File No: NA/865

January 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

1,3-Bis(Aminomethyl) Cyclohexane

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Director
Chemicals Notification and Assessment

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1,3-Bis(Aminomethyl) Cyclohexane

1. APPLICANT

Procter & Gamble Australia Pty Ltd of 99 Phillip Street PARRAMATTA NSW 2150 (ACN 008 396 245) has submitted a standard notification statement in support of their application for an assessment certificate for "1,3-bis(aminomethyl) cyclohexane".

2. IDENTITY OF THE CHEMICAL

The notifier did not apply for any information on the notified chemical to be exempted from publication in the Full Public Report and the Summary Report.

Chemical Name: 1,3-Bis(aminomethyl) cyclohexane

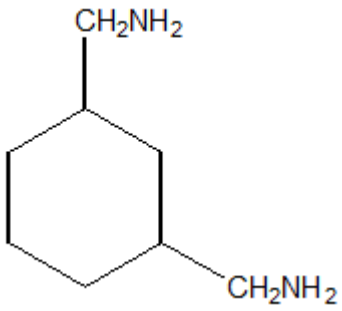
Chemical Abstracts Service (CAS) Registry No.: 2579-20-6

Other Names: 1,3-Cyclohexanedimethanamine

Marketing Name: 1,3-BAC

Molecular Formula: $C_8H_{18}N_2$

Structural Formula:



Molecular Weight: 142.2

Method of Detection and Determination: UV/Vis, IR, NMR and MS.

Spectral Data: Spectra of the notified chemical were provided.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa: Colourless liquid with slight ammonia odour.

Boiling Point: 254-255°C

Density: 0.94

Vapour Pressure: 1.24×10^{-3} kPa at 20°C

Water Solubility: ≥1 000 g/L

Partition Co-efficient (n-octanol/water): Log P_{OW} = 0.44

Hydrolysis as a Function of pH:

Number of hours	*% hydrolysis at 50°C* pH 4	pH 7	pH 9
2.4	13.8	4.2	-7
24	-2	-1	-10
48	0.3	-4	-7
53	-5	1.6	-20
144	4.9	-11	-15

Adsorption/Desorption:

Soil	*pH*	*Organic carbon, %*	K_{ad}	K_{oc}	*Log* K_{oc}
Euro 3	5.8	3.45	>12.7	>367	2.56
Euro 4	7.0	1.55	>12.9	>832	2.92
Euro 5	4.6	9.23	>13.0	>141	2.15

Dissociation Constant: pK_{a1} = 11.55
pK_{a2} = 10.92.

Flash Point: 107°C

Flammability Limits: Not provided.

Autoignition Temperature: Not provided.

Explosive Properties: Not provided.

Reactivity/Stability: Not provided.

3.1 Comments on Physico-Chemical Properties

Tests were performed according to EEC/OECD test guidelines at facilities complying with OECD Principles of Good Laboratory Practice.

The boiling point was determined by Krips (1999a) via a method based on the EEC Directive

92/69, part A.2 and OECD guideline 103 and utilised a differential scanning calorimeter with a detection limit 10 µW.

A method based on EEC Directive 92/69 Part A.3 and OECD Guideline No. 109, using a 10 mL glass pycnometer, was used to determine the density of the chemical (Krips, 1999b).

The method used to determine the vapour pressure of the chemical was based on the EEC Directive 92/69, part A.4 and OECD guideline 104. The vapour pressure was determined using the static technique, with the vapour pressure at 24.98, 31.61 and 38.32ºC being measured (Krips, 1999c). This data was then used to interpolate the vapour pressure at 20ºC, thus giving a vapour pressure of 1.24 ± 0.05 Pa (or $9.3 \pm 0.4 \times 10^{-3}$ mmHg) for the chemical.

The water solubility was determined by Wortelboer (1999a) using the flask method (OECD Guideline 105). An excess amount of the chemical (2.7131 g) was added to known amounts of water (10, 20, 50 and 100 µL), stirred and visually inspected. The temperature was maintained at 20ºC. At all water volumes the chemical completely dissolved, thus indicating that its water solubility was greater than 271 kg/L.

OECD Guideline 111 was followed to determine the likely hydrolysis as a function of pH. The hydrolytic degradation of the chemical was determined by Wortelboer (1999b) over 6 days at 50ºC in buffer solutions of pH 4, 7 and 9. The concentration of the test material in the solutions was determined using HPLC, and after the 6 days <10% of the test material had undergone hydrolysis in any buffer solution. In accordance with the protocols given in the guideline no further testing was undertaken. Under the lower temperatures encountered in the aqueous and terrestrial environmental compartments the degree of degradation would be less, and it is inferred that hydrolytic degradation is unlikely.

