File No: NA/667

April 1999

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

1,3-benzenedimethanamine, N,N,N',N'-tetrakis(oxiranylmethyl)-

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

1,3-benzenedimethanamine, N,N,N',N'-tetrakis(oxiranylmethyl)-

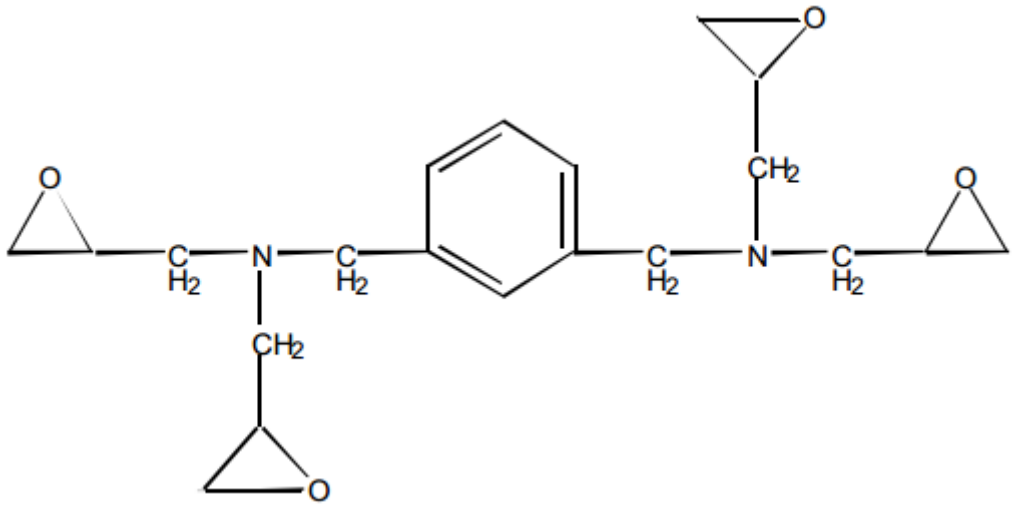
1. APPLICANT

Amtrade International of Level 2, 570 St. Kilda Rd, MELBOURNE, VIC 3004 has submitted a standard notification statement in support of their application for an assessment certificate for 1,3-benzenedimethanamine, N,N,N',N'-tetrakis(oxiranylmethyl)-

2. IDENTITY OF THE CHEMICAL

Chemical Name:	1,3-benzenedimethanamine, N,N,N',N'-tetrakis(oxiranyl-methyl)-
Chemical Abstracts Service (CAS) Registry No.:	63738-22-7
Other Names:	N,N,N',N'-tetraglycidyl-1,3-xylylenediamine, N,N,N',N'-tetraglycidyl-meta-xylylenediamine (TGMX), tetraglycidyl xylenediamine Polyglycidyl metaxylenediamine (PGA-X) Tetrad-X
Trade Name:	Amtrade B15

Structural Formula:



Molecular Formula:	$C_{20}H_{28}N_2O_4$
Molecular Weight:	360
Method of Detection and Determination:	the notified chemical can be detected using GC and identified using infrared spectrometry
Spectral Data:	IR: 3048, 2993, 2921, 2820, 2796, 1606, 1589, 1484, 1440, 1348, 1257, 1135, 1066, 993, 912, 848, 829, 792, 759, 701 cm^{-1}

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	pale yellow viscous liquid
Boiling Point:	>250°C
Specific Gravity:	ca. 1.15 at 25°C
Vapour Pressure:	<0.13 kPa at 25°C (estimated)
Water Solubility:	the notified chemical reacts with water
Partition Co-efficient (n-octanol/water):	Not determined
Hydrolysis as a Function of pH:	rapid reaction with water
Adsorption/Desorption:	not determined
Dissociation Constant:	not determined
Flash Point:	216 °C
Autoignition Temperature:	not determined
Explosive Properties:	not explosive
Reactivity/Stability:	the notified chemical reacts readily with water and other bases; the chemistry is typical of epoxy functional groups

Comments on Physico-Chemical Properties

The nature of the chemical was stated to preclude acquisition of most of the physico-chemical data pertinent to environmental issues, i.e. water solubility, hydrolytic degradation, octanol/water partition coefficient and adsorption/desorption characteristics. The notified substance reacts with water to form a gel.

