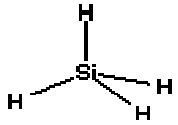
Interim 1: November 2007

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

SILANE (CAS No. 7803-62-5)

INTERIM



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PREFACE

Under the authority of the Federal Advisory Committee Act (FACA) P. L. 92-463 of 1972, the National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) has been established to identify, review and interpret relevant toxicologic and other scientific data and develop AEGLs for high priority, acutely toxic chemicals.

AEGLs represent threshold exposure limits for the general public and are applicable to emergency exposure periods ranging from 10 minutes to 8 hours. Three levels — AEGL-1, AEGL-2 and AEGL-3 — are developed for each of five exposure periods (10 and 30 minutes, 1 hour, 4 hours, and 8 hours) and are distinguished by varying degrees of severity of toxic effects. The three AEGLs are defined as follows:

AEGL-1 is the airborne concentration (expressed as parts per million or milligrams per cubic meter [ppm or mg/m^3]) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic, non sensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEGL-2 is the airborne concentration (expressed as ppm or mg/m^3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEGL-3 is the airborne concentration (expressed as ppm or mg/m^3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience life threatening health effects or death.

Airborne concentrations below the AEGL-1 represent exposure levels that could produce mild and progressively increasing but transient and nondisabling odor, taste, and sensory irritation or certain asymptomatic, non-sensory effects. With increasing airborne concentrations above each AEGL, there is a progressive increase in the likelihood of occurrence and the severity of effects described for each corresponding AEGL. Although the AEGL values represent threshold levels for the general public, including susceptible subpopulations, such as infants, children, the elderly, persons with asthma, and those with other illnesses, it is recognized that individuals, subject to unique or idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL.

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SUMMARY

Silane (CAS No. 7803-62-5) is a colorless gas that has a repulsive odor. It is used in industry in the microelectronics and is a source of hyperpure silicon used for semiconductors (Arkles 2000). Limited data are available regarding the toxicity of silane in humans or laboratory animals. Silane can ignite spontaneously in room air and can cause explosions making it difficult to conduct studies safely.

AEGL -1 values were determined from a study in which male mice were exposed to 1000 ppm silane for 1, 2, 4 or 8 hours. The NOAEL for irritation was 1,000 ppm (Omae et al. 1992). No effects were observed on mortality, hematology, clinical chemistry or histopathology. Clinical signs in treated animals included increased washing of the face and lower abdominal area after exposure. The only finding was a slight increase in inflammatory nasal cells in mice exposed to 1000 ppm silane for 6 hours/day, 5 days/week over 4 weeks. Therefore, 1000 ppm will be the point-of-departure for the 10-min., 30-min and 1 hour AEGL-1 values with no time-scaling. Derivation of 4 and 8 hour values from this data is not recommended as it would result in AEGL-1 values greater than the 4 and 8 hour AEGL-2 values. A total uncertainty factor of 10 was used, 3 for both interspecies and intraspecies because the only effect observed was mild irritation and this response is not expected to vary greatly among species or humans.

AEGL-2 values were derived from a 4 hour acute inhalation study in mice (Takebayashi 1993). In mice exposed to 2500 ppm for four hours, renal lesions observed two days post-exposure resolved within two weeks. At the next higher concentration, 5000 ppm, renal lesions were noted after both the two day and two week observations, making 2500 ppm the NOEL for irreversible effects at 4 hours. Time-scaling was performed using the formula $C^n \times t = k$ where n values range from 0.8 to 3.5 (ten Berge et al. 1986). When data are limited, the Standing Operating Procedure (SOP) for Developing AEGLs for Hazardous Chemicals (NRC 2001) states that the default value of n = 1 is used when extrapolating from shorter to longer study durations and n = 3 is used when extrapolating from longer to shorter durations. Since extrapolating from 4 hours to 10 minutes is not recommended, the 30 minute value was adopted as the 10 minute value. A total uncertainty factor of 30 was used, 3 for interspecies and 10 for intraspecies. An interspecies value of 3 was used because an LC_{50} study (MacEwen and Vernot 1972) identified the mouse as being more sensitive than the rat. The intraspecies uncertainty factor was set at the default value of 10 as there is no data to estimate human variability and the chemical was not acting as a direct irritant.

AEGL-3 values were based on a 4 hour mouse inhalation study; 5000 ppm was the concentration that induced irreversible microscopic renal lesions and was the no-effect level for lethality (Takebayashi 1993). A single exposure to the highest level tested, 10,000 ppm, caused mortality in 6/8 mice observed for two weeks post-exposure. Time-scaling was performed using the formula $C^n \times t = k$ where n values range from 0.8 to 3.5 (ten Berge et al. 1986). Scaling was performed using n =3 for extrapolating to the 30 minute and 1 hour time point and n = 1 for extrapolating to 8 hours. Since extrapolating from 4 hours to 10 minutes is not recommended, the

30 minute value was adopted as the 10 minute value. A total uncertainty factor of 30 was used, 3 for interspecies and 10 for intraspecies. An interspecies value of 3 was used because an LC_{50} study (MacEwen and Vernot 1972) identified the mouse as being more sensitive than the rat. The intraspecies uncertainty factor was set at the default value of 10 as there is no data to estimate human variability and the chemical was not acting as a direct irritant.

The AEGL-1, AEGL-2 and AEGL-3 derived values are listed in the table below.