The partition coefficient was determined by Wortelboer (1999c) via the flask shaking method following the EEC Directive 92/69 Annex V, A.8 and OECD Guideline 107. The test was run in duplicate with concentration of the notified chemical between 340 and 485 mg/L. A measured amount of the chemical was placed in a 60 mL glass centrifuge tubes and the required volumes of saturated n-octanol and saturated water were added. The tube was rotated 180º at a rate of 150 times/minute for 5 minutes and centrifuged to separate the phases. A sample from each phase was analysed via a FI/MS/MS. Log P_{ow} was determined as 0.44±0.09 from the ratio of the concentrations in the octanol and water phases. This value indicated that the chemical is hydrophilic and unlikely to bioaccumulate.

OECD Guideline 106 was used to determine the adsorption/desorption of the chemical (Wortelboer, 1999d), using three representative Euro soils. In the Euro soil 3, an acid brown forest soil, log K_{oc} was 2.56, in the Euro soil 4, gray brown podzolic soil, log K_{oc} was 2.92, and Euro soil 5, podzolized soil, log K_{oc} was 2.15. The results indicate that the compound is likely to be relatively mobile in all soils.

The dissociation constant for the chemical was determined by Wortelboer (1999e) using OECD Guideline 112, Titration Method. Five test solutions of 0.01mol/L were prepared, at initial pH 11.6. The test solutions were titrated with 0.1 mol/L HCl until after the second equivalence point. The Dissociation constant (pK_a) was calculated to be 11.05 (pK_{a1}) and 10.92 (pK_{a2}). This indicates that the chemical is highly basic and both amino groups will be protonated in the environmental pH region 4-9.

4. PURITY OF THE CHEMICAL

Degree of Purity: 99.8%

Hazardous Impurities:

Chemical name:	m-Xylylenediamine
Synonyms:	1,3-Benzenedimethanamine
CAS No.:	1477-55-0
Weight percentage:	0.01
Toxic properties:	On the NOHSC List of Designated Hazardous Substances (NOHSC, 1999a); and has NOHSC exposure standards of 0.1 mg/m^3 (TWA) and peak limitation (STEL) with "Sk" annotation (absorption through the skin may be a significant source of exposure) (NOHSC, 1995).

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

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical is a component of hand dishwashing liquid preparations, which will be used directly by householders.

Neither the notified chemical nor the product containing the notified chemical will be manufactured, formulated or repackaged in Australia. It will be imported as a component of Dawn Dishwashing Liquid. Eight tonnes of the notified chemical or approximately 1 600 tonnes Dawn Dishwashing Liquid will be imported annually into Australia in the first 5 years.

The imported dishwashing liquid preparation containing 0.5% notified chemical is packed in 375 mL bottles.

6. OCCUPATIONAL EXPOSURE

Transport and storage

After importation, products containing 0.5% notified chemical will be transported from dockside to storage site, then distributed to supermarkets and retailers. The notifier estimated that there will be 50 waterside and transport workers, and 20 to 30 warehouse workers who will handle the products containing the notified chemical for 12 times/year, 8 hours/day and 100 times/year, 4 hours/day, respectively. The waterside workers, drivers and warehouse workers would only be exposed to the notified chemical if the packaging was damaged.

Waterside, transport and warehouse personnel will wear coats or overalls and heavy duty gloves during distribution of the product.

Supermarket and retail workers
Supermarket workers and retailers will unload the dishwashing products, stack them on the shelves. The notifier estimated approximately 10 000 supermarket and retail workers Australia wide will handle the product 100 times/year for 1 hour/day. It is anticipated that they would only be exposed to the notified chemical in the event of an accident.

Retail workers normally wear coats.

Commercial premises workers
Wash-up workers in commercial premises may use and be exposed to the notified chemical.

7. PUBLIC EXPOSURE

The notified chemical, as a component (0.5%) of hand dishwashing liquid preparations will be imported into Australia in 375 mL plastic bottles and transported and stored by the notifier. There will be no manufacturing, formulation or repackaging of the notified chemical/products in Australia. To this point, the public will only be exposed to the notified chemical in the event of an accidental spill. According to the Material Safety Data Sheet (MSDS) provided for Dawn Dishwashing Liquid, containing 0.5% of notified chemical, an accidental spill should be prevented from entering drains and surface or ground water and contained with non-combustible absorbent material and shovelled into a container for disposal. Products containing the notified chemical will be sold to supermarkets and retail outlets. The public will come in contact with the chemical through their use of hand dishwashing liquids.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Given the use pattern of the dishwashing liquid almost all of the imported volume of the new compound will be released to the sewer system. Very little of the dishwashing concentrate is likely to be left in the bottles, since these are usually washed out with water prior to disposal. Any residue left in the bottles would be disposed of to landfill with general domestic waste.

