qualitative descriptions of responses where dose related
effects were seen: There were no effects of treatment on fetal body weights/litter or on the sex or incidences of malformations and variations.

Source : Epona Associates, LLC

Test condition : The objective of this study was to establish a dose-response range of test article for maternal toxicity and/or developmental toxicity when administered by gavage during organogenesis to pregnant CD® rats in order to select appropriate doses for use in a definitive developmental toxicity study. At the time of dose level selection for this study, preliminary work indicated that the water reactive test substance did not remain stable when diluted in corn oil and an appropriate solvent could not be identified. Therefore, the test substance had to be administered undiluted.

· Number of animals per dose per sex: 8

· Vehicle: none
Control group and treatment: Corn oil

· Clinical observations performed and frequency: All animals were observed twice daily for morbidity and mortality.
Prior to the treatment period, animals were observed for clinical signs once daily. During treatment, animals were observed for clinical signs immediately before (or during) dosing and approximately 1 hour following each daily dosing period. Subsequent to the treatment period, animals were observed for clinical signs once daily in the morning.

· Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): One
male and one female per cage; proof of pregnancy was an in situ copulatory plug or a dropped copulation plug.

· Parameters assessed during study (maternal and fetal): maternal parameters - clinical signs;
body weight (on GD 0, 6, 9, 12, 15, 18 and 21); necropsy; uterus, ovaries, cervix, vagina, and abdominal and thoracic cavities were examined grossly; maternal liver, kidneys, lungs and bladder were weighed and retained in 10% neutral buffered formalin; gravid uterine weight,
laparohysterectomic exam, location of viable and nonviable fetuses, early and late resorptions, total number of implantations and corpora lutea; fetal parameters - weight,

sex, examined for external variations and malformations including cleft palate

Test substance : Gamma-Aminopropyltriethoxysilane (CAS Number 919-30-2); 99.83%
Reliability : (1) valid without restriction
08.01.2004 (16)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience : Human

Result : The silane concentrations in the air samples were below the detection limits of the analytical methods. Only small quantities of 3-aminopropyltriethoxysilane were found in a few handwash samples.
Source : Epona Associates, LLC
Test condition : "Occupational hygiene samples were taken from workers and their environment in a fibreglass factory during filament forming and the handling of coated fibres. The total exposure of workers to silanes was assessed by the collection of air samples into impinger flasks at stationary sampling sites, by the use of absorbent patch samples on workers' clothes or skin and from handwash samples. During the time of our field survey, 3-aminopropyltriethoxysilane, 3-glycidoxypropyltrimethoxysilane and 3-methacryloxypropyltrimethoxysilane were being used in different sizing mixtures. The samples were analysed by gas and liquid chromatography."
Reliability : (4) not assignable
The original report was not reviewed.
08.01.2004 (42)

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