File No: NA/666

April 1999

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME**

**FULL PUBLIC REPORT**

# 1,3-Benzenedimethaneamine, Reaction Products with Epichlorohydrin

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Director
Chemicals Notification and Assessment

# FULL PUBLIC REPORT

## 1,3-Benzenedimethaneamine, Reaction Products with Epichlorohydrin

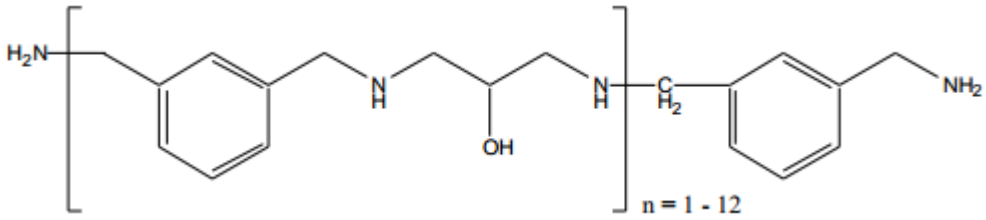
## 1. APPLICANT

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, reaction products with epichlorohydrin.

## 2. IDENTITY OF THE CHEMICAL

| | |
|---|---|
| **Chemical Name:** | 1,3-benzenedimethanamine, reaction products with epichlorohydrin |
| **Chemical Abstracts Service (CAS) Registry No.:** | 135470-04-1 |
| **Other Names:** | N,N'-bis-(3-aminomethylbenzyl)-2-hydroxy-trimethylenediamine (for component where n=1)<br>2-hydroxy-1,3-bis(N,N'-metaaminomethylbenzyl)-trimethylene-diamine (for component where n=1)<br>1,3-xylylenediamine, reaction products with epichlorohydrin<br>m-xylenediamine, reaction products with epichlorohydrin<br>m-XDA, reaction products with epichlorohydrin<br>Gaskamine 328 |
| **Trade Name:** | Amtrade A15 (72 – 76 % notified chemical) |
| **Molecular Formula:** | $(C_{11}H_{16}N_2O)_nC_8H_{12}N_2$ (n = 1 - 12) |

**Structural Formula:**




| | |
|---|---|
| **Molecular Weight:** | 328.4 (for n = 1); the NAMW for the oligomeric mixture was not provided |
| **Method of Detection and Determination:** | the notified chemical can be detected using HPLC and identified using infrared spectrometry |
| **Spectral Data:** | IR: 3353, 3297, 3054, 2915, 2848, 1606, 1589, 1486, 1456, 1378, 1157, 1114, 1039, 867, 790, 732, 701 $cm^{-1}$ |

## 3. PHYSICAL AND CHEMICAL PROPERTIES

The notified chemical is oligomeric and contains a range of different molecular weight species, including up to 28 % of 1,3-benzenedimethanamine. Several of the physico-chemical properties are estimates based on similar amine compounds. The analogue data are identified where used.

| | |
|---|---|
| **Appearance at 20°C and 101.3 kPa:** | clear pale yellow viscous liquid |
| **Boiling Point:** | >200°C |
| **Specific Gravity:** | ca. 1.14 at 25°C |
| **Vapour Pressure:** | < 0.004 kPa at 25°C<br>(value for 1,3-benzenedimethanamine, calculated) |
| **Water Solubility:** | stated to be insoluble for n > 2 |
| **Partition Co-efficient (n-octanol/water):** | log $P_{ow}$ ~ 3.3<br>(analogue data for isophoronediamine) |
| **Hydrolysis as a Function of pH:** | The notified chemical does not contain any hydrolysable functional groups |
| **Adsorption/Desorption:** | see comments below |
| **Dissociation Constant:** | $pK_a$ ~ 11<br>(analogue data for diethylamine and triethylamine) |

| | |
|---|---|
| **pH:** | 11.7 (10 % w/v aqueous N,N'-bis-(3-aminomethyl-benzyl)-2-hydroxy-trimethylenediamine |
| **Flash Point:** | 177°C |
| **Flammability Limits:** | combustible |
| **Autoignition Temperature:** | not determined |
| **Explosive Properties:** | not explosive |
| **Reactivity/Stability:** | The chemical shows reactivity typical of primary and secondary amines |

**Comments on Physico-Chemical Properties**

While the notified chemical is stated to be insoluble in water for n > 1, the amine groups present would confer some solubility in water when protonated. This would be expected to occur to a greater or lesser degree in the environmental pH range of 4-9. The lower MW moieties would also have a greater potential to be soluble.