Summary of AEGL values for Silane in ppm (mg/m^3)

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL-1 (Nondisabling)	100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	NR	NR	No-effect level (Omae et al 1993)
AEGL-2 (Disabling)	170 ppm (220 mg/m^3)	170 ppm (220 mg/m^3)	130 ppm (170 mg/m^3)	80 ppm (100 mg/m^3)	42 ppm (55 mg/m^3)	Concentration with reversible renal lesions (Takebayashi 1993)
AEGL-3 (Lethality)	300 ppm (400 mg/m^3)	300 ppm (400 mg/m^3)	270 ppm (350 mg/m^3)	170 ppm (270 mg/m^3)	80 ppm (100 mg/m^3)	No-effect level for lethality, irreversible renal lesions (Takebayashi 1993)

ppm = parts per million, m/m^3 = milligrams per cubic meter

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Takebayashi, Toru. 1993. Acute inhalation toxicity of high concentration of silane in male ICR mice. Archives of Toxicology, 67: 55-60.

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1.0 INTRODUCTION

Silane (CAS No. 7803-62-5) is in the group of inorganic silanes with boiling points and melting points similar to the simple hydrocarbons (Arkles 2000). Silane, a colorless gas, differs from hydrocarbons in that it is pyophoric and can ignite immediately on contact with air. Silane does not react with water under normal conditions. In the United States, it is often used within manufacturing operations. Most production occurs at a polycrystalline silicon production facility in Washington and Montana that has an annual capacity for up to 8000 metric tons (ASMI 2005). Another smaller plant in Texas uses approximately 1250 tons/year and the world-wide market is about 250 tons/year with the majority being used in microelectronics (Arkles 2000).

Selected chemical and physical properties are listed in Table 1.

Table 1. Chemical and physical properties of silane

Characteristic/ property	Silane	(Reference)
Synomyms	Silicon tetrahydride, silicane, monosilane	(O' Neil et al. 2001)
CAS Registry No.	7803-62-5	(O' Neil et al. 2001)
Chemical formula	H_4Si	(O' Neil et al. 2001)
Molecular weight	32.12	(O' Neil et al. 2001)
Physical state	Colorless gas	(O' Neil et al. 2001)
Odor	Repulsive odor	(O' Neil et al. 2001)
Vapor pressure	> 1 atm	(NIOSH 2005)
Melting point	- 185° C	(O' Neil et al. 2001)
Boiling point	- 112° C	(O' Neil et al. 2001)
Flash point	May spontaneously ignite on contact with air	(IPCS 2001)
Explosive limits (volume % in air)	LEL- 1.37% UEL- 100%	(IPCS 2001)
Solubility (in water)	Insoluble in water	(Lemen and Bingham 2001)
Conversion factors	1 ppm = 1.3 mg/m^3 1 mg/m^3 = 0.76 ppm	(NIOSH 2005)

2. HUMAN TOXICITY DATA

2.1 Acute Lethality

No data on the acute lethality of silane in humans were available.

2.2. Nonlethal Toxicity

No data on non-lethal toxicity of silane were available.

2.2.1. Odor Threshold

Data are not adequate to determine an odor threshold.

2.2.2. Experimental Studies

No data were available on human experimental exposure to silane.

2.2.3. Epidemiologic Studies/Occupational Exposures

The only information available regarding occupational exposure to silane states that the main exposure route for humans is through inhalation; target organs are the eyes, skin, and respiratory system (NIOSH 2005).

2.2.4. Clinical Studies

No data from clinical studies in humans are available.

2.3. Neurotoxicity

No data are available concerning neurotoxicity of silane in humans.

2.4. Developmental/Reproductive Toxicity

No data are available concerning developmental or reproductive toxicity of silane in humans.

2.5. Genotoxicity

No data are available concerning genotoxicity of silane in humans.

2.6. Carcinogenicity

No data are available concerning carcinogenicity of silane in humans.

2.7. Summary

Very limited data are available concerning human exposure.

3. ANIMAL TOXICITY DATA

Toxicity data are extremely limited.

3.1. Acute Lethality

In a whole-body inhalation study, male ICR mice were exposed to silane for 30 minutes (n = 8), 1 hour or 4 hours (n = 12) at concentrations of 0 (controls), 2500, 5000, 7500 (30-minute study only) or 10,000 ppm (Takebayashi 1993). Control animals were exposed to filtered air. Chamber concentrations were monitored every 5 minutes using gas chromatography and levels remained within 7% of the desired concentration. In the 1 and 4 hour experiments, twelve mice were divided into two groups: four were observed for two days and eight were observed for two weeks post-exposure. In the two week observation group, 6/8 mice died within 24 hours after silane exposure and 3/4 of those in the 2 day observation group died within 24 hours in the 4 hour, 10,000 ppm exposure groups. No other deaths were recorded. Clinical signs observed during exposure included face washing and licking of the lower abdomen in the silane exposed animals but severity of signs and relationship to dosing was not included in the report. Ruffled fur occurred more frequently with increasing concentration.

Animals sacrificed two days post-exposure at ≥ 2500 ppm (4 hour exposure) and 10,000 ppm group (1hr exposure) had acute renal tubular necrosis characterized by cellular degeneration and necrosis of the tubules. In the 4 hour exposure, this was seen in 1/4 mice in each of the 2500 and 5000 ppm groups and in all of the animals in the 10,000 ppm group. All mice in the 10,000 ppm group exposed for 4 hours also had enlarged kidneys. At 2 weeks post-exposure, tubulo-interstitial nephritis characterized by interstitial fibrosis and atrophy of the tubules was observed in 0/7 mice at 2500 ppm (1 and 4 hr exposures); 1/8 and 2/8 mice at 5000 ppm (1 and 4 hr exposures); 4/8 at 7500 ppm (30 min. exposure); and 7/8 and 1/2 mice at 10,000 ppm (1 and 4 hr exposures). Only two mice survived in the 10,000 ppm group. In mice exposed to 10,000 ppm for 4 hours, there were hematopoietic cells in the bone marrow and lymphocytes in the thymus in the decedents. The study author suggested this was either a result of the acute renal failure or direct silane toxicity. In the group observed two weeks post-exposure, only two mice were exposed to 10,000 ppm for 4 hours and both had a normochromic, normocytic anemia which could again be the result of prolonged renal damage or direct silane toxicity. The mouse LC_{50} was between 5000 and 10,000 for the four hour exposure and greater than 10,000 for the one hour or 30 minute exposure. The NOAEL was set at 5000 ppm for the 30 minute study, 2500 in the one hour and not determined in the four hour study. Data are shown in Table 2.

