File No: NA/648

8 November 1999

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Amino-Functional Alkoxysilane

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Amino-Functional Alkoxysilane

1. APPLICANT

Dow Corning Australia Pty Ltd of 21 Tattersall Road BLACKTOWN NSW 2148 has submitted a standard notification statement in support of their application for an assessment certificate for Amino-Functional Alkoxysilane.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae have been exempted from publication in the Full Public Report and the Summary Report.

Marketing Names:	Dow Corning 3-3362 Adhesion Promoter;
Method of Detection and Determination:	Mass spectroscopy (MS); Gas chromatography (GC)
Spectral Data:	MS and GC read-outs were provided in the submission

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Straw yellow coloured clear liquid
Particle Size:	Not applicable, substance is a liquid
Melting Point:	> 35°C
Specific Gravity:	1.05 at 25°C
Vapour Pressure:	3.33 kPa at 25°C (for analogue X3-3541, corresponds to residual trimethoxysilane)
Water Solubility:	Reacts with water (see comments below)

Partition Co-efficient (n-octanol/water):	not determined (see comments below)
Hydrolysis as a Function of pH:	not determined (see comments below)
Adsorption/Desorption:	not determined (see comments below)
Dissociation Constant:	not determined (see comments below)
Flash Point:	8.0°C (for methyltrimethoxysilane)
Flammability Limits:	Upper Explosive Limit = 10.5% Lower Explosive Limit = 1.5% (for methyltrimethoxysilane)
Autoignition Temperature:	255°C (for methyltrimethoxysilane)
Explosive Properties:	Not determined
Reactivity:	Reacts with water and moisture

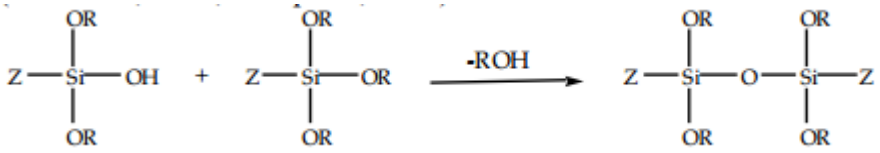
Comments on Physico-Chemical Properties

In the vapour pressure determination methanol and residual methyltrimethoxysilane were removed under vacuum. The proportion of methyltrimethoxysilane in the volatile material was determined and an equivalent amount of methyltrimethoxysilane was added to non-volatile residue. This solution was used in the vapour pressure determination. Hence, the determined vapour pressure corresponds mainly to that of methyltrimethoxysilane.

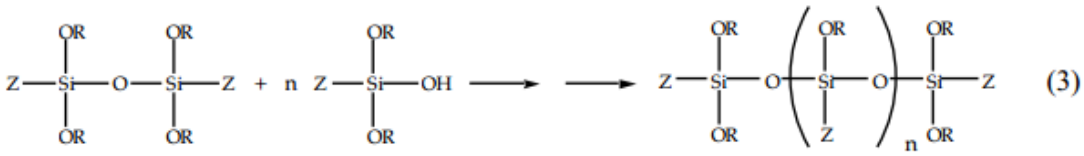
The notified chemical reacts with water including moisture in the air. A general reaction for the hydrolysis is shown below (1). The notifier has submitted data that shows the hydrolysis of the reactants used to prepare the notified chemical is catalysed at both low and high pH.

(1)

The hydrolysed product can then condense with starting material (2). The condensation product can also react with the hydrolysis product resulting in a polymerised product (3) with no significant solubility. This is supported by the literature (Hamelink, 1992, Varaprath, 1996).



(2)



(3)

The hydrolysis (1) and subsequent condensation (2) polymerisation (3) reactions are important in the curing of the sealant.

Determinations of the partition coefficient, adsorption/desorption behaviour and the dissociation constant for the notified chemical were not attempted. The moisture sensitive nature of the chemical would prevent the determination of these properties for the chemical.

The notified chemical is highly flammable and carries a Class 3 dangerous goods label.

4. PURITY OF THE CHEMICAL

Degree of Purity: 96% (approximately)

Hazardous Impurities:

Chemical name:	methanol
CAS No.:	67-56-1
Weight percentage:	3 to 7
Toxic properties:	Hazard Classification (NOHSC, 1994a): R11 – Highly flammable; R23/25 – toxic by inhalation and if swallowed. National Exposure Standard (NOHSC, 1995): 200 ppm TWA, 250 ppm STEL.
Chemical name:	ethanol
CAS No.:	67-17-5
Weight percentage:	3 to 7
Toxic properties:	National Exposure Standard (NOHSC, 1995): 1 000 ppm TWA

Non-hazardous Impurities (> 1% by weight): none

Additives/Adjuvants: none

5. USE, VOLUME AND FORMULATION

The notified chemical, will not be manufactured in Australia. The notified chemical is an adhesion promotor in silicone sealants. The formulated sealant containing the notified chemical (1 to 2%) will be imported into Australia in moisture resistant sealed 20 or 200 L metal drums or in metal tubes or polythene/polypropylene cartridges of 100 to 500 grams. Annual imports of the notified chemical over the next five years are projected to be up to 5 tonnes.

The majority of the sealant (~70%) containing the notified chemical will be used by professionals in the building industry. It will be applied in outdoor areas using either manually or pneumatically operated sealant guns. The notifier estimates that up to 30% of the notified chemical will find its way onto the do-it-yourself (D-I-Y) market. This is likely to be in the smaller 100-500 g packages sold through hardware stores nationwide.

6. OCCUPATIONAL EXPOSURE

Worker exposure during transport and storage will be limited to accidental spillage.