In the oral toxicity study supplied by the notifier, the single component of the reaction mixture for which n=1, N,N'-bis-(3-aminomethylbenzyl)-2-hydroxy-trimethylenediamine, was found to be miscible with water and pH values for a number of concentrations are quoted, ranging between 11.7 (10 % w/v) and 12.7 (90 % w/v).

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. No data for the octanol/water partition coefficient was provided. However, the notifier claims that the $P_{ow}$ value would be similar to that of isophorone diamine, a similarly structured alkylamine; it was not indicated how the $P_{ow}$ value was calculated. The hydrocarbon content of the chemical should confer an ability to adsorb onto sediments containing organic material, at least when unprotonated for the higher MW fraction.

## 4. PURITY OF THE CHEMICAL

| | |
|---|---|
| **Degree of Purity:** | 72-76 % |
| **Toxic or Hazardous Impurities:** | |

| | |
|---|---|
| *Chemical name:* | 1,3-benzenedimethanamine |
| *Synonyms:* | m-XDA, 1,3-xylylenediamine, 1,3-bis(aminomethyl)-benzene |
| *CAS No.:* | 1477-55-0 |
| *Weight percentage:* | 24-28 % |
| *Toxic properties:* | On the *List of Designated Hazardous Substances* (risk phrases not stipulated)<br>NOHSC exposure standard 0.1 mg/m$^3$ (peak limitation) with skin notation<br><br>Eye: Corrosive. Contact with eyes may cause severe irritation, and possible eye burns.<br>Skin: Corrosive. May cause severe irritation and possible burns. Skin sensitiser<br>Ingestion: Gastrointestinal irritant.<br>Inhalation: May cause severe irritation of the respiratory tract with sore throat, coughing, shortness of breath and delayed lung oedema. |
| *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* with the following risk phrases:<br><br>0.1≤Conc. ≤1 %<br>R23/24/25: Toxic by inhalation, in contact with skin and if swallowed<br>R36/38: Irritating to eyes and skin<br><br>1≤Conc. ≤10 %<br>R23/24/25: Toxic by inhalation, in contact with skin and if swallowed<br>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 A 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 3:1 ratio with Part B, and 30 % glycol ether solvent in preparation for application. The import volume is estimated to be 20 000 kg/year.

## 6. OCCUPATIONAL EXPOSURE

Routes of Exposure
The notified chemical is a viscous liquid of low volatility. It is a Type 1 category compound and the system used for handling this chemical is intended to provide total segregation. The most probable route of exposure will be dermal. The low vapour pressure and viscous nature of the chemical indicate that inhalation would be unlikely.

*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*
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 A will be mixed with a glycol ether solvent before being mixed with Part B. 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. The equipment used for mixing and applying the epoxy resin will be completely enclosed and automated, so exposure would not occur during this process. The production area is stated to have local and general ventilation to remove any vapours which may escape.

Plant operators will be working with the notified chemical for 8 hours per day for up to 250 days per year. In the coated products the notified chemical will be crosslinked and immobilised within the cured epoxy matrix. The greatest exposure is likely to occur during drum connection and disconnection, and during cleaning and maintenance of equipment, when skin contamination may occur due to drips and spills of the chemical.

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.

## 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 mixture containing the notified chemical is cured.

The cleaning of equipment is expected to lead to some residues (300 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 100 kg or 0.5 % of the yearly import volume will be released due to accidents or leaks in equipment. Any spillage of the chemical 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 chemical.