Table 2. Observations after inhalation of silane[a]

Microscopic lesions after 2-day observation			
	Nasal Cavity	Kidney –acute tubular necrosis	Lung
1-hour exposure			
Control	0/4	0/4	0/4
2500 ppm	0/4	0/4	0/4
5000 ppm	1/4	0/4	0/4
10,000 ppm	0/4	2/4	0/4
4-hour exposure			
Control	0/4	0/4	0/4
2500 ppm	0/4	1/4	0/4
5000 ppm	0/4	1/4	0/4

10,000 ppm	1/1	1/1	0/1
10,000 ppm (D)[b]	7/9	9/9	0/9
Microscopic lesions after 2-week observation			
	Nasal Cavity	Kidney- tubulo-interstitial nephritis	Lung
30-minute exposure			
Control	0/5	0/5	0/5
2500 ppm	0/8	0/8	0/8
5000 ppm	0/8	0/8	0/8
7500 ppm	0/8	4/8	0/8
10,000 ppm	0/8	6/8	0/8
1-hour exposure			
Control	0/8	0/8	0/8
2500 ppm	0/7[c]	0/7	0/7
5000 ppm	0/8	1/8	0/8
10,000 ppm	1/8	7/8	0/8
4-hour exposure			
Control	0/8	0/8	0/8
2500 ppm	0/7	0/7	0/7
5000 ppm	0/8	2/8	0/8
10,000 ppm	0/2	1/2	0/2
10,000 ppm (D)	-	-	-

[a] Data from Takebayashi 1993.
[b] 10,000 ppm (D)= dead mice exposed to 10,000 ppm silane
[c] One insufficiently fixed organ was excluded from the exam

Limited data from an older study were available (MacEwen and Vernot 1972). Male CFE rats were exposed to 0, 1000, 4000 or 10,000 ppm silane and CF1 mice to 0, 6000 or 10,000 ppm for 2 or 4 hours. Exposures took place in a 30-Liter glass bell jar with an air flow of 30 L/min. Silane concentration in the exposure chamber was measured using a Beckman infrared 5-A spectrophotometer. Table 3 shows the mortality ratio determined from these studies. Animals were observed for 14 days after exposure and gross pathology was performed on representative animals. No gross lesions were identified at sacrifice. The 4/10 mice found dead in the 10,000 ppm (4 hour exposure), between 31 and 45 hours post-exposure, had appeared normal during and after exposure. No gross examination was performed on this group of animals. Although the data are limited, they support the findings of the Takebayashi study above.

Table 3. Lethal effects of silane vapor inhalation exposures[a]

Species	Nominal conc. (ppm)	Measured conc. (ppm)	Time (hr.)	Mortality	Time to death
Rats	1000	ND[b]	1.25	0/50	-
Rats	4000	ND	1.0	0/5	-
Rats	10,000	9600	4.0	0/5	-
Mice	6000	ND	1.0	0/5	-
Mice	10,000	9600	4.0	4/10	31-45 hours
Mice	10,000	9800	2.0	0/10	-

[a] Data from MacEven and Vernot 1972
[b] ND = no data included in study

3.2. Acute Nonlethal Toxicity

3.2.1. Mice

Ten male ICR mice/dose were exposed to 1000 ppm silane for 1, 2, 4, and 8 hours (phase 1-acute) and for 6 hours/day, 5 days/week for 2 and 4 weeks (phase 2-subacute) (Omae et al. 1992). No mortalities were observed in either phase of the study. Phase 2 will be described below under Repeated Exposure. The concentration of 1000 ppm was created by a ten fold dilution of 10,000 ppm silane with filtered room air. The chamber concentration was monitored every 10 minutes using a gas chromatograph. Mice in phase 1 were sacrificed three days after the last exposure. All organs were examined grossly and the following organs examined by histopathological examination: cornea, nasal cavity, respiratory cavity, lung, liver, kidney, spleen, pancreas, thymus, thyroid, bone marrow, salivary glands, esophagus and testis. The following clinical chemistry and hematology parameters were measured: alkaline phospatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), cholinesterase (ChE), blood urea nitrogen (BUN), sodium (Na), potassium (K), red blood cell count (RBC) and total and differential white blood cell count (WBC). In the phase 1 study, no exposure-related changes were found in hematology, clinical chemistry or histopathology. Animals were observed for three days post exposure in addition to immediately after being exposed to silane. The only clinical signs were an increased amount of face washing and licking of the abdominal area in exposed mice compared to controls. Silane did not have any adverse toxicological effects on mice exposed to 1000 ppm by inhalation for up to 8 hours.

3.3. Repeat Exposure Studies

3.3.1. Mice

The Omae et al. research mentioned above included a repeated dose study (Phase 2) in which ten ICR mice/dose were exposed to 1000 ppm silane for 6 hours/day, 5 days/week, for two or four weeks (Omae et al. 1992). No mortalities occurred. The same parameters described above were measured for the Phase 2 study and body weight was monitored. The only exposure-related finding in Phase 2 was increased incidence of mucous exudates and inflammatory and/or necrotic cells in the nasal cavity in mice exposed for four weeks. Exudates in the nasal cavity were seen in 8/10 of the treated mice after the 2 week recovery versus 2/10 of the control group and inflammatory and necrotic cells in the nasal cavity were observed in 6/10 mice after the 4 week recovery versus 0/10 of the controls. The only toxicological effect in mice exposed to 1000 ppm silane for up to four weeks was minor irritation to the nasal cavity.