The compound has a moderate value for log K_{oc} 2.1–2.9 and once released to the sewer system may become associated with sewage sludge. Some of the chemical may be released to the soil compartment, because sludge is typically disposed of to landfill, or increasingly used as a soil conditioner. The K_{oc} indicates that in most soils the chemical will be relatively mobile.

8.2 Fate

Ultimately all of the notified chemical will be released to the environment, particularly the aquatic compartment, via the sewer system. Some of the chemical may become associated with sewage sediments and sludge, but the majority is more likely to stay mobile due to the high water solubility and low log K_{oc} values. Any chemical adsorbed to sewage sludge may re-enter the water compartment at a later stage.

The notifier provided a number of biodegradation studies for the notified chemical, summarised below.

OECD Guideline 301B was followed to determine the ready biodegradability of the chemical. A medium consisting of the notified chemical and a mixed population of activated sewage sludge was kept in a closed dark vessel for 28 days at 21ºC (Mead, 1998a). The initial concentration of the chemical in the vessels was 14.8 mg/L which represented 10 mg of carbon per litre. The study was done in duplicate with a control solution consisting of inoculum and sodium benzoate, as a standard. The DOC was determined on day 0 and 28. The degree of degradation was determined by measurement of the amount of carbon dioxide (CO_2) produced. CO_2 was collected and analysed irregularly throughout the course of the study from one CO_2 adsorber vessel and on the first and last day from the other. After 28 days there had been a 29% degradation, indicating that the chemical was not readily biodegradable, according to the OECD protocol. After 28 days the sodium benzoate control had undergone 94% degradation, confirming the suitability of the study parameters. Nevertheless, slow biodegradation in the environment is expected for the compound.

Test	*Duration*	*Result*	*Reference*
Ready biodegradation assessment via CO_2 evolution assessment	28 Days	29% degradation	Mead, 1998a
Activated sludge simulation test	28 days	DOC removal 96% COD removal 92%	Van der Kerken, 1998
Modified SCAS Test with tritium labelled material	36 Days	80% removal between days 25 and 36 86% removal on day 36	Debaere, 1999

A second biodegradability study was then undertaken using OECD Guideline 303A. Two model activated sludge plants were set up with a control unit, with the study running for 28 days (Van der Kerken, 1998). A nutrient solution with a COD between 350 and 450 mg/L, consisting of at least 50% (preferably 100%) raw sewage was used. The inoculum was activated sludge with a pH of 7.15, a respiration rate of 15.21 mg oxygen per litre per hour and a mixed liquor suspended solids (MLSS) level of 5.87 g/L. A solution using the notified chemical was prepared so that the organic carbon content was 0.59 mg C/mg of active ingredient. In the model plant the nutrient solution was inoculated with the activate sludge to give a concentration of 2.5 g/L and then the test solution was introduced. The level of DOC was determined 5 times a week, while COD and MLSS were determined 3 times a week. The results indicated that test units had a 96% removal of DOC and 92% removal of COD, while the control unit had a 94% removal of COD. These results indicate that the chemical is ultimately biodegradable.

A further degradation test was conducted using tritium labelled test material and biodegradation consisted of mineralisation and adsorption (Debaere, 1999). A semi-continuous activated sludge unit was set up with activated sludge to which was added an aliquot of the test material and domestic sewage. The mixture was aerated for 23 hours, allowed to settle, and the supernatant removed. This sequence was repeated. The supernatant was then analysed to determine the degree of biodegradation. The control was subjected to the same conditions and the resultant supernatant used as a comparison. The removal is the sum of mineralisation and adsorption. The test indicated that by day 36 there had been an 86% removal (12% adsorption and 74% mineralisation). It also indicated that the biodegradation process was very slow initially but that between days 25 and 36 the removal rate was 80%. These results indicated that ultimately the notified chemical is biodegradable.

The chemical is unlikely to bioaccumulate due to the highly water solubility, low log P_{ow} and inherent biodegradability.