Any residue of the notified substance remaining in the 200 L drums, estimated to be 300 kg annually or 1.5 % of the drum contents, will be mixed with part B of the resin. 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 chemical are likely to be recycled or disposed of to a liquid waste handling facility where the ultimate fate of any remaining material would presumably be incineration.

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

Incineration of the notified chemical 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 be protonated in the environment or reacted with the other part of the surface coating.

## 9. EVALUATION OF TOXICOLOGICAL DATA

No toxicological data on the notified chemical itself were submitted. Some studies on the dimer, N,N'-bis-(3-aminomethylbenzyl)-2-hydroxy-trimethylenediamine (MW = 328), which is a major component of the notified chemical, were available and were included as part of the submission.

Analogue data for a number of related organic amine compounds have been provided by the notifier. The data was in the form of readily available compilations of hazardous properties, from ACGIH (American Conference of Government Industrial Hygienists, 1998), RTECS (National Institute of Occupational Safety and Health, 1997) and HSDB (National Library of Medicine, 1997). The analogue chemicals were 1,3-benzenedimethanamine (m-xylylenediamine, m-XDA) which is the starting material and major impurity (24 - 28 %) in the notified chemical, isophoronediamine (IPD), diethylenetriamine (DETA) and triethylenetetramine (TETA).

The analogue data is accepted in this report as a suitable surrogate for the notified chemical. Consequently, the findings are taken as representing the toxicity of the notified chemical.

### 9.1 Acute Toxicity

**Summary of the acute toxicity of 1,3-benzenedimethanamine, reaction products with epichlorohydrin, and related compounds**

| *Test substance* | *Species* | *Outcome* | *Reference* |
|---|---|---|---|
| **Acute oral toxicity** | | | |
| dimer | rat | $LD_{50}$ = 646 mg/kg (males)<br>$LD_{50}$ = 744 mg/kg (females) | (Nagai & Hirota, 1983a) |
| **Acute dermal toxicity** | | | |
| m-XDA | rabbit | $LD_{50}$ = 2000 mg/kg | ACGIH |
| DETA | | $LD_{50}$ = 1090 mg/kg | ACGIH, RTECS |
| TETA | | $LD_{50}$ = 805 mg/kg | RTECS |

| | | | |
|---|---|---|---|
| **Acute inhalation toxicity** | | | |
| m-XDA | rat | $LC_{50}$ = 3.75 mg/L (1 hour, equivalent to $LC_{50}$ of 1.9 mg/L for 4 hours) | ACGIH |
| DETA | | no deaths following 300 ppm exposure for 8 hours | ACGIH |
| **Skin irritation** | | | |
| dimer | rabbit | corrosive | (Nagai & Hirota, 1983b) |
| m-XDA | | corrosive | ACGIH |
| DETA | | moderate to severe irritation | RTECS |
| TETA | | severe irritation | RTECS |
| **Eye irritation** | | | |
| m-XDA | rat | exposure to aerosol produced ocular irritation and lacrimation | ACGIH |
| DETA | human | severe corneal injury after application of a 15 % solution | ACGIH |
| **Skin sensitisation** | | | |
| m-XDA | human | reported to be a potent | ACGIH |
| IPD | | sensitiser | (Patussi et al., 1995) |
| | | sensitiser | (Guerra et al., 1992) |
| DETA | | | ACGIH |
| TETA | | respiratory and skin sensitiser | HSDB |
| m-XDA | guinea pig | marked sensitisation in 6 out of 20 workers in one factory<br>mild sensitiser | RTECS |

The toxicological properties of the notified chemical would be expected to be dominated by the presence of primary and secondary amine groups. Of the analogue compounds, m-XDA would be expected to be the closest to the notified chemical in toxicological properties, having the same type of primary aromatic amines. DETA and TETA both contain secondary amines as well. The overall toxicological properties of the four analogue chemicals show a similar pattern, and so it would be expected that the notified chemical would also have similar toxicological properties.

The notified chemical is of significantly higher molecular weight than any of the analogue chemicals and should not be absorbed across biological membranes as readily as the analogues are.