The notifier estimates that 200 to 500 workers in the building industry may be involved in application of the sealant containing the notified chemical and could be using the sealant 8 hours/day, 5 days/week. The method of use is first to prepare the surface then extrude "beads" of sealant either by hand from the cartridge or by using a compressor operated gun to force beads from the cartridge or from the drums. Once extruded, the "beads" are spread by means of a spatula or a finger dipped in soapy water (to prevent sticking). Dermal exposure to the sealant may, therefore, be frequent. Some secondary exposure of the eyes or mouth may occur by transfer from fingers. Uncured sealant is typically removed using solvents such as white spirit or acetone. Cured material can only be removed with a blade. Most of the work will be conducted on outdoor building sites where vapours are unlikely to accumulate. The notifier stated that goggles, rubber gloves and overalls would be worn during application.

Home handypersons may also be exposed to the notified chemical as the tubes and cartridges are to be available in hardware stores. In these cases, the sealant is applied by hand or by the use of a compressor-operated sealant gun. Exposure is expected to be similar, but on a smaller scale, to that described above for building industry workers. The level of personal protection worn is likely to be less stringent than for building workers.

Domestic and building site waste is commonly collected and disposed of to landfill. At this point the sealant should be cured and, although dermal exposure may occur, the notified chemical will not be bioavailable.

7. PUBLIC EXPOSURE

It is expected that during transport and storage, exposure of the general public to the notified chemical will be minimal, except in the event of an accidental spill. According to the MSDS spills should be prevented from spreading and soaked up with absorbent material, which is then disposed of according to regulations. The notified chemical reacts with ambient moisture on contact to form solid material, which would limit the potential for spills to spread.

Public exposure to the notified chemical will occur through contact with the cured sealant following its use in building and also via contact with the sealant material in use as a D-I-Y product.

8. ENVIRONMENTAL EXPOSURE

Release

The notified chemical is imported as a minor component of a ready-to-use sealant formulation. After use, the majority of the chemical will be crosslinked into the cured sealant matrix bound to building materials.

The notifier expects that the residues in the empty sealant containers will be kept to a minimum due the high cost of the sealant. The environmental assessment supports this view for industrial applications, however, the residual in containers used in the D-I-Y market is likely to be higher.

For the industrial applications of the sealants, container residues are expected to be sent to licensed waste contractors for disposal. It is likely that used containers from the D-I-Y market will be disposed of with household garbage. In both cases the residual sealants in the containers are expected to have cured prior to disposal.

Fate

No data on the biodegradability of the notified chemical has been supplied. The notifier refers to the literature, indicating that in general polysiloxanes are not biodegradable. Polydimethylsiloxanes are thought to be unstable in terrestrial environments where clays can catalyse cleavage of the siloxane linkage. They are probably more stable in aquatic sediment, as the catalytic action of clays is inversely related to their degree of hydration (Hamelink, 1992).

The vast majority of the silicone sealant, containing the notified chemical crosslinked within the sealant matrix, will share the fate of the building material to which it has

been applied. Incineration is the recommended means of disposal of the container residues consigned to licensed waste contractors. This would destroy the silicones and liberate water and oxides of carbon, nitrogen and silicon. If disposed of to landfill, the notified chemical is expected to remain immobile as it is crosslinked within the sealant matrix.

9. EVALUATION OF TOXICOLOGICAL DATA

Claims, by the notifier, were made and accepted for variation to Part C Schedule Requirements for Acute (except skin sensitisation where specific data are available), Repeated Dose and Genetic Toxicity.

The skin sensitising potential of the notified chemical has been investigated using the Magnusson and Kligman Guineapig Maximisation Test.

To support the claim toxicity studies on substances considered analogous to the notified chemical have been submitted as follows:

- Dow Corning X3-3541 - acute oral and dermal toxicity, skin and eye irritation tests and a reverse bacterial mutagenicity test. This substance has three methoxy groups on one of its constituent silanes, whereas the notified chemical has three ethoxy groups. Ethoxy components after hydrolysis produce ethanol and methoxy components produce methanol. The notifier considers methoxy components to be more toxic than ethoxy components, consequently, the notified chemical is considered by the notifier to be less toxic than Dow Corning X3-3541.

- Silane A-1120 (N-(β-aminoethyl)-γ-aminopropyltrimethoxysilane, CAS No. 1760-24-3) range finding toxicity studies (acute oral, inhalation and dermal toxicity), skin and eye irritation tests and a repeat human patch test. The submission states that Silane A-1120 is a precursor of the notified chemical. Brief summaries only of these studies were provided.

- Silane A-1110 - a human patch test (brief summary only).

- Trimethoxysilane (CAS No. 2487-90-3) - repeat dose studies (5 day subchronic inhalation study in 4 rodent species and 20 day repeated inhalation dose study in rats). The submission states that this substance is of the same chemical family as the notified chemical and it is significantly more volatile. It is claimed that because of the higher volatility, this chemical would have more adverse toxicity and can be considered as the worse case effect.

- Triethoxysilane (CAS No. 998-30-1) – a study investigating the induction of point mutations in mammalian cells *in vitro*. The submission states that this substance is of the same chemical family as the notified chemical but of a significantly lower molecular weight. It is claimed that because of its lower molecular weight, this chemical would have a more adverse effect on chromosome damage, therefore it can be considered as the worse case effect.

- Methyltriethyoxylsilane (CAS No. 2031-67-6) - studies investigating point mutations, chromosome alterations and DNA damage. The submission states that the triethoxysilane tested in this study is said to be of the same chemical family as the notified chemical but of lower molecular weight. It is claimed that because of its lower molecular weight this chemical would have a more adverse effect on chromosome damage, therefore it can be considered as the worse case effect.

This assessment accepts the analogue data as default data for the notified chemical.