3.4 Neurotoxcity

No data are available on neurotoxicity of silane.

3.5. Developmental/Reproductive Toxicity

No data are available on developmental/reproductive toxicity of silane.

3.6. Genotoxicity

No data are available on genotoxicity of silane.

3.7. Chronic Toxicity/Carcinogenicity

No data are available for evaluation of carcinogenicity and/or chronic toxicity of silane in laboratory animals.

3.8. Summary

Both human and animal data on silane toxicity are limited. Part of the difficulty in conducting studies is the highly explosive nature of silane. Both MacEwen and Vernot (1972) and Takebayashi (1993) used 10,000 ppm as the highest concentration due to safety concerns above this level. In the MacEwen and Vernot (1972) 4 hour study, an LC_{50} of 9600 ppm in mice was established, and Takebayashi (1993set the 4 hour LC_{50} for mice between 5000 and 10,000 ppm. Rats exposed to 9600 ppm for 4 hours had no mortality and no gross lesions (MacEwen and Vernot 1972). In the Takebayashi study, the only mortalities were in mice exposed to 10,000 ppm for 4 hours. Mice exposed to 5000 ppm group had tubulo-interstitial nephritis in the kidney. Mice exposed to 2500 ppm had lesions in the kidney two days after exposure that resolved within two weeks. Omae et al. (1992) found no toxicological effects in mice exposed to 1000 ppm silane for 1, 2, 4 or 8 hours. Repeated exposures to the same concentration for up to four weeks caused nasal irritation in mice.

4.0 SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

Based on the limited data, silane does appear to be a strong irritant. Only a slight increase in nasal exudates and inflammatory cells were found in histopathological examination after four weeks of exposure to 1000 ppm of silane (Omae et al. 1992). The increased washing behavior observed in rats exposed to silane at all levels may also be indicative of irritation; however, it could also be a reaction to the strong odor. Mice exposed to 5000 ppm and 10,000 ppm (Takebayashi 1993) for 1 and 4 hours had evidence of renal lesions in the renal tubules. The mechanism for this effect was not discussed.

4.2. Mechanism of Toxicity

The mechanism of toxicity for silane was not found.

4.3. Structure Activity Relationships

Silicone forms a series of silicon hydride compounds similar to the alkane series of hydrocarbons. The simplest of this series is silane. Like hydrocarbons, hydrogen atoms can be replaced by other groups such as halogens and hydroxyl groups to form a parallel series of compounds. The silicon hydrogen bond in silane is much weaker that that found in a similar carbon hydrogen bond making this chemical more reactive. Silane is a colorless gas that is pyrophoric and can ignite immediately upon contact with air. Silane is used less often in industry than its less toxic counterpart, trichlorosilane (Lemen and Bingham 2001).

4.4. Other Relevant Information

No additional relevant information was available.

4.4.1. Species Variability

Very limited data are available on human or animal exposure to silane. Animal studies included a subactue study in mice (Omae et al. 1992) and LC_{50} studies in rats and mice. Rats appeared to be less sensitive to silane (MacEwen and Vernot 1972), exhibiting no lesions or mortality at concentrations which caused enlarged kidneys and mortality in mice (Takebayashi 1993).

4.4.2. Susceptible Populations

Little is known about the effect of silane on humans. While this is a gas with suspected irritating properties as demonstrated in mouse studies, it also has a distinct repulsive odor which would likely limit exposure, thus decreasing the possibility for substantial inhalation.

4.4.3. Concentration-Exposure Duration Relationship

The concentration-exposure time relationship for many irritant and systemically-acting vapors and gases can be described by the relationship $c^n \times t = k$, where the exponent, n, ranges from 0.8 to 3.5 (ten Berge et al. 1986). Data were unavailable for an empirical derivation of *n* in the equation, $C^n \times t = k$. In the absence of chemical specific data, an *n* of 3 will be applied to extrapolate to shorter time periods, and an *n* of 1 will be applied to extrapolate to longer time periods, to provide AEGL values that would be protective of human health (NRC 2001).

5.0 DATA ANALYSIS for AEGL-1

5.1. Summary of Human Data Relevant to AEGL-1

No human data were available for determining AEGL-1 values.

5.2. Summary of Animal Data Relevant to AEGL-1

In an acute inhalation study, mice exposed to 1000 ppm silane for 1 to 8 hours showed no adverse effects (Omae et al. 1992). In a subacute study of mice, effects were limited to nasal

irritation after exposure to 1000 ppm, 6 hours/day, 5 days/week for 4 weeks. No mortalities occurred in either study. Adequate clinical chemistry, hematology parameters were measured and histopathology was performed. The only treatment-related effect was a slight increase in the number of inflammatory and/or necrotic cells in the nasal cavity in mice exposed for four weeks.

5.3. Derivation of AEGL-1

AEGL -1 values (shown in Table 4) were derived from the 1000 ppm NOEL for irritation in mice (Omae et al. 1992). Male mice were exposed to 1000 ppm silane for 1, 2, 4 and 8 hours. No effects were observed on mortality, hematology, clinical chemistry or histopathology. Clinical signs in treated animals included increased washing of the face and lower abdominal area after exposure. In the repeated dose Phase of the study, the only other finding was a slight increase in inflammatory/necrotic nasal cells in mice exposed to 1000 ppm silane 6 hours/day, 5 days/week for 4 weeks. Therefore, 1000 ppm will be the point-of-departure for the 10-min., 30-min and 1 hour AEGL-1 values with no time-scaling. Extrapolating values for the 4 and 8 hour time-points from this data is not recommended because the derived value would result in AEGL-1 values greater than the 4 and 8 hour AEGL-2 values. A total uncertainty factor of 10 was used, 3 for interspecies and 3 for intraspecies. Both were set at 3 because the only effect observed was mild irritation and this response is not expected to vary greatly among species or humans.