The notified substance does not contain any dissociable groups.

4. PURITY OF THE CHEMICAL

Degree of Purity: 100 %

Toxic or Hazardous Impurities:

Chemical name:	Oxirane, (chloromethyl)-
Synonyms:	epichlorohydrin
CAS No.:	106-89-8
Weight percentage:	< 10 ppm
Toxic properties:	On the NOHSC *List of Designated Hazardous Substances* (National Occupational Health and Safety Commission, 1994a) 0.1≤Conc. ≤1 % R23/24/25: Toxic by inhalation, in contact with skin and if swallowed R36/38: Irritating to eyes and skin 1≤Conc. ≤10 % R23/24/25: Toxic by inhalation, in contact with skin and if swallowed R34: Causes burns

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

5. USE, VOLUME AND FORMULATION

The notified chemical is an epoxy curing agent and will be used in Part B of a two part epoxy coating for application to plastic surfaces.

The notified chemical will not be manufactured in Australia, nor will it be reformulated other than by mixing in a 1:3 ratio with Part A, and 30 % glycol ether solvent in preparation for application. The import volume is estimated to be 7 000 kg/year. One site for the surface coating process has been identified in Australia.

6. OCCUPATIONAL EXPOSURE

Transport and Storage
Transport and storage workers may be involved with the notified chemical for 2-3 hours per day on 10-15 days per year. The notified chemical will be imported in 200 kg drums. The drums will be transported directly from the docks to the customer facility where they will be stored in a chemical warehouse prior to use on the same site. Waterside workers, transport drivers and warehouse workers would only be exposed to the notified chemical in the case of an accident involving rupture of the packaging.

Plant Operators
Plant operators will be working with the notified chemical for 8 hours per day for up to 250 days per year. The equipment used for mixing and applying the epoxy resin will be completely enclosed and automated. The products will contain the cured epoxy resin in which the notified chemical will be crosslinked and immobilised. The most significant exposure is therefore likely to occur during drum connection and disconnection, cleaning and equipment maintenance.

Metered quantities of the notified substance will be pumped or gravity fed from the 200 kg drums directly into the application machinery. The epoxy resin Part B will be mixed with a mixture of glycol ether solvent and Part A. The mixing will be automated. The coating mix will then be sprayed onto the plastic material using an electrostatic mechanism to minimise overspray. The treated material will then be heated to 63°C for 15 minutes within the process line to complete the curing of the resin before the article is removed from the enclosed environment. The production area is stated to have local and general ventilation to remove any vapours which may escape.

Cleaning of the equipment will be carried out using a suitable solvent which will be collected and disposed of to a liquid waste facility by a licensed contractor.

The notifier states that plant operators will be required to wear impervious gloves, coveralls, suitable respirator and eye protection during connection and disconnection of containers to transfer lines and during cleaning and maintenance of equipment.

7. PUBLIC EXPOSURE

There is little potential for exposure of the public to the notified chemical, as it is not available for retail sale. The public will only come in contact with the coated materials where the notified chemical will be trapped inside the cured matrix of the coating. The low exposure indicates a low risk to public health.

8. ENVIRONMENTAL EXPOSURE

Release

The process of mixing and applying the resin is in a closed system with no exposure to the environment until the notified substance is cured.

The cleaning of equipment is expected to lead to some residues (105 kg per year or 1.5 % of yearly import volume) which will be collected by a licensed waste contractor.

During the surface coating process the notifier estimates that 35 kg or 0.5 % of the yearly import volume will be released due to accidents or leaks in equipment. Any spillage of the polymer would be absorbed into sand or other suitable material, and disposed of to landfill. The Material Safety Data Sheet (MSDS) gives instructions for dealing with spills of the imported product containing the notified polymer.

Any residue of the notified substance remaining in the 200L drums, estimated to be 105 kg annually or 1.5 % of the drum contents, will be mixed with part A. After hardening, the drums containing the residues will be disposed of by a licensed contractor to landfill.

Fate

The notified substance will form part of a surface coating on plastic components and fixed strongly to the coated articles, thus sharing their fate. At the end of their useful lives these would be disposed of to landfill, or possibly incinerated.

Released material resulting from the surface coating process would also be placed into landfill. Solvents used in cleaning of equipment and other activities connected with use of the polymer are likely to be recycled or disposed of to a liquid waste handling facility where the ultimate fate of any remaining polymeric material is assumed to be incineration.