9.1 Acute Toxicity

Summary of the acute toxicity of:

Test Substance	*Test*	*Species*	*Outcome*
Amino-Functional Alkoxysilane (notified chemical)	Skin sensitisation	Rabbit	Non-sensitising
Dow Corning X3-3541	Acute oral toxicity	Rat	LD_{50} > 2 000 mg/kg
	Acute dermal toxicity	Rabbit	LD_{50} > 2 000 mg/kg
	Skin irritation	Rabbit	Non irritating
	Eye irritation	Rabbit	Severe irritant
Silane A-1120	Acute oral toxicity	Rat	LD_{50} > 5 000 mg/kg
	Acute dermal toxicity	Rabbit	LD_{50} > 5 000 mg/kg
	Acute inhalation	Rat	LC_{50} > saturated vapour concentration
	Skin irritation	Rabbit	Moderate irritant
	Eye irritation	Rabbit	Moderate to severe irritant
Silane A-1100	Human patch test	Males	Sensitising

9.1.1.1 Acute Oral Toxicity (Stanton, 1990c)

Test Substance:	Dow Corning X3-3541
Species/strain:	rat/Sprague-Dawley albino
Number/sex of animals:	5/sex
Observation period:	14 days

Method of administration:	oral (gavage)
Clinical observations:	nil
Mortality:	1 female died spontaneously from gavage injury
Morphological findings:	nil
Test method:	OECD TG 401
LD_{50}:	> 2 000 mg/kg
Result:	Dow Corning X3-3541 was of very low acute oral toxicity in rats

9.1.1.2 Acute Oral Toxicity (Carpenter, 1966)

Test Substance:	Silane A-1120
Species/strain:	rat/Wistar
Number/sex of animals:	5 males per dose group
Observation period:	Not stated
Dose/Method of administration:	Dosages of 0, 2.0, 4.0, 8.0 or 16.0 mL/kg via stomach intubation
Clinical observations:	None observed
Mortality:	All high dose animals died on the first day of treatment; three animals dosed at 8 mL/kg died on Day 2
Gross Pathology:	Congestion throughout the lungs and the abdominal viscera with some haemorrhage present in the intestines. The surface of the livers, stomachs and intestines were whitish in appearance
Test method:	Similar to OECD TG 401
LD_{50}:	7.46 mL/kg (> 5 000 mg/kg)
Result:	Silane A-1120 was of very low acute oral toxicity in rats

9.1.2.1 Acute Dermal Toxicity (Stanton, 1990a)

Test Substance:	Dow Corning X3-3541
Species/strain:	Rabbit/New Zealand White

Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	a dermal application to clipped trunk region under a semi-occlusive dressing for 24 hours
Clinical observations:	nil
Mortality:	nil
Morphological findings:	all animals had changes in the skin and subcutaneous tissue which consisted of petechial haemorrhage, dermal thickening, and yellowish-brown discolouration.
Test method:	Similar to OECD TG 402
LD_{50}:	> 2 000 mg/kg
Result:	Dow Corning X3-3541 was of low dermal toxicity in rabbits

9.1.2.2 Acute Dermal Toxicity (Carpenter, 1966)

Test Substance:	Silane A-1120
Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	Neat test material – 2 males Diluted test material – 4 males
Observation period:	Not stated
Method of administration:	dermal application of neat test material, 16 mL/kg or diluted test material, 8 mL/kg to an intact skin site of the trunk under occlusive dressing for 24 hours
Clinical observations:	Marked erythema
Mortality:	Neat test material – 1 male on Day 7
Gross pathology:	Congested lungs, liver and spleen and pale kidneys
Test method:	Similar to OECD TG 402
LD_{50}:	16 mL/kg (> 5 000 mg/kg)
Result:	Silane A-1120 was of low dermal toxicity in rabbits

9.1.3. Acute Inhalation Toxicity (Carpenter, 1966)

Test Substance:	Silane A-1120
Species/strain:	Rats, strain not specified
Number/sex of animals:	6 males
Observation period:	Not stated
Method of administration:	Saturated vapour pressure generated by spreading 50g of test substance over 200 cm^2 area on a shallow tray placed near the top of a 120L glass chamber and sealed for 16 hours while a fan intermittently agitated the chamber atmosphere; rats were then introduced into the test chamber via a gasketed drawer type cage
Clinical observations:	None observed
Mortality:	nil
Gross pathology:	unremarkable
Test method:	Not an established guideline method
LC_{50}:	> saturated vapour concentration (not stated)
Result:	Silane A-1120 was of low inhalation toxicity in rabbits

9.1.4.1 Skin Irritation (Stanton, 1990d)

Test Substance:	Dow Corning X3-3541
Species/strain:	rabbit/New Zealand White
Number/sex of animals:	4 male
Observation period:	72 hours
Method of administration:	Dow Corning X3-3541 (0.5 mL) was applied to intact skin under a semi-occlusive dressing for 4 hours
Draize scores:	All individual scores were zero for erythema and oedema
Test method:	OECD TG 404
Result:	Dow Corning X3-3541 was non irritating to rabbit skin

9.1.4.2 Skin Irritation (Carpenter, 1966)

Test Substance:	Silane A-1120
Species/strain:	rabbit/New Zealand White
Number/sex of animals:	5 animals, sex not stated
Method of administration/Dermal response evaluation :	Test substance applied in 0.1 mL amounts to clipped, intact skin of the belly either undiluted or in progressive dilutions of 10, 1, 0.1 or 0.01% solvent. Ten grades are recognised based on appearance of moderate or marked capillary injection, erythema, oedema, necrosis within 24 hours. Grade 1 = No injury from undiluted.
Response:	Moderate erythema on one animal and from moderate to marked capillary injection on four others. Grade 3. (No individual scores provided)
Test method:	Not stated
Result:	Silane A-1120 was moderately irritating to rabbit skin

9.1.5.1 Eye Irritation (Stanton, 1990b)

Test Substance:	Dow Corning X3-3541
Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3 male/group
Observation period:	14 days (group 1), 7 days (group 2).
Method of administration:	Dow Corning X3-3541 (0.1 mL) was instilled into the right eye of each rabbit. Group 1 eyes were dosed and not washed. Group 2 eyes were dosed and washed 30 seconds after treatment.
Test method:	similar to OECD TG 405

Draize scores for Group 1 nonirrigated eyes:

	Time after instillation											
Animal	***1 hour***		***1 days***		***2 days***		***3 days***		***7 days***		***14 days***	
Cornea			***o***		***o***		***o***		***o***		***o***	
1	-		2		2		1		0		0	
2	-		2		2		1		0		0	
3	-		2		2		1		0		0	
Iris												
1	1		1		1		1		0		0	
2	1		1		1		1		0		0	
3	1		1		1		1		0		0	
Conjunctiva	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***
1	2	2	3	2	3	2	3	2	1	0	0	0
2	2	3	3	3	3	3	3	3	0	0	0	0
3	2	2	3	2	3	2	3	2	0	0	0	0

o: opacity, r: redness, c: chemosis

Comment:

Rabbits experienced slight to moderate pain after instillation. After one hour, all three rabbits showed moderate conjunctival redness and moderate to severe sweling and iritis. The 24, 48 and 72 hour readings revealed slight to moderate swelling, iritis and slight damage to the cornea. At 7 days, one animal still showed slight conjunctiva redness. All eyes were normal at 14 days.