### 9.1.1 Oral Toxicity (Nagai & Hirota, 1983a)

The test was conducted using 2-hydroxy-1,3-bis (N, N'-metaaminomethylbenzyl) trimethylene-diamine (the dimer; N,N'-bis-(3-aminomethylbenzyl)- 2-hydroxy-trimethylenediamine), a single component of Amtrade A15. The test material contained only 0.69 % (w/w)

1,3-benzenedimethanamine, rather than the 24-28 % (w/w) in the notified chemical. The aqueous solution used in the test had a pH of 11.5.

| | |
|---|---|
| *Species/strain:* | rat/Wistar |
| *Number/sex of animals:* | 10/sex/dose |
| *Observation period:* | 14 days |
| *Method of administration:* | gavage, 10 % (w/v) aqueous solution |
| *Dose range:* | males: 415, 490, 578, 682, 805, 950 mg/kg<br>females: 490, 578, 682, 805, 950, mg/kg |
| *Test method:* | OECD TG 401 (Organisation for Economic Cooperation and Development, 1987) |

*Mortality:* males

| dose (mg/kg) | mortality |
|---|---|
| 0 (control) | 0/10 |
| 415 | 0/10 |
| 490 | 2/10 |
| 578 | 4/10 |
| 682 | 3/10 |
| 805 | 9/10 |
| 950 | 10/10 |

females

| dose (mg/kg) | mortality |
|---|---|
| 0 (control) | 0/10 |
| 490 | 0/10 |
| 578 | 1/10 |
| 682 | 4/10 |
| 805 | 7/10 |
| 950 | 8/10 |
| 1121 | 10/10 |

*Clinical observations:* transient signs of excitement were observed in the animals immediately after administration; sudden collapse due to ataxia resulting in death was seen in a number of the animals, generally within two hours of administration and always within the first day; partial recovery from the symptoms was seen in the surviving animals by the second day

| | |
|---|---|
| *Morphological findings:* | the rats which died during the test exhibited high fusion of mucous membranes of the stomach and intestinal canal, and sligh pulmonary congestion; no major changes in other organs were reported; in the animals sacrificed at the end of the observation period no noticeable abnormalities were found |
| *$LD_{50}$:* | males: 646 mg/kg, females: 744 mg/kg |
| *Result:* | the test substance was of low acute oral toxicity in rats |

### 9.1.2 Dermal Toxicity

A summary of analogue data was provided by the notifier. The findings are tabulated in Section 9.1 above.

### 9.1.3 Inhalation Toxicity

A summary of analogue data was provided by the notifier. The findings are tabulated in Section 9.1 above.

### 9.1.4 Skin Irritation (Nagai & Hirota, 1983b)

The test was conducted using 2-hydroxy-1,3-bis(N,N'-metaaminomethylbenzyl)trimethylene-diamine (the dimer; N,N'-bis-(3-aminomethylbenzyl)-2-hydroxy-trimethylenediamine), a single component of Amtrade A15. The test material contained only 0.69 % (w/w) 1,3-benzenedimethanamine, rather than the 24-28 % (w/w) in the notified chemical.

| | |
|---|---|
| *Species/strain:* | rabbit/Japanese native strain |
| *Number/sex of animals:* | 6 male |
| *Observation period:* | 7 days |
| *Method of administration:* | semi-occlusive patch; 0.5 mL neat liquid; intact and abraded skin for both 4 hours and 24 hours; after this time, the remaining material was removed with warm water and gauze |

*Test method:* Draize method (Draize et al., 1944)

*Draize scores (Draize, 1959):*

4 hour exposure
Intact skin

| ***Time after treatment (hours)*** | ***Animal #*** | | | | | |
|---|---|---|---|---|---|---|
| | ***1*** | ***2*** | ***3*** | ***4*** | ***5*** | ***6*** |
| ***Erythema*** | | | | | | |
| 4 | 0[a] | 0 | 0 | 0 | 0 | 0 |
| 24 | 0 | 0 | 0 | 0 | 0 | 0 |
| 48 | 0 | 0 | 0 | 0 | 0 | 0 |
| ***Oedema*** | | | | | | |
| 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| 24 | 0 | 0 | 0 | 0 | 0 | 0 |
| 48 | 0 | 0 | 0 | 0 | 0 | 0 |