When disposed of to landfill, the highly crosslinked nature of the material will preclude significant leaching, and the polymer would be subject to the slow biodegradation processes operative in landfill situations.

Incineration of the polymer would result in the production of water and oxides of carbon and nitrogen.

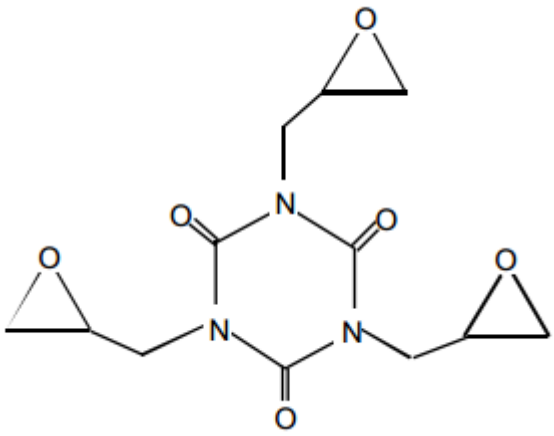
The notified substance is not expected to bioaccumulate because it will either react with water in the environment to form a gel, or have been reacted with the other part of the surface coating.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Reports of acute oral toxicity and skin irritation tests using the notified chemical were provided as part of the notification statement.

Analogue data for triglycidylisocyanurate (TGIC; structure shown below) have been provided by the notifier for acute dermal toxicity, eye irritation, acute inhalation toxicity and skin sensitisation. The analogue data is from the NOHSC Priority Existing Chemicals report (National Occupational Health and Safety Commission, 1994c). The toxic properties of TGIC are expected to be dominated by the reactivity of the glycidyl groups, and thus it should serve as an appropriate model for the glycidyl groups on the notified chemical. TGIC is reasonably similar in size to the notified chemical, but does not have the same basic properties caused by the tertiary amine nitrogens.



To compensate for this discrepancy, analogue data for the toxicity of primary and secondary amine nitrogens which has been provided as part of the notification for Part A of the epoxy system has also been considered. The amine compounds for which the data has been provided are isophoronediamine, diethylenetriamine, m-xylylenediamine and triethylenetetramine. The data consisted of a compilation of summaries from the common sources RTECS (National Institute of Occupational Safety and Health, 1997), HSDB (National Library of Medicine, 1997) and ACGIH (American Conference of Government Industrial Hygienists, 1998).

The combined analogue data is accepted in this report as a suitable surrogate for the notified chemical. The findings are taken as representing in part the toxicity of the notified chemical. The acceptance is qualified because the properties of the amine nitrogens on the notified chemical may, for certain end points, increase the overall toxicity. Unless specifically indicated, the toxicity of the notified chemical is taken as that of the analogue showing the highest toxicity.

Summary of the acute toxicity of 1,3-benzenedimethanamine, N,N,N',N'-tetrakis(oxiranylmethyl)-

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD50 = 730 mg/kg (males) LD50 = 630 mg/kg (females)	(Mitsubishi Gas Chemical Company, undated)
acute dermal toxicity	rat	not determined	
skin irritation	rabbit	moderate irritant	(Mitsubishi-Kasei Institute of Toxicological and Environmental Sciences, 1978a) (Mitsubishi-Kasei Institute of Toxicological and Environmental Sciences, 1978b)
eye irritation	rabbit	not determined	
skin sensitisation	guinea pig	not determined	

9.1.1 Oral Toxicity (Mitsubishi Gas Chemical Company, undated)

The test material used for this study was Epoxy Resin PGA-X, which was estimated by the study author to contain 75 % notified chemical. No details of the identity of impurities was given.