9. EVALUATION OF TOXICOLOGICAL DATA

The toxicity studies on the notified chemical were conducted at Safepharm Laboratories Limited in UK, Huntingdon Research Center and BioReliance in USA, Covance Laboratories Ltd in UK and USA with Good Laboratory Practice compliance statements and quality assurance statements. Most of the studies were performed in compliance with the OECD Guidelines for Testing Chemicals.

9.1 Acute Toxicity

Summary of the acute toxicity of 1,3-bis (aminomethyl) cyclohexane

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	200 - 2 000 mg/kg	Allen, 1998a
acute dermal toxicity	rabbit	1 700 mg/kg	Upman, 1975
skin irritation	rabbit	Corrosive	Allen, 1998b
skin sensitisation	guinea pig	Not sensitising	Allen, 1998c

9.1.1 Oral Toxicity (Allen, 1998a)

Species/strain: Rat/Sprague Dawley.

Number/sex of animals: 5/sex.

Observation period: 14 days.

Method of administration: A single oral dose of 200 mg/kg (vehicle: water) was given by gavage.

Test method: OECD TG 401.

Mortality: None.

Clinical observations: 2 females had hunched posture and/or noisy respiration.

Morphological findings: None.

Comment: In a range-finding study, all rats (2/sex) died after receiving 2 000 mg/kg notified chemical by gavage.

LD_{50}: Between 200 mg/kg and 2 000 mg/kg.

Result: The notified chemical was of low to moderate acute oral toxicity in rats.

9.1.2 Dermal Toxicity (Upman, 1975)

Species/strain: Rabbit/New Zealand White.

Number/sex of animals: 4 per group (sex not provided).

Observation period: 14 days.

Method of administration: The notified chemical was applied in each test group to intact (2 rabbits) and abraded (2 rabbits) skin at levels of 2 510, 2 000, 1 580 and 1 260 mg/kg under an occlusive dressing for 24 hours.

Test method: OECD TG

Mortality:

Dose (mg/kg)	***No. Dead***	***No. Tested***
2 510	4	4
2 000	2 (both unabraded)	4
1 580	2 (1 each)	4
1 260	0	4

Clinical observations: All animals displayed vocalization and hyperactivity after dosing. At 24 hours, severe erythema and oedema were observed in all rabbits. The oedema subsided within a few days and the skin became "leathery" in appearance and to the touch.

One rabbit at the highest dose became lethargic prior to death. All surviving rabbits lost bodyweight during the study.

Morphological findings: None.

Comment: No details of the results or Draize scores were provided in

	the report.
LD_{50}:	1 700 mg/kg.
Result:	The notified chemical was of moderate dermal toxicity in rabbits.

9.1.3 Inhalation Toxicity

The notifier did not provide a report of inhalation toxicity on the notified chemical.

9.1.4 Skin Irritation (Allen, 1998b)

Species/strain:	Rabbit/New Zealand White.
Number/sex of animals:	1 male.
Observation period:	1 hour.
Method of administration:	A single 3-minute semi-occluded application (0.5 mL notified chemical) to the intact skin.
Test method:	OECD TG 404.
Draize scores:	At 1 hour after dosing, Draize scores for erythema and oedema were 4 and 0, respectively.
Comment:	Green coloured necrosis, a loss of elasticity and drying of the skin were observed. The rabbit was killed for humane reasons. There was no further testing.
Result:	The notified chemical was corrosive to the skin of rabbit.

9.1.5 Eye Irritation

Since the notified chemical was corrosive to rabbit skin, eye irritation study was not conducted. This assessment accepts that the notified chemical is corrosive to eyes.

9.1.6 Skin Sensitisation (Allen, 1998c)

Species/strain:	Guinea pig/Dunkin Hartley.
Number of animals:	19 females and 6 males (including preliminary studies); 15 guinea pigs were used for the main study, 10 test and 5 control.

Induction procedure:

test group:	Intradermal Induction:
day 0	Three pairs of intradermal injections (0.1 mL) into the dorsal area in the shoulder region: - Freund's complete adjuvant (FCA) 1:1 in distilled water; - 0.05% notified chemical in distilled water; - 0.05% notified chemical in a 1:1 mixture of FCA and distilled water.
day 7	Topical Induction: A 48-hour occluded application of the notified chemical (5% in water) to the test area.
control group:	Treated similarly to the test animals using distilled water instead of the notified chemical in the intradermal injections and topical application.

Challenge procedure:

day 21	Test and Control animals: Occluded applications of a patch of 2% notified chemical in water on the right flank and a patch of 1% notified chemical in water on left flank of each animal.