Abraded skin

| ***Time after treatment (hours)*** | ***Animal #*** | | | | | |
|---|---|---|---|---|---|---|
| | ***1*** | ***2*** | ***3*** | ***4*** | ***5*** | ***6*** |
| ***Erythema*** | | | | | | |
| 4 | 0 | 0 | 0 | 1 | 0 | 0 |
| 24 | 0 | 0 | 0 | 1 | 0 | 1 |
| 48 | 0 | 0 | 0 | 1 | 0 | 1 |
| ***Oedema*** | | | | | | |
| 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| 24 | 0 | 0 | 0 | 0 | 0 | 0 |
| 48 | 0 | 0 | 0 | 0 | 0 | 0 |

24 hour exposure
Intact skin

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

Abraded skin

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

[a] see Attachment 1 for Draize scales

*Comment:*

in addition to oedema and erythema, the animals were scored for bleeding and necrosis; in the area which had been exposed to the notified chemical for 24 hours, three out of six animals showed necrosis of intact skin while one animal also showed bleeding, and five of the animals showed necrosis of the abraded skin area; only a topical corrosive change on the abraded area of one animal was observed for the area exposed for 4 hours

the report indicated that the difference between the 4 hour and 24 hour exposed regions indicates that the test substance permeates through the skin relatively slowly; the corrosive

| | |
|---|---|
| | effects after 24 hour exposure were to be expected on the basis of the $pK_a$ of the test material |
| *Result:* | the test substance was a slight irritant to the skin of rabbits on the basis of the standard test, but is classified as corrosive on the basis of the pH of the aqueous solutions (11.7 for 10 % w/v, 12.7 for 90 % w/v). |

### 9.1.5 Eye Irritation

A summary of analogue data was provided by the notifier. The findings are tabulated in Section 9.1 above.

### 9.1.6 Skin Sensitisation

A summary of analogue data was provided by the notifier. The findings are tabulated in Section 9.1 above. Two case reports of sensitisation by exposure to IPD have been provided as part of the notification package.

A 53 year old male with a four year history laying impermeable floors coated with epoxy resins including IPD showed an eruption of the face which disappeared on spending two weeks away from work. The eruption recurred 2 months later, and disappeared with treatment with oral corticosteroids and time away from work. He tried four more times to recommence work after this, with dermatitis reappearing each time. Patch testing with the chemicals used in the epoxy mixtures gave a positive result for IPD (Patussi et al., 1995).

A 36 year old male with a ten year history as a wine vat varnisher, with dermatitis of the hands and face, a 44 year old male with an eruption of the face following use of and adhesive, and a 37 year old female worker in a car factory with dermatitis on the hands and a history of exposure to plastics, rubbers and adhesives, all tested positive to IPD in patch testing (Guerra et al., 1992).

No skin sensitisation study of the notified chemical has been provided. All of the amines for which analogue data has been provided have been reported to be human skin sensitisers. On this basis, the notified chemical must be classified as a skin sensitiser.

## 9.2 Repeated Dose Toxicity (Greenman et al., 1996)

A published report of a 92 day oral subchronic study using the dihydrochloride of TETA has been supplied by the notifier as analogue data. It is not possible to draw more than indicative conclusions about the notified chemical from this analogue study. The main reason is that TETA is a strong chelating agent, and is used for reducing tissue copper levels in some cases of Wilson's disease. It is therefore likely that many of the subchronic effects caused by TETA will be due to the changes in body metal ion concentrations. The notified chemical

does not have the structural features which make TETA such a potent chelating agent, and the *in vivo* effects would therefore be expected to be very different. The other reason for being cautious in extrapolating the effects for the analogue chemical is that in subchronic toxicity, the metabolites of the administered compound play an important role. TETA has a very different carbon skeleton to the notified chemical and a very different group of metabolites would be expected.