Draize scores for Group 2 irrigated eyes:

	Time after instillation									
Animal	***1 hour***		***1 day***		***2 days***		***3 days***		***7 days***	
Cornea	***o***		***o***		***o***		***o***		***o***	
1	-		0		0		0		0	
2	-		0		0		0		0	
3	-		1		1		0		0	
Iris										
1	0		0		0		0		0	
2	0		0		0		0		0	
3	0		0		1		0		0	
Conjunctiva	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***
1	2	1	2	1	1	1	1	0	0	0
2	2	2	1	1	0	0	0	0	0	0
3	1	2	1	1	1	1	1	0	0	0

o: opacity, r: redness, c: chemosis

Comment: Rabbits experienced slight to moderate pain after instillation. The one and 24 hour readings revealed slight to moderate conjunctival redness with swelling in all rabbits and slight corneal injury was observed in one animal at 24 hours. At 48 hours, slight redness with swelling was seen in 2 rabbits and one animal still showed slight corneal injury and slight iritis. All eyes were normal at 7 days.

Result: Dow Corning X3 - 3541 was moderately to severely irritating to rabbit eye

9.1.5.2 Eye Irritation (Carpenter, 1966)

Test Substance: Silane A-1120

Species/strain: rabbit/New Zealand White

Number/sex of animals: 5 animals, sex not stated

Method of administration/Ocular response evaluation : Single instillations into the conjunctival sac of 0.005, 0.02, 0.10 or 0.5 mL undiluted or of 0.5 mL of 40, 15, 5 and 1% dilutions. Eye responses were read within one hour unstained and after fluorescein application at 24 hours, with ten grades recognised. Trace or no injury from 0.5 mL undiluted = Grade 1.

Response:	Moderately severe corneal necrosis from instillation of either 0.005 mL amounts in undiluted form or from an excess (0.5mL) of a 15% solution in propylene glycol. A 5% solution caused no injury in 2 eyes and traces of diffuse corneal necrosis in three others. Grade 8.
Test method:	Not stated
Result:	Silane A-1120 was severely irritating to rabbit eye

9.1.6.1 Skin Sensitisation – Guineapig Maximisation Test (Blaszcak, 1998)

Test Substance:	Notified chemical
Species/strain:	Guineapig/
Number/sex of animals:	Test animals, Group 1a – 10 males; Group IIa – 20 males. Irritation Control animals, Group Ib – 10 males; Group IIb – 10 males.
Study Design:	Group Ia and Group Ib animals were treated with the positive control, hexylcinnamic aldehyde (HCA); Group IIa and IIb animals were treated with the test substance

Induction/Challenge Procedure:

		Induction Concentration % ***(Shoulder)***				***Challenge Concentration %*** ***(Right Flank)***	
		Intradermal Injection			*Topical*[A]	*Topical*	
		Site 1	*Site 2*	*Site 3*	*Site 4*	*Site 1*	*Site 2*
			Day 1		*Day 8*	*Day 22*	
Test Animals:							
Ia	Positive control	B	30C	30D	100F	100G	50G, H
IIa	Test substance	B	5C	5E	100F	100G	50G, I
Irritation Control Animals:							
Ib	Positive control	B	J	B	L	100G	50G,H
IIb	Test Substance	B	J	K	L	100G	50G, I

A all animals treated with sodium lauryl sulfate before induction.
B animals received 0.1 mL dose/ site of 50% Freund's complete adjuvant (FCA)/water emulsion.
C Vehicle: propylene glycol – 0.1mL/site.
D Vehicle: 50% FCA/water emulsion – 0.1mL/site.
E Vehicle: 50% FCA/mineral oil – 0.1mL/site.
F 0.2 mL administered via saturated filter patch.
G 0.2 mL administered via saturated filter paper.
H Vehicle: propylene glycol.
I Vehicle: acetone.
J 100% propylene glycol administered – 0.1 mL/site.
K 50% propylene glycol in FCA/mineral oil – 0.1mL/site.
L Sham treated with filter paper patch.

Challenge outcome:	All 20 test animals and 10 irritation control animals were free of clear dermal responses at both 50 and 100% challenge concentrations. Positive responses to HCA demonstrated the susceptibility of animals in this test to a mild to moderate known sensitiser.
Test method:	OECD TG 406
Result:	the notified chemical was non sensitising to guineapig skin

9.1.6.2 Human Patch Test (Anon)

Only the following details were supplied concerning this investigation.