Test method: OECD TG 406

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
2%	**0/10	0/10	0/5	0/5
1%	0/10	0/10	0/5	0/5

* time after patch removal
** number of animals exhibiting positive response

Comment: Well-defined to severe erythema was observed after intradermal induction. Very slight to well-defined erythema and slight oedema were observed after topical induction.

Result: The notified chemical was not sensitising to the skin of guinea pigs.

9.2 Repeated Dose Toxicity (Lambert, 2000)

Species/strain: Rat/Wistar

Number/sex of animals: 10/sex/group

Method of administration: Dietary administration for 28 days.

Dose/Study duration: Control group: 0 mg/kg/day;
Low dose group: 50 mg/kg/day;
Mid dose group: 250 mg/kg/day; and
High dose group: 1 000 mg/kg/day
(vehicle: distilled water).

Test method: OECD TG 407

Clinical observations:
One female at low dose was sacrificed due to a blockage in its bladder, that was not considered to be related to the treatment. A replacement animal was then used in the study.

In both males and females at high dose, food consumption was reduced throughout the treatment period, and the bodyweight gains were also reduced particularly over the last week of the study.

Clinical chemistry/Haematology
Some changes such as the activated partial thromboplastin time and the proportions of neutrophils and lymphocytes in high dose females were observed. These changes considered to be within expected ranges for untreated animals such as the historical control values. In the absence of similar findings in the males, or other corroborative findings, the changes were considered to be of negligible toxicological significance.

Pathology:
Absolute and/or relative weights of brain, spleen and liver were reduced in high dose animals of both sexes. In high dose males, adrenal, kidney, heart and prostate weights were also reduced.

There were no macroscopic or microscopic findings suggestive of toxicity.

Comment:
All test groups were slightly overdosed in the first week and under dosed in week 3 and 4.

Result:
The No Observed Effect Level (NOEL) established from this study is 250 mg/kg/day based on the reduction of food consumption and bodyweight gains, and absolute and/or relative weights of brain, spleen and liver at 1 000 mg/kg/day.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *E. coli* Reverse Mutation Assay (Wagner and Twardzik, 1998)

Strains: *S. typhimurium* TA98, TA100, TA1535, TA1537 and TA1538;
E. coli WP2*uvr*A (pKM101) and WP2 (pKM101).

Metabolic activation:	Liver fraction (S9 mix) from rats pretreated with Aroclor 1254.
Concentration range:	The assay was performed in triplicates and by both pre-incubation and plate incorporation methods in the presence and absence of metabolic activation. Concentrations were 25, 75, 200, 600, 1 800 and 5 000 μg/plate for all strains with and without S9-mix (vehicle: water). Positive control: (without S9-mix) 2-nitrofluorene for TA98 and TA1538; sodium azide for TA100 and TA1535; 9-aminoacridine for TA1537; and methyl methanesulfonate for *E. coli* strains. Positive control: (with S9-mix) Sterigmatocystin for WP2 (pKM101); and 2-aminoanthracene for the remaining strains.
Test method:	OECD TG 471
Comment:	Test article was soluble at 100 mg/mL, the maximum concentration tested. Toxicity was observed at 5 000 and ≥1 800 μg per plate, with and without S9-mix, respectively when using preincubation method. No appreciable toxicity was observed in the tests using plate incorporation method. There were no significant increases in revertant colony numbers at any concentration, in the presence or absence of metabolic activation. Concurrent positive controls used in the tests induced marked increases in the frequency of revertant colonies and the activity of the S9 fraction was found to be satisfactory. Historic data were included to support the study findings.
Result:	The notified chemical was non mutagenic under the conditions of the test.

9.3.2 Clonal Transformation Assay in Syrian Golden Hamster Embryo (SHE) Cells (Custer, 1999)

Cells:	Syrian golden hamster embryo (SHE) cells
Dosing schedule:	Each experiment consisted of 40 dishes per treatment group including at least one vehicle control and one positive

control.

Experiment	*Test concentration (μg/mL)*	*Controls*
treatment time = 24 hours	0, 15*, 35*, 40, 50*, 150*, 250*, 350 and 625 μg/mL. Vehicle: DMEM culture medium	Positive: Benzo(a)pyrene in DMSO
treatment time = 7 days	0, 5*, 20*, 35*, (42*), 50*, (60*), 65, 80 and 100 μg/mL. Vehicle: DMEM culture medium	Positive: Benzo(a)pyrene in DMSO

DMSO – dimethylsulphoxide
Concentrations in parentheses were conducted in the 5th tests of 7-day tests.
* - cultures selected for morphological transformation analysis

Test method: In-house protocol.