Table 4. AEGL-1 Values for Silane in ppm (mg/m^3)

10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	NR	NR

6.0 DATA ANALYSIS FOR AEGL-2

6.1. Summary of Human Data Relevant to AEGL-2

No human data are available in determining AEGL-2 values.

6.2. Summary of Animal Data Relevant to AEGL-2

ICR mice were exposed to 2500, 5000 or 10,000 ppm silane for four hours in an acute inhalation study (Takebayashi 1993). All deaths occurred at the 10,000 ppm level. At the 2500 ppm concentration, mice sacrificed two days after exposure showed acute tubular nephritis. However, in those sacrificed two weeks post-exposure, tubulo-interstitial nephritis was seen only at dose levels ≥ 5000 ppm. Renal lesions at 2500 ppm were reversible, justifying this dose as the point-of-departure for calculating AEGL-2 values.

6.3. Derivation of AEGL-2

AEGL-2 values (Table 5) were determined using the 2500 ppm concentration from the 4 hour acute inhalation study in mice (Takebayashi 1993). This concentration caused reversible renal

lesions. At 2500 ppm, renal lesions observed two days post-exposure resolved within two weeks. At the next highest concentration, 5000 ppm, renal lesions were noted at both after the two day and two week observation period, thus making 2500 ppm the 4 hour NOEL for irreversible effects. Time-scaling was performed using the formula $C^n \times t = k$ where n values range from 0.8 to 3.5 (ten Berge et al. 1986). Due to limited data available, scaling was performed using n =3 for extrapolating to the 30 minute and 1 hour time point and n = 1 for extrapolating to 8 hours. According the AEGL SOP (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of 4 hours. Therefore, the 30-minute AEGL-2 value was adopted as the 10-minute value. A total uncertainty factor of 30 was used, 3 for interspecies and 10 for intraspecies. An interspecies value of 3 was because the mouse was identified as being more sensitive than the rat (MacEwen and Vernot 1972). No deaths occurred and no gross lesions were observed in rats after a single 4 hour exposure to 9600 ppm silane. However, 4/10 mice died at the same concentration and in another 4 hour study (Takebayashi 1993), renal enlargement was found in mice exposed to 10,000 ppm. The intraspecies uncertainty factor was set at the default value of 10 as there is no data to estimate intrahuman variability and the chemical was not acting as a direct irritant.

Table 5. AEGL-2 Values for Silane in ppm (mg/m^3)

10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
170 ppm (220 mg/m^3)	170 ppm (220 mg/m^3)	130 ppm (170 mg/m^3)	80 ppm (100 mg/m^3)	42 ppm (55 mg/m^3)

7.0 DATA ANALYSIS FOR AEGL-3

7.1. Summary of Human Data Relevant to AEGL-3

No human data were available for determining AEGL-3 values.

7.2. Summary of Animal Data Relevant to AEGL-3

An acute LC_{50} study was used to determine the AEGL-3 values. Exposure to 5000 ppm for 4 hours resulted in no mortalities but caused irreversible renal lesions in mice (Takebayashi 1993). In this same study, 10,000 ppm, caused deaths in 6/8 mice. At the 5000 ppm concentration, acute tubular necrosis was seen at the two day observation and tubulo-interstitial nephritis at the twoweek observation. Another earlier study (MacEwen and Vernot 1972) identified 9600 ppm as the LC_{50} in mice, indicating 5000 ppm is a conservative basis for the AEGL-3 derivation.

7.3. Derivation of AEGL-3

AEGL-3 values, seen in Table 6, were based on a 4 hour mouse inhalation study in which 5000 ppm induced irreversible renal lesions with no mortality (Takebayashi 1993). The highest level tested, 10,000 ppm, caused mortality in 6/8 mice. Time-scaling was performed using the formula $C^n \times t = k$ where n values range from 0.8 to 3.5 (ten Berge et al. 1986). Due to limited data available, scaling was performed using n =3 for extrapolating to the 30- minute and 1 hour time

point and n = 1 for extrapolating to 8 hours. According the AEGL SOP (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of 4 hours. Therefore, the 30-minute AEGL-3 value was adopted as the 10-minute value. A total uncertainty factor of 30 was used, 3 for interspecies and 10 for intraspecies. The interspecies value of 3 was used because an LC_{50} study (MacEwen and Vernot 1972) identified the mouse as being more sensitive than the rat. No deaths occurred and no gross lesions were observed in rats after a 4-hour exposure to 9600 ppm silane. However, 4/10 mice died at the same concentration and in another 4 hour study (Takebayashi 1993), renal enlargement in mice exposed to 10,000 ppm was observed. The intraspecies uncertainty factor was set at the default value of 10 as there is no data to estimate human variability and the chemical was not acting as a direct irritant.

Table 6. AEGL-3 Values for Silane in ppm (mg/m^3)

10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
300 ppm (400 mg/m^3)	300 ppm (400 mg/m^3)	270 ppm (350 mg/m^3)	170 ppm (270 mg/m^3)	80 ppm (100 mg/m^3)

8.0 SUMMARY OF AEGLS

8.1. AEGL Values and Toxicity Endpoints

The derived AEGL values are shown in Table 7. The AEGL-1 values were based on the NOEL for irritation in mice. AEGL-2 values were based on reversible renal lesions in mice. AEGL-3 values were based on irreversible renal lesions and the NOEL for lethality in mice.