Test Substance:	Silane A-1100
Induction Procedure:	Cotton cloth patches soaked in test substance (25% aqueous) and applied to the skin of the backs of 52 male volunteers. Fresh applications were on alternate days for a total of 15 consecutive induction applications.
Induction outcome:	From about the 11th application onwards, close to 30% of volunteers experienced dermal responses (mainly grade 1+) during the induction
Challenge Procedure:	A challenge patch was applied 12 days after the final induction patch.
Challenge Outcome:	At challenge, 11 volunteers recorded signs of grade 1+ (just detectable erythema) and one volunteer recorded grade 2+ (moderate erythema) which when retested 8 days later was still 2+
Result:	On the basis of the data provided Silane A-1100 is considered a skin sensitiser to humans

9.2.1 Repeated Dose Toxicity – 5-Day Inhalation Study with Rats, Mice, Rabbits and Syrian Hamsters (Groh, 1981)

Test Substance trimethoxysilane

Study Design:

Species/Strain	*No of animals/dose group*
rat/Sprague Dawley;	5/sex
mouse/ICR;	5/sex
Syrian hamster/LVG;	5/sex
rabbit/New Zealand White	2/sex

Dose/ Method of Administration/Study Duration:
all species received whole body vapour exposure to 0, 10, 25 or 50 ppm trimethoxysilane for 7 hours/day for 5 consecutive days, followed by a 14-day post-exposure observation period; mean vapour concentration measured over 5 days was: 0, 12, 28 and 49 ppm.

Test method: in-house study

Mortality: Number of decedents per dose group

Species	0 ppm	10 ppm	25 ppm	50 ppm
rat	0/10	3/10	9/10	10/10
mouse	0/10	5/10	4/10	10/10
Syrian hamster	0/10	0/10	3/10	3/10
rabbit	0/4	4/4	4/4	4/4

Clinical observations:
Gasping, weakness, nasal discharge and a general debilitating condition.
Severe lung conjestion, atelectosis and haemorrhage were found in those animals that spontaneously died during the exposure period or the 14 day observation period; Animals sacrificed at the end of the observation period had lesser degrees of the same findings.

Comment:
Results indicate the relative order of mortality is hamsters < rats or mice < rabbits. In view of the significant different mortality results between the four species, the study authors considered that a large safety factor is required when extrapolating the results for safety evaluation in humans. However, the study authors also suggested that the rabbits may have had a subclinical viral infection and the rabbit LC_{50} values should be viewed with skepticism.

LC_{50}	Rat:	13 ppm
	Mouse:	14 ppm
	Syrian hamster:	72 ppm
	Rabbit:	1 ppm

Result: trimethoxysilane was of high inhalation toxicity to rats, mice, hamsters and rabbits

9.2.2 Repeated Dose Toxicity – 4 Week Inhalation Study with Rats (Beckenridge, 1980)

Test Substance: Trimethoxysilane

Species/strain: rat/Sprague-Dawley

Number/sex of animals: 10/sex/dose group

Method of administration:
whole body exposure to 0, 0.5, 5.0 or 10 ppm for 7 hours/day, five days/week for 4 weeks, except the high dose group which was sacrificed prior to study termination

Mortality:
Four of 10 rats of each sex of the mid dose group and all animals of the high dose group were found dead or sacrificed in a moribund condition during the course of treatment.

Clinical observations:
Clinical symptoms in the mid and high dose groups consisted primarily of lung congestion during the first week of treatment with nose discharge and a general weakness developing during week 2, leading to eventual death. No abnormalities were observed in the low dose group.

Significant dose dependent reduction in body weights of treated male and female rats. The magnitude of this reduction was greatest in the high dose group, less in the intermediate dose group and only marginally different from the controls in the low dose males. Bodyweight did not differ from the control group for females in the low dose group.

Significant dose-dependent reduction in absolute food consumption of treated male and female rats. The magnitude of this reduction was greatest in the high dose group, less in the intermediate dose group and only marginally different from the controls in the low dose group.

Haematology:
A decreased leucocyte count was observed in females of the low dose group. In mid and high dose animals a dose dependent increase in erythrocyte count, haemoglobin, and haematocrit was accompanied by a dose dependent decrease in leucocyte count and the proportion of lymphocytes and an increase in the proportion of segmented neutrophils.

Blood Chemistry
There was no effect on blood chemistry parameters in treated animals of the low and mid dose group compared to the control group. Abnormal blood chemistry parameters were observed in surviving animals of the high dose group.

Urinalysis
There was no effect on the urinary parameters in treated animals of the low and mid dose group compared to the control group. High mortality in the high dose group precluded analysis.

Morphological findings:
Gross Pathology
All animals had diffuse congestion of the lung and focal reddening in the gastrointestinal tract however, the incidence and severity was greater in treated animals. Findings in mid and high dose animals included areas of atelectasis and focal reddening in the lung and a failure of the lung to collapse when removed from the thoracic cavity.

Organ Weight
Increased lung weight in males of the mid and high dose groups.

Histopathology
High dose animals had pulmonary lesions consisting of bronchitis and bronchiolitis in the large and medium sized bronchii as well as smaller bronchioles. This was accompanied by, in severe cases, complete desquamation of the bronchial epithelium with replacement by mixed inflammatory cells and obliteration of the bronchial lumina with a mucopurulent exudate. Mucous metaplasia of the bronchial epithelium was revealed in several cases and this change extended sometimes to the submucosal glands.
No treatment related findings were observed in low dose group animals.
Examination of bone marrow smears revealed in high dose animals marked change with general reversal of the myeloid-erythroid ratio (which correlated with the changes in erythocyte and leucocyte counts found in the peripheral circulation), hypocellularity and general changes associated with moribund condition of the animals. Abundant megakaryocytes were noted in low dose animals.
Histopathological evaluation was not conducted on mid dose animals.

Test method: similar to OECD TG 407

Result:
Inhalation of trimethoxysilane over 4 weeks resulted in chronic inflammatory changes to the lung, dose related changes in haematological indices and morphological changes to the bone marrow in treated rats. Changes in leucocyte counts were seen in females at the lowest dose tested a No Observed Adverse Effect Level (NOAEL) cannot be determined for this study.