In mice administered 0, 120, 600 or 3000 ppm of TETA.2HCl in drinking water, a number of symptoms were reported to not be related to copper deficiency, unless localised. These included inflammation of the lung interstitium, haematopoietic cell proliferation of the spleen, liver periportal fatty infiltration, kidney weight reduction, reduced renal cytoplasmic vacuolation and body weight gain reduction.

In rats administered the same dose, the only sign that was not considered related to the effects on copper levels was a dose dependent increase in uterine dilation in the females. On the basis of this effect, the NOAEL for the study was 120 ppm, equivalent to 55 mg/kg/day for males and 70 mg/kg/day for females.

It is not clear which effects would be common to a range of amines and which will be specific to the particular compound, and the repeated dose toxicity of the notified chemical even as a hydrochloride salt could be quite different to that of TETA.2HCl.

## 9.3 Genotoxicity

### 9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Mitsubishi Gas Chemical Company, 1983)

The test was conducted using 2-hydroxy-1,3-bis(N,N'-metaaminomethylbenzyl)trimethylene-diamine (the dimer; N,N'-bis-(3-aminomethylbenzyl)-2-hydroxy-trimethylenediamine), a single component of Amtrade A15. The test material contained only 0.69 % (w/w) 1,3-benzenedimethanamine, rather than the 24-28 % (w/w) in the notified chemical.

| | |
|---|---|
| *Strains:* | *Salmonella typhimurium*: TA98, TA100, TA1535, TA1537, TA1538<br>*Escherichia coli*: WP2 *uvrA* |
| *Concentration range:* | 10, 50, 100, 500, 1000 and 5000 µg/plate |
| *Metabolic Activation System:* | rat liver S9 fraction from animals pretreated with PB-5.6 BF |
| *Test method:* | OECD TG 471 (Organisation for Economic Cooperation and Development, 1983) |

| | |
|---|---|
| *Positive controls* | N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG); 3 µg/plate –TA100; 2 µg/plate – *E. coli* WP2 *uvrA*; 5 µg/plate – TA1535 (without metabolic activation)<br>2-nitro-fluorene (2-NF) 1 µg/plate – TA 98; 2 µg/plate –TA 1538, (without metabolic activation)<br>9-aminoacridine (9-AA): 80 µg/plate – TA1537 (without metabolic activation)<br><br>2-aminoanthracene (2-AA): 0.5 µg/plate - TA100, TA98, TA1538; 2 µg/plate – TA1535, TA1537; 80 µg/plate – *E. coli* WP2 (with metabolic activation) |
| *Comment:* | increased numbers of revertant colonies were not observed for any strain at any dose either in the presence or absence of metabolic activation<br><br>toxic effects occurred both in the presence and absence of metabolic activation for the highest dose used for all strains and at 1000 µg/plate for strains TA1535, TA1537 and TA1538 in the absence of metabolic activation<br><br>the positive controls produced clear positive results indicating that the test system responded appropriately |
| *Result:* | no mutagenicity was observed for any of the strains in the presence or absence of metabolic activation |

### 9.3.2 Analogue Genotoxicity Results

The notifier provided a reference which described the genotoxicity of a number of alkylamines, ethylenediamine (EDA), aminoethylethanolamine (AEEA), aminoethyl-piperazine (AEP), DETA, TETA and tetraethylenepentamine (TEPA). Among the compounds tested, only triethylenetetramine (TETA) was considered to be mutagenic (Leung, 1994).

| Test | Result | | | | | |
|---|---|---|---|---|---|---|
| | EDA | AEEA | AEP | DETA | TETA | TEPA |
| S*almonella typhimurium* reverse mutation | N | N | N | N | Y | N |
| sister chromatid exchange | N | N | Y | N | Y | Y |
| unscheduled DNA synthesis | N | N | N | N | Y | Y |
| *in vivo* micronucleus | N | N | I | N | N | N |
| gene mutation assay | N | N | I | N | N | N |

N = negative result  Y = positive result  I = inconclusive result

The clearest genotoxicity results, for TETA, corresponded to a positive s*almonella typhimurium* reverse mutation assay. Despite some positive findings in *in vitro* assays, the lack of positive finding in *in vivo* studies suggests that the class of chemicals is at most weakly mutagenic.