Table 7. Summary of AEGL Values in ppm (mg/m^3)

Classification	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
AEGL-1 (Nondisabling)	100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	NR	NR
AEGL-2 (Disabling)	170 ppm (220 mg/m^3)	170 ppm (220 mg/m^3)	130 ppm (170 mg/m^3)	80 ppm (100 mg/m^3)	42 ppm (55 mg/m^3)
AEGL-3 (Lethality)	300 ppm (400 mg/m^3)	300 ppm (400 mg/m^3)	270 ppm (350 mg/m^3)	170 ppm (220 mg/m^3)	80 ppm (100 mg/m^3)

8.2. Comparisons with Other Standards and Guidelines

Only two other standards/guidelines have been established for silane. Both the REL-TWA (NIOSH 2005) and the TLV-TWA (ACGIH 2005), shown in Table 8, are set at 5 ppm. No other standards were found. Due to a lack of data on silane, the ACGIH TLV-TWA for silane (silicone tetrahydride) was based on a related chemical, germanium tetrahydride. The document states that the toxicity of silane is approximately $1/10^{th}$ that of germanium tetrahydride which has a TLV-TWA of 0.2 ppm (0.63 mg/m^3). The only study mentioned was the MacEwen and Vernot (1972). The NIOSH REL-TWA was also based on toxicity of other tetrahydrides.

Table 8. Extant Standards and Guidelines for Chemical					
Guideline	**Exposure Duration**				
	10 minute	**30 minute**	**1 hour**	**4 hour**	**8 hour**
AEGL-1	100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	100 ppm (130 mg/m^3)	NR	NR
AEGL-2	170 ppm (220 mg/m^3)	170 ppm (220 mg/m^3)	130 ppm (170 mg/m^3)	80 ppm (100 mg/m^3)	42 ppm (55 mg/m^3)
AEGL-3	300 ppm (400 mg/m^3)	300 ppm (400 mg/m^3)	270 ppm (350 mg/m^3)	170 ppm (270 mg/m^3)	80 ppm (100 mg/m^3)
REL-TWA (NIOSH)[a]					5 ppm
TLV-TWA (ACGIH)[b]					5 ppm

a- NIOSH REL-TWA (National Institute of Occupational Safety and Health, Recommended Exposure Limits - Time Weighted Average) (NIOSH 2005)

b- ACGIH TLV-TWA (American Conference of Governmental Industrial Hygienists, Threshold Limit Value - Time Weighted Average) (ACGIH 2005) is the time-weighted average concentration for a normal 8-hour workday and a 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect**.**

8.3. Data Adequacy and Research Needs

Very limited data are available on silane. Since it is used primarily in closed-loop processes in manufacturing and is very explosive, additional testing is not recommended. No data were found on reproduction/developmental toxicity, genotoxicity, neurotoxicity, and chronic toxicity/carcinogenicity, in animals or humans.

9.0 REFERENCES

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Appendix A: Derivation of AEGL values for Silane

Derivation of AEGL-1

Key Study:	Omae et al. 1992
Toxicity Endpoint:	Acute and subacute study causing no treatment-related adverse effects
Scaling:	Time-scaling was not performed as 1000 ppm was the NOAEL for irritation
Uncertainty factors:	3 for interspecies variability 3 for intraspecies variability Total UF = 10
10-min.AEGL-1:	$\frac{1000}{10}$ = 100 ppm (130 mg/m^3)
30-min. AEGL-1:	$\frac{1000}{10}$ = 100 ppm (130 mg/m^3)
1-hr. AEGL-1:	$\frac{1000}{10}$ = 100 ppm (130 mg/m^3)
4-hr. AEGL-1:	NR
8-hr. AEGL-1:	NR

Derivation of AEGL-2

Key Study:	Takebayashi 1993
Toxicity Endpoint:	Acute inhalation study in mice; reversible renal lesions
Scaling:	$C^n \times t = k$ n = 3 for extrapolating to the 30-min, 1-hour, 4-hour time-points $(2500 \text{ ppm})^3 \times 4 \text{ hours} = 6.25 \times 10^{10}$ ppm hr (30 min and 1 hr AEGL) n = 1 for extrapolating to the 8-hour time-point $(2500 \text{ ppm})^1 \times 4 \text{ hours} = 10{,}000$ ppm hr (8 hrs AEGL)
Uncertainty factors:	3 for interspecies variability 10 for intraspecies variability
10-min.AEGL-2:	170 ppm (220 mg/m^3) (30 min. AEGL value adopted as 10 min.)
30-min. AEGL-2:	$C^3 \times 0.5$ hr. $= 6.25 \times 10^{10}$ ppm ·hr $C^3 = 1.25 \times 10^{11}$ ppm C = 5000 ppm 30-min. AEGL-2 = 5000/30 = 170 ppm (220 mg/m^3)
1-hr. AEGL-2:	$C^3 \times 1$ hr $= 6.25 \times 10^{10}$ ppm ·hr $C^3 = 6.25 \times 10^{10}$ ppm C = 4000 ppm 1 hr AEGL-2 = 4000 ppm/30 = 130 ppm (170 mg/m^3)
4-hr. AEGL-2:	C = 2500 ppm 4 hr. AEGL-2 = 2500 ppm/30 = 80 ppm (100 mg/m^3)
8-hr. AEGL-2:	$C^1 \times 8$ hr = 10,000 ppm · hr $C^1 = 1250$ ppm 8 hr AEGL-2 = 1250 ppm/30 = 42 ppm (55 mg/m^3)