9.3 Genotoxicity

9.3.1.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Henrich, 1990)

Test Substance:	Dow Corning X3-3541
Strains:	*S typhimurium* TA 98, TA 100, TA 1535 and TA 1537; *E coli* WP2
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Concentration range:	312.5, 625, 1 250, 2 500 and 5 000 µg/plate with and without S9 metabolic activation; appropriate strain specific positive control reference substances were used

Test method:	OECD TG 471/472
Comment:	there were no significant increases in revertant colony numbers in any tester strain at any dose, both in the presence or absence of metabolic activation; concurrent positive controls used in the test induced marked increases in the frequency of revertant colonies and the activity of the S9 fraction was found to be satisfactory
Result:	Dow Corning X3-3541 was not considered mutagenic in the bacterial strains tested

9.3.1.2 *Salmonella typhimurium*, *Escherichia coli* and *Saccharomyces cerevisiae* Reverse Mutation Assay (Brusick, 1978)

Test Substance:	methyltriethoxysilane
Strains:	*Salmonella typhimurium* TA 1537, TA 1535, TA 100 and TA 98; *Escherichia coli* W3110/*po1A*$^{+}$, P3478/*po1A*$^{-}$; *Saccharomyces cerevisiae* D4
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Concentration range:	0.001 to 5 µl/plate, appropriate strain specific positive control reference substances were used
Test method:	OECD TG 472 – plate incorporation assay
Comment:	there were no significant increases in revertant colony numbers in any of the tester strains at any dose level, both in the presence or absence of metabolic activation; concurrent positive controls used in the test induced marked increases in the frequency of revertant colonies and the activity of the S9 fraction was found to be satisfactory
Result:	methyltriethoxysilane was not considered mutagenic in yeast cells and the bacterial strains tested

9.3.1.3 *In Vitro* Mammalian Cell Gene Mutation Test (Brusick, 1978)

Test Substance:	methyltriethoxysilane
Cells:	L5178Y mouse lymphoma cell line
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254

Concentration range:	Experiment 1: 0.1 to 1.6 μL/mL – with and without metabolic activation; Experiment 2: 0.4 to 2.40μL/mL – without metabolic activation; 0.4 to 3.20μL/mL – with metabolic activation, Positive Controls: appropriate positive control reference substances were used
Test method:	Similar to OECD TG 476
Comment:	The study authors indicated the results of the first experiment were slightly variable, whereas, the results of the second experiment were more uniform. Overall the results of both tests were consistent and considered negative. No treated cultures exhibited a mutant frequency greater than two times the mean mutant frequency of the solvent controls; no dose-dependent response was noted in the treated cultures. Concurrent positive controls used in the test induced marked increases in mutant frequencies and the activity of the S9 fraction was found to be satisfactory.
Result:	methyltriethoxysilane did not induce forward mutations at the thymidine kinase locus on L5178Y mouse lymphoma cells *in vitro*

9.3.1.4 *In Vitro* Mammalian Cell Gene Mutation Test (San, 1995)

Test Substance:	Triethoxysilane
Cells:	$L5178Y^{+/-}$ mouse lymphoma cell line
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Concentration range:	The following test substance concentrations were tested in duplicate, both in the presence and absence of metabolic activation: 0, 313, 625, 1 250, 2 500, 5 000 μg/mL Positive Controls: ethylmethansulfonate (-S9) ; 7,12-dimethylbenz[a]anthracene (+S9); Solvent controls: as the test substance is capable of releasing ethanol, additional controls were set up to match the amount of ethanol releasable at the highest test substance concentration;

Test method:	Similar to OECD TG 476
Comment:	Toxicity was observed at 2 500 and 5 000 µg/mL both in the presence and absence of metabolic activation; No treated cultures exhibited a mutant frequency greater than two times the mean mutant frequency of the solvent controls; no dose-dependent response was noted in the treated cultures; concurrent positive controls used in the test induced marked increases in mutant frequencies and the activity of the S9 fraction was found to be satisfactory
Result:	triethoxysilane did not induce forward mutations at the thymidine kinase locus on L5178Y$^{+/-}$ mouse lymphoma cells *in vitro.*

9.3.1.5 *In Vitro* Sister Chromatid Exchange (SCE) and Chromosome Aberration Assay in Mammalian Cells (Brusick, 1979)

This study represents a repeat of the earlier study (Brusick, 1978) in which there were some indications of a positive response, but these were erratic with the study authors concluding that methyltriethoxysilane was inactive. The study was repeated with improvements and modifications to the protocol. The second study is summarised below.

Test Substance:	methyltriethoxysilane
Cells:	L5178Y mouse lymphoma cell line
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Concentration range:	The following test substance concentrations were tested in duplicate, both in the presence and absence of metabolic activation: 0.125, 0.25, 0.50, 1.0, 2.0 µL/mL Positive Controls: ethylmethansulfonate 0.5 µL/mL (-S9) ; cyclophosphamide (CP) 0.5µM (+S9);
Test method:	Similar to OECD TG 479
Comment:	Toxicity noted at 1.0 and 2.0 µL/mL without metabolic activation and 2.0 µL/mL with metabolic activation;
Chromosome aberrations	In the absence of metabolic activation, methyltriethoxysilane

(CA):	induced a small increase in CA at 0.25 and 0.50 μL/mL. In the presence of metabolic activation, the results are similar, with indications of a dose response and noted higher frequency of CA.
Sister Chromatid Exchange (SCE):	In the absence of metabolic activation, a small but consistent increase in SCE was found. However, the increase was not dose-dependent and was not observed at 2.0 μL/mL, in parallel with the results from the CA assay. In the presence of metabolic activation, the frequency of SCE was increased more than 3-fold, although there was no dose response. (The positive control did not respond appropriately in the test with metabolic activation - the concentration of CP caused cell cycle delay preventing cells from progressing through two cell cycles)
Result:	Methyltriethoxysilane is weakly positive in the induction of chromosome aberrations in the presence and absence of metabolic activation. Methyltriethoxysilane induced marked SCE in the presence of metabolic activation and weakly induced SCE in the absence of metabolic activation.

9.3.1.6 DNA damage – Alkaline Elution Technique (Brusick, 1978)

Test Substance:	methyltriethoxysilane
Cells:	L5178Y mouse lymphoma cell line
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Study Design:	Cleansed lymphoma cells exposed to 0.5 μCi/mL ^{3}H-thymidine for 20 hours. Following a rinsing period of 24 hours, the test substance is added to the cells for a treatment period of 4 hours in the absence of metabolic activation and 2 hours in the presence of metabolic activation
Concentration range:	The following test substance concentrations were tested in duplicate as follows: Without S9: 0, 0.3, 0.6, 1.2 μL/mL, Positive Control: Methylmethanesulfonate.