Comment: The notified chemical was soluble in the culture medium at 23.7 mg/mL. The pH was adjusted with HCl.

Five 24-hour tests were conducted with only one meeting assay acceptance criteria. Sufficient cytotoxicity (50%) was seen at 250 μg/mL.

Five 7-day tests were conducted with 3rd and 5th tests meeting assay acceptance criteria. Concentrations of 42, 50 and 60 μg/mL were tested in the 5th test. Sufficient cytotoxicity (55%) was seen at 60 μg/mL.

Historic data were provided to support the study.

24 hour and 7 day experiments did not produce statistically significant increases in the frequency of morphological changes when compared with controls.

Result: The notified chemical had no potential to induce morphological transformation in SHE cells under the conditions of the test.

9.4 Overall Assessment of Toxicological Data

The notified chemical was of low to moderate acute oral toxicity (LD_{50} between 200 and 2 000 mg/kg) in rats and moderate acute dermal toxicity (LD_{50} = 1 700 mg/kg) in rabbits. A literature report (RTECS) indicated that the acute oral toxicity was low (LD_{50} = 880 mg/kg) in rats. The notified chemical was corrosive to rabbit skin and is expected to be corrosive to eyes (not tested). The notified chemical was not a skin sensitiser in guinea pigs.

In a 28-day dietary study in rats, the notified chemical caused decreases in food consumption, bodyweight gains and absolute and/or relative weights of brain, spleen and liver in the animals at 1 000 mg/kg/day. Male rats at 1 000 mg/kg/day also had adrenal, kidney, heart and prostate weight reductions. The NOEL was established to be 250 mg/kg/day from this study based on the reduction of food consumption and bodyweight gains, and absolute and/or relative weights of brain, spleen and liver at 1 000 mg/kg/day.

The notified chemical was non-mutagenic in bacteria. The notifier provided a report of clonal transformation assay in SHE cells with the test protocol similar to the draft OECD guidelines. The three tests that met the acceptance criteria did not demonstrate a statistically significant increase in frequency of morphological changes. The notifier provided comment on genotoxicity on the analogs of the notified chemical and additional comment and published literature on the use of the SHE cell transformation assay. All the available information did not indicate any potential for chromosomal damage to be caused by the notified chemical.

According to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999b), the notified chemical is classified as hazardous based on acute lethal toxicity and corrosive effects on skin and eyes. The risk phrases assigned are:

R21/22: Harmful in contact with skin and if swallowed;
R35: Causes severe burns.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies were supplied by the notifier, and carried out according to OECD Test Methods.

Species	***Test***	***Concentrations[a] (mg/L)***	***Result (mg/L)***	***Reference***
Zebra fish *(Brachydanio rerio)*	96 h acute semi-static	0, 0.32, 0.56, 1.0, 1.8, 3.2 and 5.6	LC_{50} = 2.4 mg/L NOEC = 1.8 mg/L	Hooftman and Borst, 1999
Water Flea (*Daphnia magna*)	48 h acute	0, 0.32, 0.56, 1.0, 1.8, 3.2, 5.610, 18, 32, 56 and 100	EC_{50} = 2.4 mg/L NOEC = 0.32 mg/L	Hooftman et al, 1999
Algae (*Selenastrum capricornutum*)	96 h growth inhibition	1, 10, 50 and 100	EC_{50} > 100 mg/L	Shorter and Nuck, 1999
Bacteria *(Pseudomonas putida)*	Acute	1, 2, 4, 8, 16, 32, 64, 128, 256, 512,1024 and 2048	EC_{50} = 330 mg/L EC_{10} = 90 mg/L	Mead, 1998b

Earthworm *(Eisenia fetida)*	Acute	10, 32, 100, 320 and 1000 mg/kg	$EC_{50} \geq 1000$ mg/kg soil	Henzen, 1999a
Terrestrial-Lettuce *(Luctuca sativa)*	Growth conditions	0, 10, 32, 100, 320 and 1000 mg/kg	NOEC = 320 mg/kg soil	Henzen, 1999b
Terrestrial-lettuce *(Luctuca sativa)*	Emergence, survival	0, 10, 32, 100, 320 and 1000 mg/kg	NOEC≥1000 mg/kg soil	Henzen, 1999b
Terrestrial-oat *(Avena sativa)*	Growth, emergence, survival	0, 10, 32, 100, 320 and 1000 mg/kg	NOEC≥1000 mg/kg soil	Henzen, 1999b
Terrestrial-tomato *(Lycopersicum esculentum)*	Growth, emergence, survival	0, 10, 32, 100, 320 and 1000 mg/kg	NOEC≥1000 mg/kg soil	Henzen, 1999b