Derivation of AEGL-3

Key Study:	Takebayashi 1993
Toxicity Endpoint:	Acute study in mice; irreversible renal lesions and NOEL for lethality
Scaling:	$C^n \times t = k$ n = 3 for extrapolating to the 30-min, 1-hour, 4-hour time-points $(5000 \text{ ppm})^3 \times 4 \text{ hours} = 5.0 \times 10^{11}$ ppm (30 min and 1 hr AEGL) n = 1 for extrapolating to the 8-hour time-point $(5000 \text{ ppm})^1 \times 4 \text{ hours} = 20{,}000$ ppm (8 hrs AEGL)
Uncertainty factors:	3 for interspecies variability 10 for intraspecies variability Total UF = 30
10-min.AEGL-3:	300 ppm (400 mg/m^3) (30 minute AEGL-3 value adopted as 10 min.)
30-min. AEGL-3:	$C^3 \times 0.5$ hr. $= 5.0 \times 10^{11}$ ppm ·hr $C^3 = 1 \times 10^{12}$ ppm C = 10,000 ppm 30-min. AEGL-3 = 10,000/30 = 300 ppm (400 mg/m^3)
1-hr. AEGL-3:	$C^3 \times 1$ hr $= 5.0 \times 10^{11}$ ppm ·hr $C^3 = 5.0 \times 10^{11}$ ppm C = 8000 ppm 1 hr AEGL-3 = 8000 ppm/30 = 270 ppm (350 mg/m^3)
4-hr. AEGL-3	C = 5000 ppm 4 hr. AEGL-3 = 5000 ppm/30 = 170 ppm (220 mg/m^3)
8-hr. AEGL-3:	$C^1 \times 8$ hr $= 20{,}000$ ppm ·hr $C^1 = 2500$ ppm 8 hr AEGL-3 = 2500 ppm/30 = 80 ppm (100 mg/m^3)

APPENDIX B: Derivation Summary for Silane

SILANE (CAS No. 7803-62-5)
DERIVATION SUMMARY

AEGL-1 VALUES				
10-minute	**30-minute**	**1-hour**	**4-hour**	**8-hour**
100 ppm	100 ppm	100 ppm	NR	NR

Key Reference: Omae et al. 1992

Test Species/Strain/Number: 10 Male ICR mice

Exposure Route/Concentrations/Durations: Inhalation study; mice exposed to 1000 ppm silane for 1, 2, 4 and 8 hours or 6 hrs/day for up to 2 and 4 weeks

Effects: Increased washing after exposure, mild lesions associated with irritation in nasal cavity in animals exposed up to 4 weeks.

Endpoint/Concentration/Rationale: Because this concentration is a no-effect level, 1000 ppm will be the point-of-departure for the 10-min., 30-min and 1 hour AEGL-1 values with no time-scaling. Values are not recommended for the 4 and 8 hour time-points because the derived value would result in AEGL-1 values greater than the 4 and 8 hour AEGL-2 values.

Uncertainty Factors/Rationale: 10; 3 for interspecies and 3 for intraspecies. Both uncertainty factors were 3 because the only effect observed was mild irritation and this response is not expected to vary greatly between species or humans.

Modifying Factor: None

Animal to Human Dosimetric Adjustment: Not applicable

Time Scaling: Not applicable

Data Adequacy: Data is adequate in this study for determining AEGL-1 values for 10 min, 30 min. and 1 hour.

AEGL-2 VALUES				
10-minute	**30-minute**	**1-hour**	**4-hour**	**8-hour**
170 ppm	170 ppm	130 ppm	80 ppm	42 ppm

Key Reference: Takebayashi 1993

Test Species/Strain/Number: 12 Male ICR mice

Exposure Route/Concentrations/Durations: Inhalation study; mice exposed to 0, 2500, 5000 or 10,000 ppm silane for 4 hours

Effects: 0: No signs in control mice

2500 ppm**:** Increased face and body washing, ruffled fur, reversible renal lesions (acute-tubular necrosis) observed after 2 days but not 2 weeks (1/4 mice)

5000 ppm: Increased face and body washing, ruffled fur, renal lesions observed at 2 days (acute tubular necrosis) and 2 weeks (tubulo-interstitial nephritis).

10,000 ppm: 6/8 mice died within 24 hours of exposure, 10/10 mice had acute tubular necrosis including decedents and those that survived to the 2 day observation; 1/2 mice had tubulo-interstitial nephritis at 2 week observation.

Endpoint/Concentration/Rationale: 2500 ppm had no mortalities and reversible renal effect.

Uncertainty Factors/Rationale: 30; 3 for interspecies and 10 for intraspecies. An interspecies value of 3 was used because an LC_{50} study (MacEwen and Vernot 1972) identified the mouse as being more sensitive than the rat. In this study, no deaths occurred and no gross lesions were observed in rats after a 4-hour exposure to 9600 ppm silane. However, 4/10 mice died at the same concentration and in another 4 hour study (Takebayashi 1993), renal enlargement in mice exposed to 10,000 ppm was observed. The intraspecies uncertainty factor was set at the default value of 10 as there is no data to estimate human variability and the chemical was not acting as a direct irritant.

Modifying Factor: None

Animal to Human Dosimetric Adjustment: Not applicable

Time Scaling: Time-scaling was performed using the formula $C^n \times t = k$ where n values range from 0.8 to 3.5 (ten Berge et al. 1986). Due to limited data available, scaling was performed using n =3 for extrapolating to the 10- and 30- minute and 1 hour time points and n = 1 for extrapolating to the 8 hour time point. According the AEGL SOP (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of 4 hours. Therefore, the 30-minute AEGL-2 value was adopted as the 10-minute value.

Data Adequacy: Data in this study are adequate for determining AEGL-2 values.