## 9.4 Overall Assessment of Toxicological Data

The notifier has indicated that Amtrade A15 is classified as a category I hazardous substance.

The acute oral toxicity of the tested component of the notified chemical is low. The analogue data indicates that the acute dermal toxicity is likely to be moderate. On the basis of the analogue data, the inhalation toxicity is likely to be moderate. The $LD_{50}$ values for oral toxicity of the dimer, the $LD_{50}$ values for dermal toxicity of the analogue compounds and $LC_{50}$ value for inhalation of the analogue compounds indicates that the risk phrase R20/21/22 'Harmful by inhalation, in contact with skin and if swallowed' should be applied.

The NOHSC exposure standards for m-XDA and DETA have skin notations, indicating potential for skin absorption. As the notified chemical contains similar functional groups, the lower molecular weight components of the notified chemical may also be absorbed through the skin. The higher molecular weight components would be too large for skin absorption.

The results of the skin irritation study showed the component of the notified chemical to be corrosive when applied for 24 hours. The standard test using 4 hour exposure resulted in only slight irritation being observed. On the basis of the structure of the chemical, it is expected to be strongly basic (analogous chemicals having a $pK_a$ of 11). In the *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (National Occupational Health and Safety Commission, 1994a) it is stated that a chemical with a pH of 11.5 or greater should be classified as corrosive.

It was noted in the skin irritation study that the corrosive effects required comparatively long exposures to develop. It was suggested that the skin permeability is slow, which is reasonable as the molecular weight of the substance tested is 328.4. The notified chemical should be classified as corrosive with the risk phrase R34 'Causes burns' applied. The product in which the notified chemical is imported also contains 24-28 % (w/w) of the lower molecular weight amine, m-XDA, as a consequence of the manufacturing process. Therefore the slow skin permeability of the dimer which was used in the test will not be representative of the product Amtrade A15. Corrosive substances are also considered assumed to cause serious eye damage.

Chemicals of the organic amine class of chemicals to which the notified chemical belongs are commonly found to be skin sensitisers, and all of the analogue chemicals for which data was provided by the notifier were subject to reports of occupational skin sensitisation. The notified chemical should therefore also be considered a skin sensitiser with the risk phrase

R43 'May cause sensitisation by skin contact' applied.

The analogue data which was provided for repeat dose toxicity could not be extrapolated to cover the notified chemical, due to significant structural differences. Therefore, on the available analogue data, the effects of prolonged or repeated exposure to the notified chemical can be regarded as unknown. The notified chemical will not be used in neutralised or highly diluted form, and the repeat exposure should be limited by the serious effects of acute exposure to the chemical.
The component of the notified chemical gave a negative result in a *Salmonella typhimurium* reverse mutation assay. A report on the mutagenic potential of a number of organic amines showed that the class of chemicals is likely to be at most weakly mutagenic. Therefore, it is unlikely that the notified chemical will be a strong mutagen.

## 10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies have been supplied by the notifier. The tests were carried out according to OECD Test Methods (Organisation for Economic Co-operation and Development, 1995-1996)

Both test reports note that the notified chemical was dispersed in reverse osmosis water to make the stock solutions of 1 g/L (fish) and 128 mg/L (bacteria). The toxicity of the notified chemical might be underestimated as it is not known what proportion of the dispersed material was dissolved. Given that some of the test substance is likely to be in solution, particularly that fraction with a lower MW, the true toxicity is likely to be much higher.

| ***Test*** | ***Species*** | ***Results*** |
|---|---|---|
| 96 h acute toxicity<br>(Wetton, 1997) | Golden orfe *(Leuciscus idus)* | $LC_{50}$ = 4 mg/L<br>NOEC ≥ 1.8 mg/L |
| 16 h inhibition<br>(Mead, 1997) | Bacteria (*Pseudomonas putida*) | $EC_{10}$ ≥ 0.23 mg/L<br>$EC_{50}$ ≥ 0.42 mg/L<br>NOEC = 0.16 mg/L |

* NOEC - no observable effect concentration

*Fish*

A 96 hour toxicity test, performed in accordance with the test guidelines, demonstrated that the notified chemical had toxic effects on the test fish at nominal concentrations of > 1.8 mg/L. The report notes that a cosolvent was used and a solvent control was included.