Species/strain:	rat/Wistar
Number/sex of animals:	10/sex/dose
Observation period:	14 days
Method of administration:	gavage, neat liquid, estimated purity 75 %
Dose range:	males: 0.392, 0.485, 0.606, 0.714, 0.825, 0.918, 1.170 mL/kg females: 0.349, 0.471, 0.588, 0.741, 0.864, 0.988 mL/kg
Test method:	OECD TG 401 (Organisation for Economic Cooperation and Development, 1987c)

Mortality: males

dose (mL/kg)	mortality
0 (control)	0/10
0.392	1/10
0.485	5/10
0.606	3/10
0.714	5/10
0.825	6/10
0.918	9/10
1.170	10/10

females

dose (mL/kg)	mortality
0 (control)	0/10
0.349	0/10
0.471	5/10
0.588	7/10
0.741	6/10
0.864	8/10
0.988	10/10

Clinical observations: no clinical signs of toxicity were observed for the first two days after administration; on the third day, severe diarrhea, reddish brown vomit or lacrimation, decline of spontaneous movement and blepharoptosis (drooping of eyelids due to paralysis) commenced; these symptoms persisted until around day 14; ataxia and oppression in breathing preceded the deaths; mortality was confined to days 4 to 8

bodyweights of treated animals decreased substantially between days 1 and 5; from day 5 the rate of bodyweight increase was similar to controls

Morphological findings: the rats which died during the test exhibited ulceration or necrosis of the stomach and intestinal canal, with the stomach symptoms being particularly pronounced; no major changes in other organs were observed; in the males sacrificed at the end of the observation period, accretion of the stomach (mainly anteriorly) with thoracic peritoneum was observed with a tendency to increased accretion at higher doses; this was not observed in the females

LD_{50}: males: 730 mg/kg, females: 630 mg/kg

Result: the test material was of low acute oral toxicity in rats; the risk phrase R22 'Harmful if swallowed' is required

9.1.2 Dermal Toxicity

No dermal toxicity studies of the notified chemical were provided. The summary of toxicological data for TGIC which was provided as analogue data listed the results from three acute dermal toxicity studies performed according to OECD TG 402 (Organisation for Economic Cooperation and Development, 1987a). For each of the studies, the LD_{50} was found to be > 2000 mg/kg. TGIC was therefore found to have low dermal toxicity.

The acute dermal toxicity of a number of primary and secondary amines showed these to be of moderate dermal toxicity, with LD_{50} values between 805 and 2000 mg/kg. The notified chemical would therefore be expected to be of low to moderate acute dermal toxicity. The risk phrase R21 'Harmful in contact with skin' is required.

9.1.3 Inhalation Toxicity

No acute inhalation toxicity studies of the notified chemical were provided. A summary of the inhalational toxicity for the analogue compound TGIC was provided. Four studies are summarised; of these, two were studies with rats according to OECD TG 403 (Organisation for Economic Cooperation and Development, 1981). The results showed a LC_{50} of 650 mg/m^3 for females and > 650 mg/m^3 for males. Partial haemmorhage in the lungs of the dead animals was the main observation. TGIC is therefore classified as moderately toxic by inhalation.

The acute inhalation toxicity of xylylenediamine, which can be used as an analogue for the amine functionalities in the notified chemical, is moderate, with a 4 hour LC50 of 1900 mg/m^3. The notified chemical can be expected to be of moderate inhalation toxicity.

On the basis of the analogue data for TGIC, the notified chemical is classified as toxic with the risk phrase R23 'Toxic by inhalation'.

9.1.4 Skin Irritation (Mitsubishi-Kasei Institute of Toxicological and Environmental Sciences, 1978a), (Mitsubishi-Kasei Institute of Toxicological and Environmental Sciences, 1978b)

The test material used for this study was Epoxy Resin PGA-X, containing an estimated 75 % notified chemical.

Two separate experiments were conducted; the first used neat test material, as supplied, while in the second, the test material was applied diluted in acetone at concentrations of 0.1, 0.4, 1.6, 6.4 and 25.6 % (v/v).

Species/strain:	rabbit/Japanese native strain
Number/sex of animals:	6 males per experiment
Observation period:	7 days

Method of administration: semi-occlusive patch

experiment 1:
0.5 mL of test material as received was applied to both intact and abraded skin for 24 h; the area of application was rinsed with tepid water

experiment 2:
0.15 mL of each test dilution and 0.15 mL of acetone were applied individually to intact skin for 24 h; the area of application was rinsed with tepid water

Test method: U.S. Consumer Product Safety Commission (CPSC)

Draize scores (Draize, 1959):

Experiment 1
neat test material; intact skin

Time after treatment (days)	***Animal #***					
	1	***2***	***3***	***4***	***5***	***6***
Erythema						
1	3[a]	3	3	3	3	3
2	2	3	2	3	3	2
3	2	2	2	3	3	2
7	1	0	1	1	1	1
Oedema						
1	2	3	1	3	3	2
2	1	2	1	2	2	1
3	0	0	0	1	1	1
7	0	0	0	0	0	0