OECD Guideline 203 was used for the fish study (Zebra fish (*Brachydanio rerio*)). In the study by Hooftman and Borst (1999) each exposure concentration used 10 fish, with diluted river water as the diluent. Every day the test medium was replaced. The actual concentration of the notified chemical in the test solutions was never determined. No abnormal behaviour or mortality was observed up to and including the concentration 1.8 mg/L and the NOEC=1.8 mg/L. At 3.2 mg/L all the fish were dead. The LC_{50} was determined to be 2.4 mg/L, indicating that the chemical is moderately toxic to fish.

The daphnia study by Hooftman et al (1999) followed the OECD Guideline 202, using four replicates with 5 daphnia in each. Diluted river water was the diluent. The actual concentration of the notified chemical in the test solutions was not determined. The oxygen content and mobility of daphnia were checked every 24 hours. The mobility of the daphnia was observed to be normal up to and including the concentration 0.32 mg/L, and the NOEC=0.32 mg/L. The EC_{50} was determined to be 2.4 mg/L, indicating that the chemical is moderately toxic to daphnia.

The algae toxicity study by Shorter and Nuck (1999) was conducted using 250 mL Erlenmeyer flasks with an initial algae cell density of 10 000 cells/mL. The flasks were continually rotated at approximately 24ºC while being exposed to a continuous lighting. Cell counts were made after 72 and 96 hours, and no inhibition was noted. The result of EC_{50} > 100 mg/L, indicated that the chemical is practically non toxic to algae.

The bacteria study by Mead (1998b) followed the German Water Hazard Classification Scheme and ISO 10712 "Determination of the inhibitory effect of water constituents on bacteria" (*Pseudomonas* cell multiplication inhibition test). The study was done in duplicate for each concentration while the temperature was maintained at 25ºC. The test was run for 16.5 hours. The absorbance of the bacteria/test solution at 436 nm was determined both before the test commenced and after 16 hours. This indicated the degree of growth inhibition, if any. Bacteria were affected at concentrations above 64 mg/L, indicating that the chemical is, at worst, slightly toxic to bacteria.

OECD Guideline 207 was followed for the earthworm study (Henzen, 1999a). The study was conducted in quadruplicate for 14 days at 20ºC under continuous low intensity illumination.

The condition, behaviour and number of worms were determined on days 7 and 14. At the end of the study on day 14 the surviving worms were weighed. Throughout the study there were no deaths and the no change in condition of the worms. The EC_{50} was determined to be greater than 1000 mg/kg soil, indicating that the chemical is practically non toxic to earthworms.

The terrestrial toxicity studies using three plant species by Henzen (1999b) were conducted following the OECD Guideline 208. The tests were done in quadruplicate with 5 plants per pot. The growth medium was a mixture of agricultural soil and coarse sand. The tests lasted 18/19 days, at 22ºC, pH 5.0 to 7.5 and a 16 hour light/8 hour dark light regime. Plants were assessed visually once or twice a week for the critical milestones of emergence and growth/condition. In all three species the test material did not affect emergence. However, when considering growth/condition, lettuce was affected at concentrations greater than 320 mg/kg, while the other two species were not affected.

The ecotoxicity data for the notified chemical indicate that the notified chemical is moderately toxic to fish and daphnia, and practically non toxic to algae, bacteria and earthworms.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified chemical is to be used as a component in domestic dishwashing formulations, therefore almost all will be released to the sewer system. Although it does not meet the criteria for "ready biodegradability" as defined in OECD TG 301B, the chemical has been shown to be extensively degraded under aerobic conditions, including tests designed to simulate an activated sludge sewage treatment plant.

The chemical is moderately toxic to zebra fish (LC_{50}=2.4 mg/L) and daphnia (EC_{50}=2.4 mg/L) and practically non toxic to algae and sewage bacteria.

Since the dishwashing liquid is likely to be used throughout Australia, an estimate of the Predicted Environmental Concentration (PEC) may be made on a national basis.

The following PEC calculation assumes that the dishwashing formulations (containing the notified chemical) is used nationwide, that all is released to the sewer system and that 150 L of sewage are generated each day by each person. Due to the very high water solubility, almost all the new chemical is expected to remain in the water column.