1
2

AEGL-3 VALUES				
10-minute	**30-minute**	**1-hour**	**4-hour**	**8-hour**
300 ppm	300 ppm	270 ppm	170 ppm	80 ppm

Key Reference: Takebayashi 1993

Test Species/Strain/Number: 12 Male ICR mice

Exposure Route/Concentrations/Durations: Inhalation study; mice exposed to 0, 2500, 5000 or 10,000 ppm silane for 4 hours

Effects: 0: No signs in control mice

2500 ppm**:** Increased face and body washing, ruffled fur, reversible renal lesions (acute tubular necrosis) observed after 2 days but not 2 weeks (1/4 mice)

5000 ppm: Increased face and body washing, ruffled fur, renal lesions observed at 2 days (acute tubular necrosis) and 2 weeks (tubulo-interstitial nephritis).

10,000 ppm: 6/8 mice died within 24 hours of exposure, 10/10 mice had acute tubular necrosis including decedents and those that survived to the 2 day observation; 1/2 mice had tubulo-interstitial nephritis at 2 week observation.

Endpoint/Concentration/Rationale: At 5000 ppm, no mortality and irreversible renal lesions

Uncertainty Factors/Rationale: 30; 3 for interspecies and 10 for intraspecies. An interspecies value of 3 was used because an LC_{50} study (MacEwen and Vernot 1972) identified the mouse as being more sensitive than the rat. In this study, no deaths occurred and no gross lesions were observed in rats after a 4-hour exposure to 9600 ppm silane. However, 4/10 mice died at the same concentration and in another 4 hour study (Takebayashi 1993), renal enlargement in mice exposed to 10,000 ppm was observed. The intraspecies uncertainty factor was set at the default value of 10 as there is no data to estimate human variability and the chemical was not acting as a direct irritant.

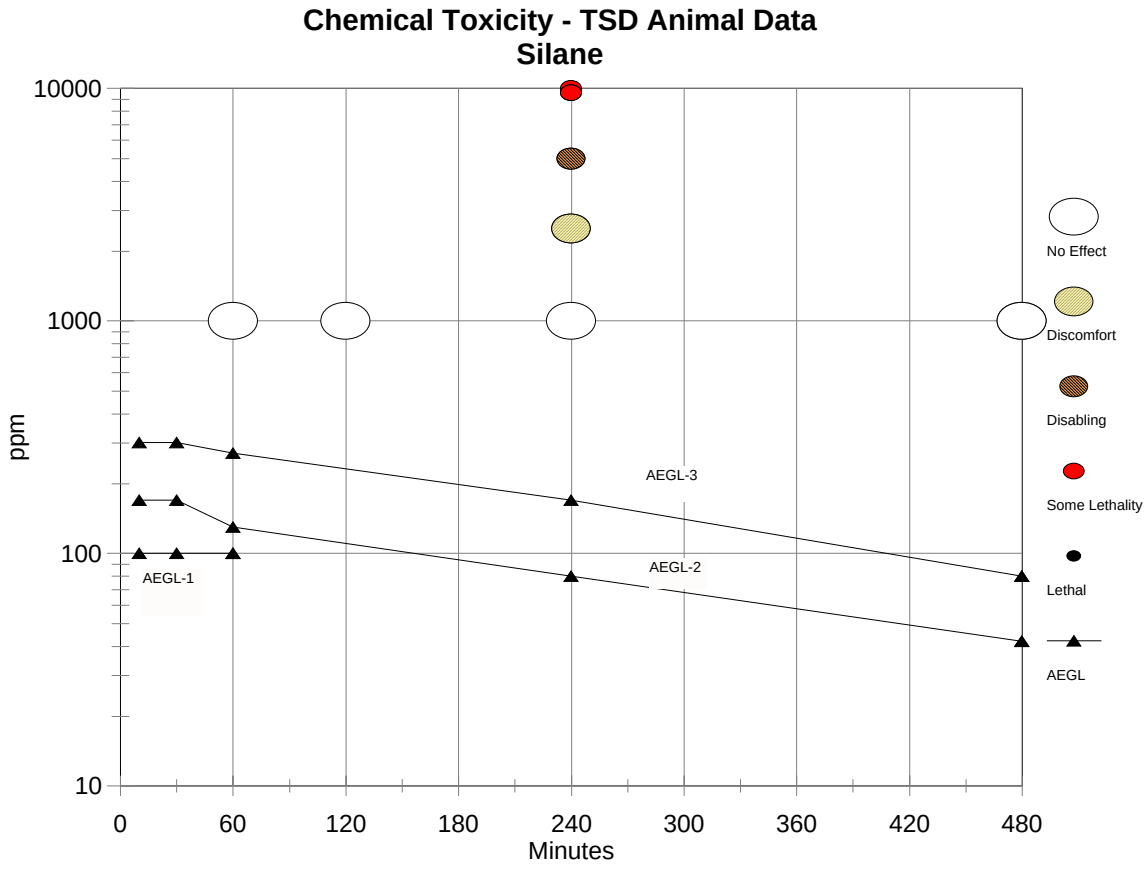
Modifying Factor: None

Animal to Human Dosimetric Adjustment: Not applicable

Time Scaling: Time-scaling was performed using the formula $C^n \times t = k$ where n values range from 0.8 to 3.5 (ten Berge et al. 1986). Due to limited data available, scaling was performed using n =3 for extrapolating to the 10- and 30- minute and 1 hour time points and n = 1 for extrapolating to the 8 hour time point. According AEGL SOP (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of 4 hours. Therefore, the 30-minute AEGL-3 value was adopted as the 10-minute value.

Data Adequacy: Data are adequate in this study for determining AEGL-3 values.

APPENDIX C: Time-Scaling Category Plot for Silane



No effect= No effect or mild discomfort
Discomfort= Notable transient discomfort/irritation
Disabling= Irreversible/long lasting effects or impaired ability to escape
Some lethality= Some, but not all, exposed animals died
Lethal= All exposed animals died