[a] see Attachment 1 for Draize scales

neat test material; abraded skin

Time after treatment (days)	*Animal #*					
	1	*2*	*3*	*4*	*5*	*6*
Erythema						
1	4	4	4	4	4	4
2	4	4	4	4	4	4
3	4	4	4	4	4	4
7	4	4	4	4	4	4
Oedema						
1	4	4	4	4	4	4
2	4	4	4	4	4	3
3	3	3	3	3	4	3
7	3	1	2	2	3	2

Experiment 2
0.1 % (v/v) test material in acetone; intact skin

Time after treatment (days)	*Animal #*					
	1	*2*	*3*	*4*	*5*	*6*
Erythema						
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
7	0	0	0	0	0	0
Oedema						
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
7	0	0	0	0	0	0

0.4 % (v/v) test material in acetone; intact skin

Time after treatment (days)	*Animal #*					
	1	*2*	*3*	*4*	*5*	*6*
Erythema						
1	0	0	1	1	0	1
2	0	0	1	1	0	0
3	0	0	1	1	0	0
7	0	0	0	0	0	0
Oedema						
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
7	0	0	0	0	0	0

1.6 % (v/v) test material in acetone; intact skin

Time after treatment (days)	*Animal #*					
	1	*2*	*3*	*4*	*5*	*6*
Erythema						
1	1	1	1	1	1	2
2	0	0	1	1	1	1
3	0	0	1	1	1	1
7	0	0	0	0	0	0
Oedema						
1	0	0	0	0	0	1
2	0	0	0	0	0	0
3	0	0	0	0	0	0
7	0	0	0	0	0	0

6.4 % (v/v) test material in acetone; intact skin

Time after treatment (days)	*Animal #*					
	1	*2*	*3*	*4*	*5*	*6*
Erythema						
1	2	1	3	2	2	3
2	2	1	2	2	2	2
3	1	1	2	1	1	1
7	0	0	1	0	0	0
Oedema						
1	2	0	1	1	1	1
2	1	0	1	1	0	0
3	0	0	0	0	0	0
7	0	0	0	0	0	0

25.6 % (v/v) test material in acetone; intact skin

Time after treatment (days)	*Animal #*					
	1	*2*	*3*	*4*	*5*	*6*
Erythema						
1	3	2	3	3	3	3
2	3	2	3	2	2	2
3	2	1	2	2	1	1
7	1	0	1	1	0	0
Oedema						
1	1	1	2	1	1	1
2	1	0	2	1	0	0
3	0	0	1	0	0	0
7	0	0	0	0	0	0

Comment: for the lower concentrations of the test material in acetone (6.4 % (v/v) and below), the skin effects were below the levels which would lead to classification as an irritant; the neat liquid, which is the form in which the test material will be used, was found to be a moderate irritant to skin, and was also observed to have corrosive effects on abraded skin.

Result: the test material was moderately irritating to the skin of rabbits when applied for a 24 hour period

the neat chemical and the 25.6 % (v/v) solution would warrant the health effects classification R38 'Irritating to skin'

9.1.5 Eye Irritation

A summary of the analogue data for TGIC was provided. Three studies were carried out according to OECD TG 405 (Organisation for Economic Cooperation and Development, 1987b). In one of the studies, TGIC was found to not be an eye irritant. The other two studies indicated severe eye reactions including moderate to severe corneal opacity, redness, chemosis and discharge, persisting for up to 7 days. It was concluded on the basis of the latter studies that TGIC presents a risk of serious damage to the eyes and warrants the risk phrase R41.

The analogue data presented for a number of primary and secondary amines indicated that the amine functionality would have potential for severe eye irritation, and it would therefore be unlikely that the notified chemical would be less irritating to the eye than TGIC. The notified chemical is therefore classified with the risk phrase R41 "Risk of serious damage to eyes".

9.1.6 Skin Sensitisation

No skin sensitisation study has been provided for the notified chemical. The results of two skin sensitisation studies using the analogue compound, TGIC, have been provided (National Occupational Health and Safety Commission, 1994c). TGIC was considered to be a skin sensitiser on the basis of these studies. The TGIC assessment also quotes reports of cases of human skin sensitisation caused by handling TGIC.