Import rate = release rate	8 000 kg per annum
National population	18 million
Volume of sewerage per annum	365x150x18 000 000= $9.86x10^{11}$
Concentration of chemical in sewage	8.11 µg/L
Dilution in receiving waters	1:10
Concentration in receiving waters	0.811 µg/L

The calculation assumes that no biodegradation or adsorption of the compound occurs in the sewage treatment plants prior to discharge to receiving waters. The calculation is a worst case scenario because it is likely that most of the chemical will have been destroyed prior to

discharge. However, even assuming no biodegradation, the estimated PEC is at least 5 orders of magnitude below levels which have been shown to be toxic to fish and daphnia.

The chemical is assessed as having low potential for bioaccumulation. The chemical is not expected to have affinity for the organic component of soils or sediments, and the high water solubility indicates that it is likely to be relatively mobile in soil. The terrestrial studies indicate that chemical applied to soil with sewage sludge will not have an effect on earthworms or on the emergence of seedlings, but it may have a slight inhibitory impact on seedling growth at high concentrations.

It is concluded that the new chemical presents a low hazard to the environment when used as a component of dishwashing liquid as indicated by the notifier.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical was of low to moderate acute oral toxicity in rats and moderate acute dermal toxicity in rabbits. The notified chemical was corrosive to rabbit skin and is expected to be corrosive to eyes. The notified chemical was not a skin sensitiser in guinea pigs.

In a 28 day repeat dose study in rats, food consumption and body weight gain were reduced and changes in clinical chemistry and haematology parameters occurred at 1 000 mg/kg bw/day. The NOEL was 250 mg/kg bw/day. The notified chemical was not mutagenic in an Ames test performed in *Salmonella typhimurium* and *Escherichia coli* strains. In a clonal transformation assay in Syrian Golden Hamster Embryo (SHE) cells, one 24-hour assay and two 7-day assays met the acceptance criteria for the study. In these assays, the notified chemical was negative for inducing morphological transformation in SHE cells. There were no *in vivo* mutagenicity or clastogenicity studies.

According to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999b), the notified chemical is classified as a hazardous substance with risk phrases of R21/22 (Harmful in contact with skin and if swallowed) and R35 (Causes severe burns).

Occupational health and safety
Occupational exposure to the notified chemical prior to end user is expected to be negligible, as it will be imported as a component of a formulated dishwashing liquid, and will not require formulation or repackaging in Australia. The health risk for transport, storage and retail workers is expected to be negligible unless packaging is breached. Little expected when cleaning up spills because the notified chemical will be present at a concentration of 0.5% in the imported product and workers are expected to wear coats and gloves.

Wash-up workers in commercial premises may be exposure to the chemical, but the risk would be similar to that of the public.

Public health
The notified chemical will be imported into Australia in hand dishwashing liquid preparations, such as Dawn Dishwashing Liquid and sold to the public. It is corrosive to skin

and likely to be an eye irritant. The public will come in contact with liquid dishwashing product preparations containing 0.5% of the notified chemical and described as slightly irritating to the skin and slight to moderately irritating to eyes. It is not uncommon for dishwashing agents to be eye irritants and users can avoid slight skin irritation by following a recommendation to use gloves. Therefore, the risk of the notified chemical to the general public is considered to be low, when formulated as a 0.5% component of liquid dishwashing preparations.

13. RECOMMENDATIONS

To minimise occupational exposure to "1,3-Bis(Aminomethyl) Cyclohexane", the following guidelines and precautions should be observed:

- Industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.2 (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.

Further recommendations may be required if the occupational use of the notified chemical is varied from the notified use. In this case, secondary notification may be 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.

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* (NOHSC, 1994).

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

Secondary notification under Section 64 of the Act may be required if:

1. the annual import levels of the chemical exceed 8 tonnes

2. the method of use changes in such a way as to greatly increase the environmental exposure of the notified chemical, particularly to natural waters, or if additional information becomes available on adverse environmental effects of the chemical

3. the conditions of use are varied from its use as a component of dishwashing liquid preparations, or the concentration of the notified chemical in consumer products is to be increased beyond 0.5%

4. occupational and environmental exposure is varied form the exposure described in this assessment

Secondary notification of the notified chemical may also be required if any of the circumstances stipulated under subsection 64(2) of the Act arise.

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Attachment 1

The Draize Scale (Draize, 1959) 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 (Draize *et al*., 1944) 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.
		Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
Diffuse beefy red	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

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