*Microorganisms*

The inhibitory effect of the notified chemical on bacterial growth was investigated in a respiration test. The notified chemical showed inhibitory effects on cell growth at test concentrations greater than 0.16 mg/L after 16 hours of exposure.

***Conclusions***
The ecotoxicity data for the notified chemical indicate that it is moderately toxic to fish and highly toxic to bacteria (*Pseudomonas putida*).

## 11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified substance in its unreacted form may have some potential to be water soluble particularly the lower MW fraction when protonated. In case of exposure to the aquatic environment from accidental spillage in transport, there may be some risk of toxicity to aquatic species and bacteria.

The notified substance is not expected to bioaccumulate because it will either be protonated in the environment or reacted with the other part of the surface coating.

The environmental hazard from the notified chemical is however considered low when it is reacted to form a surface coating on plastic components. It is not expected to be mobile or achieve any significant environmental exposure. The residue resulting from use of the material would be reacted with the other part and share a similar fate and hazard as the surface coating on the plastic components at the end of their service. These will be 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. The imported material, Amtrade A15, which contains up to 28 % of 1,3-benzenedimethanamine (m-XDA) as a consequence of the manufacturing process, is also a category I hazardous substance.

The acute oral toxicity of the tested component of the notified chemical is low. From the toxicological properties of related compounds, the notified chemical is expected to be of moderate acute dermal and acute inhalation toxicity. The lower molecular weight components of the notified chemical can be expected on the basis of the properties of related materials to be absorbed through the skin. The chemical is classified as corrosive because of its basicity, although the corrosive action was shown to be slow. The mixture of reaction products, which includes m-XDA, will be classified as corrosive. On the basis of analogue data, the notified chemical is a skin sensitiser. The risk phrases R20/21/22 ‘Harmful by inhalation, in contact with skin and if swallowed’, R34 ‘Causes burns’ and R43 ‘May cause sensitisation by skin contact’ are therefore required.

Insufficient data was supplied in the notification on which to base an assessment of the effects of prolonged exposure to the notified chemical. The notified chemical is unlikely to be used in a diluted or neutralised form, where chronic exposure would be possible without serious acute effects. The notified chemical was not mutagenic in a *Salmonella typhimurium* reverse mutation assay, and similar chemicals were found to be at most, weak mutagens. The

main hazard associated with this chemical is therefore likely to be the serious acute effects associated with the high basicity of the amine groups.

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 acute hazard (systemic and topical) associated with the notified chemical, stringent measures to prevent occupational exposure are required. 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, and during cleaning and maintenance of equipment, where skin contamination may occur. The m-XDA contained in the mixture of reaction products may also pose an inhalation hazard.

The production area is stated to have local and general ventilation to remove any solvent 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.

Therefore the risk of adverse health effects arising from exposure to the notified chemical are confined to possible skin irritation and sensitisation and eye irritation during operations outside the main process, which is fully enclosed. Due to the toxic nature of the notified chemical, brief exposures may be harmful.

The imported product also contains m-XDA as a major constituent. This chemical has a low NOHSC exposure standard (0.1 $mg/m^3$ peak limitation) with skin notation. Stringent precautions are required to minimise exposure to the product Amtrade A15.

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, and the pattern of exposure will be intermittent. It is therefore considered that the notified chemical will not pose a significant hazard to public health.

## 13. RECOMMENDATIONS

To minimise occupational exposure to 1,3-benzenedimethanamine, reaction products with epichlorohydrin, 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.

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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 |