The analogue data provided for primary and secondary amines indicated that these are known sensitisers in occupational health monitoring studies, and therefore the amine functionality in the notified chemical would most likely increase the sensitising potential of this chemical relative to TGIC.

The notified chemical is therefore taken as being a skin sensitiser which warrants the risk phrase R43, 'May cause sensitisation by skin contact'.

9.2 Repeated Dose Toxicity

No repeat dose toxicity study of the notified chemical has been provided. Analogue data for TGIC includes a summary of a 7 day oral study in rats, and of a 5 day inhalational study in male mice (National Occupational Health and Safety Commission, 1994c).

In the oral study, the main observations were renal tubular damage (for 54 and 216 mg/kg/day males and 43 and 172 mg/kg/day females) and haemorrhagic and degenerative changes of the gastric and duodenal mucosa (for 216 mg/kg/day males and 172 mg/kg/day females). No NOAEL was established.

In the inhalation study, mice were exposed nose-only to 0, 10, 40 or 140 mg/m^3 of TGIC for 6 hours per day for 5 days. The mortalities were 1/10 (non-treatment related) in the low dose group; 4/10 in the intermediate dose group and 9/10 in the high dose group. Clinical signs of toxicity, including hunched posture, piloerection, lethargy, ptosis (drooping of the eyelid), decreased respiratory rate and noisy or gasping respiration, were observed for the intermediate and high dose groups. The intermediate dose animals which died showed dark or reddened lungs (in some animals), while for the high dose group, dark or reddened lungs, pale liver, pale kidneys and congestion of the small intestine were observed. Based on the effects seen in the mid and high dose groups, the NOAEL is 10 mg/m^3. Cytotoxicity in germ cells was also investigated in this study. No effect of the test substance was seen.

A summary of testicular and haemopoietic (blood forming) effects of the glycidyl ethers was also supplied as part of the notification (National Institute for Occupational Safety and Health, 1978). This gives some indication of further toxic effects which can be expected from contact with epoxide functional groups.

The results from the short term oral and inhalation studies are similar to those seen in acute lethal studies and reflect the highly irritant nature of the notified chemical. The results suggest that the chemical warrants a health effects classification, but the data are insufficient to classify the chemical according to the *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1994d).

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Mitsubishi Gas Chemical Company, 1980)

The test material used for this study was Epoxy Resin PGA-X, containing an estimated 75 % notified chemical.

Strains:	*Salmonella typhimurium*: TA98, TA100, TA1535, TA1537, TA1538 *Escherichia coli*: WP2
Concentration range:	10, 50, 100, 500, 1000 and 5000 µg/plate
Metabolic Activation System:	rat liver S9 fraction from animals pretreated with PCB
Test method:	OECD TG 471 (Organisation for Economic Cooperation and Development, 1983b) and TG 472 (Organisation for Economic Cooperation and Development, 1983a)

Positive controls	N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG); 2 µg/plate –TA100; 5 µg/plate – *E. coli* WP2; 10 µg/plate – TA1535 (without metabolic activation) 2-nitro-fluorene (2-NF) 2 µg/plate – TA 98; 5 µg/plate –TA 1538, (without metabolic activation) 9-aminoacridine (9-AA): 50 µg/plate – TA1537 (without metabolic activation) 2-aminoanthracene (2-AA): 5 µg/plate - TA100, TA98, TA1538; 20 µg/plate – TA1535, TA1537; 40 µg/plate – *E. coli* WP2 (with metabolic activation)
Comment:	toxic effects occurred in the absence of metabolic activation for the highest dose used for all strains; a substantial increase in the number of revertant colonies with an indication of clear dose response occurred for strains TA100 (500-5000 µg/plate), TA1535 (1000-5000 µg/plate) and *E. Coli* WP2 (5000 µg/plate) in the presence of metabolic activation the positive controls produced clear positive results indicating that the test system responded appropriately
Result:	the test material was weakly mutagenic in the bacterial strains which detect base substitution (TA100, TA1535 and WP2) in the presence of metabolic activation provided by rat liver S9 fraction

9.3.2 Analogue Genotoxicity Results

Positive evidence of genotoxicity for the analogue compound TGIC was found in a number of studies quoted in the summary of TGIC toxicity provided by the notifier (National Occupational Health and Safety Commission, 1994c).