	With S9: 0, 0.8, 1.6, 3.2 μL/mL, Positive Control: Benzo[a]pyrene
Test method:	Kohn (Biochemistry 13:4134-4139, 1974)
Comment:	The study authors reported the test for primary DNA damage was negative. Increased ^{3}H-thymidine in the elution at 3.2 μL/mL was elevated because of toxicity. The positive controls induced responses within the expected ranges.
Result:	Methyltriethoxysilane did not induce DNA damage

9.4 Overall Assessment of Toxicological Data

Data submitted on the notified chemical was limited to a Magnusson and Kligman Guineapig Maximisation Test. In their claim for Variation of Schedule Requirements the notifier has provided toxicity studies on substances considered analogous to the notified chemical.

Acute Toxicity
The notified chemical is not expected to cause acute systemic toxicity based on the results of very low acute oral and low acute dermal toxicity of Dow Corning X3-3541 and
Silane A-1100 in rats and rabbits. Based on the results of Silane A-1100, it is probable that the notified chemical will also have low acute inhalation toxicity.

Skin and Eye Irritation
Dow Corning X3-3541 was non-irritating and Silane A-1120 was moderately irritating to rabbit skin. Severe effects were seen in the eye. Using Silane A-1100, rabbit eyes suffered moderate to severe corneal injury from very small amounts undiluted and from an excess of a 15% solution in propylene glycol. A 5% solution caused minor corneal irritation. Dow Corning X3-3541 was moderately to severely irritating to rabbit eye, with corneal, iris and conjunctiva involvement. Based on these findings the notified chemical is expected to have severe irritant effects to the eye and some skin irritant potential.

Sensitisation
The notified chemical was non–sensitising in an adjuvant type test in guineapigs. In a human patch test on a precursor substance, Silane A-1100, there was evidence of skin sensitisation. Unreacted, residual precursors of the notified chemical may cause skin sensitisation.

Repeat Dose Toxicity
Short-term repeated exposure (5 days) to trimethoxysilane in four rodent species resulted in high inhalation toxicity. In a 20 day repeat dose inhalation study, administration of trimethoxysilane (0.5, 5.0 or 10 ppm) resulted in chronic inflammatory changes to the lung and dose related changes in haematological indices and morphological changes to the bone marrow in treated rats. Changes in leucocyte

counts were seen at the lowest dose tested and no NOAEL is determined for this study. Methoxy silanes such as trimethoxysilane may produce methanol toxicity. Methanol is converted by alcohol dehydrogenase (the affinity for methanol is much less than that for ethanol) in human liver into formaldehyde and formic acid. These two metabolites are highly toxic and produce severe metabolic acidosis, ocular toxicity and neurotoxicity. The notified chemical is of high molecular weight and is stated to have negligible vapour pressure. Given the structure of the the notified chemical and any unreacted alkoxysilanes contained therein will have similar toxicity to that of trimethoxysilane.

Genotoxicity
Dow Corning X3-3541 was not mutagenic to bacteria. Triethoxysilane did not induce point mutations in mouse lymphoma cells *in vitro*. Methyltriethoxysilane did not induce point mutations in bacterial or yeast cells or mammalian cells *in vitro* and did not induce DNA damage in mammalian cells *in vitro*. However, it is considered weakly positive in the induction of chromosome aberrations in the presence and absence of metabolic activation, and induces sister chromatid exchanges in mammalian cells. The notified chemical is expected to display genotoxic activity similar to that of the analogue substances.

Hazard Classification
Based on the analogue data submitted, the notified chemical is expected to have skin and severe eye irritation. The Material Safety Data Sheet for the notified chemical alerts to respiratory irritation as well. The notified chemical was negative for skin sensitisation in guineapigs, however, results from a human repeat patch test on a precursor substance do not preclude the notified chemical having some skin sensitisation potential. It is not expected the notified chemical will display effects more adverse than those observed with trimethoxysilane in repeat dose inhalation studies. The notified chemical may display some genotoxic activity *in vitro* but the data is insufficient for a health effects classification. Further testing on the notified chemical would be required for a satisfactory assessment of effects from repeated exposure or genotoxic potential.

The analogue data supports the hazard classification Irritant (Xi) (NOHSC, 1999) and the following risk phrases, for the notified chemical: R41 - Risk of Serious Damage to Eyes; and R37/38 – Irritating to Respiratory System and Skin.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No ecotoxicity data for the notified chemical has been provided. However, the following ecotoxicity studies for methyltriethoxysilane [$(CH_3CH_2O)_3SiCH_3$] have been supplied by the notifier.

Test/ Concentration mg/L[a]	*Species*	*Results*	*Reference*[b]
acute 96 hour toxicity 0, 100, 180, 320, 560, 1 000	Rainbow trout *(Oncorhyncus mykiss)*	LC_{50} = 400 (95% CI 264-608) NOEC = 320	(Rausina, 1976)
acute 96 hour toxicity 0, 10, 100, 1 000	Bluegill sunfish *(Lepomis macrochirus)*	LC_{50} > 1 000	(Rausina, 1976)
acute 96 hour toxicity 0, 10, 100, 1 000	Mummichogs *(Fundulus heteroclitus)*	LC_{50} > 1 000	(Rausina, 1976)
acute 96 hour toxicity 0, 240, 320, 420, 560, 750	Shore crabs *(Pachygrapsus crassipes)*	LC_{50} = 421 (95% CI 353-501) NOEC = 320	(Rausina, 1976)
acute 96 hour toxicity 0, 18, 32, 56, 100, 180	Grass shrimp *(Palaemonetes vulgaris)*	LC_{50} = 58 (95% CI 41-83) NOEC = 32	(Rausina, 1976)
acute 48 hour toxicity 0, 10, 100, 500, 1 000	Water flea *(Daphnia magnus)*	EC_{50} > 1 000	(Annelin, 1976)
14 day growth 0, 10, 100, 500, 1 000	Algae *(Selenastrum capricornutum)*	EC_{50} > 1 000	(Cerro, 1976)
14 day growth 0, 10, 100, 500, 1 000	Algae *(Anabaena flos-aquae)*	EC_{50} > 1 000	(Cerro, 1976)

* NOEC - no observable effect concentration
[a]Nominal concentrations. [b]Full test details are only available for results obtained by (Rausina, 1976).