A TGIC Ames test showed it to be a weak mutagen to TA98 and TA100 in the presence and absence of metabolic activation. It was also found to be mutagenic in a mouse lymphoma cell forward mutation assay both in the presence and absence of metabolic activation. It was also found to be damaging to DNA as measured by induction of unscheduled DNA synthesis in rat hepatocytes *in vitro*, although it was negative in a similar test using human fibroblasts.

In other *in vitro* studies, TGIC did not cause chromosomal aberrations in human lymphocytes, nor cell transformation in mouse embryo fibroblasts. It was found to induce sister chromatid exchanges in Chinese Hamster ovary cells and to induce chromosomal aberrations in Chinese Hamster lung cells.

It was also found to be genotoxic in *in vivo* studies, where it induced nuclear anomalies and sister chromatid exchanges by oral administration to Chinese Hamsters, although it was found to be negative in a mammalian spot test in mice.

Potential for TGIC to alkylate DNA was found in an *in vitro* study using the model DNA substrate, p-nitrobenzyl-pyridine, and in *in vivo* studies of the alkylation of mouse liver, stomach and testis DNA and rat liver DNA.

The analogue chemical, TGIC, was found to produce chromosomal damage in germ cells in a number of studies of mouse spermatogonia, but the data from a number of dominant lethal tests proved equivocal.

The results from the genotoxicity studies on TGIC were sufficient for the chemical to be classified as toxic, with the risk phrase R46(2), 'May cause heritable genetic damage'. As the notified chemical is structurally similar to TGIC, and was found to be mutagenic in the Ames test, the same classification should be applied to the notified chemical in the absence of other specific data.

9.4 Reproductive Toxicity

In tests on laboratory animals, a number of glycidyl ethers were found to cause atrophy and necrosis of the testes, with reduction in spermatogenic activity (National Institute for Occupational Safety and Health, 1978).

9.5 Overall Assessment of Toxicological Data

The notifier has indicated that Amtrade B15 is classified as a category I hazardous substance.

The acute oral toxicity of Epoxy Resin PGA-X, containing the notified chemical, is low. The risk phrase R22 'Harmful if swallowed' is required on the basis of the reported LD_{50} values. The analogue data indicates that the acute dermal toxicity is likely to be low to moderate, requiring the risk phrase R21 'Harmful in contact with skin'. On the basis of the analogue data, the inhalation toxicity is likely to be moderate. The LC_{50} value for the analogue ,TGIC, indicates that the risk phrase R23 'Toxic by inhalation' should be applied.

Epoxy Resin PGA-X, containing the notified chemical, is a moderate skin irritant. The risk phrase R38 'Irritating to skin' should be applied for concentrations above 6.4 % (v/v). The chemical is a slight skin irritant at lower concentrations. Eye irritation would also be expected on the basis of this result. Analogue data for TGIC was provided which shows that the

potential for eye irritation is very high, and the appropriate risk phrase on the basis of the effects of the analogue compound is R41, 'Risk of serious damage to eyes'. The analogue, TGIC, also showed skin sensitising effects, and the presence of amine functionalities on the notified chemical indicate that it is more likely to be a skin sensitiser than the analogue, so the risk phrase R43 'May cause sensitisation by skin contact' is warranted.

There has been a report cited in Concise International Chemical Assessment Document 8, Triglycidyl Isocyanurate (World Health Organisation, 1998), where asthma-like symptoms were reported following exposure to TGIC. This matter is being considered during the current secondary notification of TGIC. Classification of the notified chemical with respect to respiratory sensitisation should be revised, if necessary, after the TGIC assessment is complete.

In the repeat dose toxicity studies of the analogue compound, by gavage for seven days and by inhalation for five days, substantial toxic effects were observed. Due to the limited duration of these studies, they are of limited usefulness in determining the effects of prolonged exposure. The major findings involved renal tubular damage and haemorrhagic and degenerative changes of the gastric and duodenal mucosa (in the oral study) and discolouration of the lungs with pale liver and kidneys and congestion of the small intestine (in the inhalation study). The gastrointestinal and respiratory tract effects were similar to those seen in acute lethal studies of TGIC and the notified chemical and can be attributed to the irritant effects of these chemicals.

Epoxy Resin PGA-X, containing the notified chemical, was found to be mutagenic in an Ames test, and there is strong evidence that the analogue chemical TGIC is capable of producing mutations from both *in vitro* and *in vivo* tests, and that it can cause germ cell damage. The glycidyl ethers were found to produce germ cell damage, and it is probable that this was because of the presence of the epoxide groups. By analogy to TGIC, the notified chemical should be regarded as a Category 2 mutagen, with the risk phrase R46(2), 'May cause heritable genetic damage'.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No ecotoxicological data were provided as the notifier states there will be no deliberate release to the environment.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Significant environmental exposure of the notified substance is only likely to occur after reaction with part A of the resin. Any unreacted material is likely to rapidly react with water (including soil and air moisture, to form a gel) severely limiting its bioavailability and mobility.

The notified substance is therefore not expected to bioaccumulate and the environmental hazard is considered low. The residue resulting from use of the material would be reacted with Part A and share a similar fate and hazard as the surface coating on the plastic components at

the end of their service (i.e. placed in landfill with little hazard expected as a consequence of leaching).

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical is a category I hazardous substance. From the toxicological studies of the notified chemical, it is classified as hazardous with the risk phrases R22 'Harmful if swallowed' and R38 'Irritating to skin'. The notified chemical was found to be mutagenic in an Ames test.

Further information on the likely toxicity of the notified chemical was obtained from analysis of analogue toxicity data, for TGIC and for a number of amines. On the basis of the probable toxicity of the notified chemical derived from the analogue data, the risk phrases R21 'Harmful in contact with skin', R23 'Toxic by inhalation', R41 'Risk of serious damage to eyes, R43 'May cause sensitisation by skin contact' and R46(2) 'May cause heritable genetic damage' are also required.

The notified chemical may be recommended to the National Occupational Health and Safety Commission for consideration for inclusion in the NOHSC List of Designated Hazardous Substances.

Considering the high level of acute hazard (systemic and topical) and genotoxic potential associated with the notified chemical, a high level of precautions to prevent occupational exposure should be used. The occupational health and safety data provided with this notification indicated that this will be the case. The equipment used for mixing and applying the epoxy resin will be completely enclosed and automated. The resin mixture will remain in the enclosed system until it is heat treated to effect crosslinking, which will immobilise the notified chemical as part of the resin matrix. The most significant exposure is therefore likely to occur during drum connection and disconnection, cleaning and equipment maintenance.

The production area is stated to have local and general ventilation to remove any vapours which may escape. The notifier states that plant operators will be required to wear impervious gloves, coveralls, suitable respirator and eye protection during connection and disconnection of containers to transfer lines and during cleaning and maintenance of equipment.

Workers other than the production workers applying the resin should not be exposed to the notified chemical, as it will be imported and transferred to the site where it is used in sealed containers, and will not be generally available. It will not be available for retail sale.

There is negligible potential for public exposure to the notified chemical arising from its use as a curing agent as part of epoxy coatings applied to plastic surfaces. There will be public contact with the notified chemical when incorporated into products, but since the notified chemical is an integral part of the epoxy matrix, no significant exposure should occur. The

pattern of exposure will be intermittent.

An exposure limit for TGIC of 0.08 mg/m^3 (TWA) with a sensitiser notation has been set by NOHSC. As the notified chemical is likely to have similar toxicity to TGIC, the notified chemical may be recommended to NOHSC for consideration for an exposure standard.

13. RECOMMENDATIONS

To minimise occupational exposure to 1,3-benzenedimethanamine, N,N,N',N'-tetrakis-(oxiranylmethyl)- 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/Standards New Zealand, 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 be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the MSDS should be easily accessible to employees.

The following regulatory action is recommended:

- The notified chemical may be recommended to NOHSC for consideration for an exposure standard;
- The notified chemical may be recommended to the National Occupational Health and Safety Commission for consideration for inclusion in the NOHSC List of Designated Hazardous Substances.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (National Occupational Health and Safety Commission, 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.

16. REFERENCES

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Standards Australia/Standards New Zealand (1998) Australian/New Zealand Standard 2161.2-1998, Occupational protective gloves, Part 2: General requirements. Standards Association of Australia, Sydney.

World Health Organisation (1998) Concise International Chemical Assessment Document 8: Triglycidyl Isocyanurate, Geneva.

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