In all tests, methyltriethoxysilane was allowed to equilibrate for 24 hours in the test media prior to the addition of test animals. In the daphnia and algal studies, the submission claims that this was to allow time for complete hydrolysis of the methyltriethoxysilane to $CH_3Si(OH)_3$. Complete hydrolysis of the test material is unlikely given the propensity of these materials to polymerise after hydrolysis (see Section 3). Hence the exact composition of the chemical to which the test organisms were exposed is unknown.

The submitted ecotoxicity data indicate that the test material is slightly toxic to grass shrimp and practically non-toxic to all other test organisms. The relevance of these toxicity studies to the notified chemical is uncertain given the polymerisation reactions which are possible. However, the limited environmental exposure of the notified chemical would minimise any potential environmental effects.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified chemical is a minor component of silicone sealants. The vast majority of the silicone sealant containing the notified chemical crosslinked within the sealant matrix, will share the fate of the building material to which it has been applied. Incineration is the recommended means of disposal of container residues in the containers, which are consigned to licensed waste contractors. This would destroy the silicones and liberate water and oxides of carbon, nitrogen and silicon. If disposed of to landfill, the notified chemical is expected to remain immobile, as it is crosslinked within the sealant matrix. Hence, the potential environmental hazard of the notified chemical incorporated into formulated sealant products is expected to be low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Based on the analogue data submitted, the notified chemical is expected to be a skin and severe eye irritant. The MSDS for the notified chemical alerts workers to respiratory irritation as well. The notified chemical was negative for skin sensitisation in guineapigs, however, results from a human repeat patch test on a precursor substance suggest that the notified chemical may have skin sensitisation potential. Inhalation of trimethoxysilane over 4 weeks resulted in chronic inflammatory changes to the lung, dose related changes in haematological indices and morphological changes to the bone marrow in treated rats. Changes in leucocyte counts were seen at the lowest dose tested (0.5 ppm) and no NOAEL can be determined for this study. It is not expected the notified chemical will display effects more adverse than those observed with trimethoxysilane in this repeat dose inhalation study. The notified chemical may display some genotoxic activity *in vitro* but the data is insufficient for a health effects classification. Further testing on the notified chemical would be required for a satisfactory assessment of effects from repeated exposure or genotoxic potential.

The analogue data supports the hazard classification Irritant (Xi) (NOHSC, 1999) and the following risk phrases, for the notified chemical: R41 - Risk of Serious Damage to Eyes; and R37/38 – Irritating to Respiratory System and Skin.

Occupational Health and Safety

The notified chemical is to be imported at a concentration of up to 1 to 2% in an adhesive sealant in tubes, cartridges and 20 L or 200 L drums. The sealant will be used by building industry workers and home handymen. The sealant will be extruded

from the cartridge or drum line as "beads" which are then spread, typically with a spatula or finger dipped in soapy water and the excess uncured sealant removed.

Exposure of transport and storage workers is unlikely even in the event of accidental spillage, considering the physical form of the sealant and the packaging.

Exposure is possible for workers cleaning off excess sealant after it is has been applied to a substrate. Beads of sealant may be spread by hand and tools contaminated with uncured sealant are cleaned by hand. Some secondary exposure to the eyes and mouth may occur through hand contamination.

At the concentration of the notified chemical (1 to 2%) in the sealant product the risk of eye, skin and respiratory irritation during application is expected to be minimal. The risk of skin sensitisation cannot be excluded, however. Protective gloves, goggles and overalls should be worn when handling the sealant containing the notified chemical, removing excess sealant and disposing of uncured sealant to minimise the risk of adverse effects. The notified chemical should at all times be used in well ventilated areas.

Public Health
As the notified chemical will be used in silicon sealant products available for purchase by consumers, there is the potential for widespread exposure to the public. Major concerns identified in toxicity tests with analogue chemicals were the potential for skin sensitisation in humans, the high inhalation toxicity of analogue chemicals and a weakly positive response *in vitro* chromosome aberration test. The notified chemical is of high molecular weight and is stated to have a low vapour pressure. This, combined with the presentation of the notified chemical at a low percent (1 to 2%) in silicone sealant which would be expected to cure relatively rapidly, limit the concerns relating to inhalation exposure. The normal precautions for use of silicone sealants should also limit the dermal exposure to the notified chemical. Consequently, the potential hazard from use of the notified chemical is considered to be low. There will be minimal public exposure from transport and storage, and the public exposure to the notified chemical from contact with the cured sealant is also expected to be minimal.

Based on the above information, it is considered that the notified chemical will not pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

To minimise occupational exposure to products containing the notified chemical the following guidelines and precautions should be observed:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);

- Industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.1 (Standards Australia, 1990);
- Impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia, 1998);
- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994);
- Spillage of the notified chemical should be avoided, spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion; and
- A copy of the MSDS should be easily accessible to employees.

If the conditions of use are varied, such as the concentration used in the product is varied or additional products containing the notified chemical enter the public domain, then greater exposure of the public may occur. In such circumstances, further information may be required to assess the hazards to public health.

14. MATERIAL SAFETY DATA SHEET

The MSDS for Dow Corning 3-3362 Adhesion Promoter containing the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994b).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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Attachment 1

The Draize Scale for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema 0 Very slight erythema (barely	
perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
Diffuse beefy red	3 severe	Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
		Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe