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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Trialkylene glycol ether

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Trialkylene glycol ether

1. APPLICANT

Dow Chemical (Australia) Limited of Kororoit Creek Road ALTONA VIC 3018 and Colgate-Palmolive Pty Ltd of 345 George Street SYDNEY NSW 2000 have jointly submitted a standard notification statement in support of their application for an assessment certificate for 'trialkylene glycol ether'.

2. IDENTITY OF THE CHEMICAL

Trialkylene glycol ether is not considered to be hazardous based on the nature of the chemical and the data provided. Therefore the chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data and details of exact import volume have been exempted from publication in the Full Public Report and the Summary Report.

Generic Name: trialkylene glycol ether

Method of Detection and Determination: infrared spectral analysis

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa: colourless liquid

Boiling Point: 274°C (calculated)

Freezing Point: < -50°C

Specific Gravity: 0.932 at 20°C

Vapour Pressure: < 0.001 kPa at 20°C

Water Solubility: 40.2 g/L at 25°C

Partition Co-efficient (n-octanol/water):	log P_{ow} = 1.896
Hydrolysis as a Function of pH:	not determined - see comments below
Adsorption/Desorption:	not determined - see comments below
Dissociation Constant:	pK_a > 10 (calculated)
Evaporation Rate:	<< 0.01 (where butyl acetate - 1.0) (from product information dossier)
Surface Tension:	29.9 mN/m at 20°C (from product information dossier)
Flash Point:	124°C (PMCC) 130°C (Setaflash)
Flammability Limits:	not determined
Autoignition Temperature:	202°C
Explosive Properties:	not determined
Reactivity/Stability:	not determined

Comments on Physico-Chemical Properties

The boiling point has been calculated from the vapour pressure data. No sign of freezing was observed after a period of five days at -55°C.

The notifiers do not expect the notified chemical to hydrolyse, based on its structure. It is agreed that hydrolysis is unlikely as the chemical contains no hydrolysable functional groups. Ethers are known to be generally resistant to hydrolysis (1).

The log K_{ow} value for the notified chemical was estimated to be 1.896 using the MedChem method (Medicinal Chemistry Project - MedChem Release 3.54). This program calculates the partition coefficient from the chemical's structure by an additive-constitutive procedure, using fragment constants for various structural pieces using the method reported by Hansch and Leo. The log K_{ow} was estimated to be 1.34 by SRC estimation software (2). This program estimates Log K_{ow} of chemicals using an atom/fragment contribution method.

The adsorption of the notified chemical to soil was calculated by the notifiers to be less than 20%. This was estimated from the octanol/water partition coefficient (K_{ow}) using linear regression relationships. It is expected that adsorption to common soils will be low based on the chemical's high water solubility.

The supplied dissociation data is based on calculations using extrapolated data for

alcohols. It was demonstrated that the bulk of the molecule has little effect on the end pK_a value when the hydroxyl functionality is present as in an alcohol or a glycol ether. Therefore, the notifiers claim that the dissociation constant will be greater than 10. It is accepted that the notified chemical is unlikely to dissociate in the expected environmental pH ranges.

Values for the evaporation rate and surface tension were taken from the notified chemical's product information sheet. Test reports for these values were not supplied. Note that these tests are not required under the Act, but that the results indicate low volatility and high surface activity (3).

4. PURITY OF THE CHEMICAL

Degree of Purity: > 95% (w/w)

Non-hazardous Impurities (> 1% by weight): < 5% (w/w) (identity of impurities is exempt)

Toxic or Hazardous Impurities: none

5. USE, VOLUME AND FORMULATION

The notified chemical will not be manufactured in Australia. It will be imported for use as a solvent in formulations for cleaning products, paints and coatings, and industrial printing inks. Initial use in Australia will be as a component of a surface cleaning product. Import volumes are expected to be greater than 10 tonnes per year for each of the first 5 years.

6. OCCUPATIONAL EXPOSURE

General
Trialkylene glycol ether will be imported by sea in 200 L steel drums in full container lots. Containers will be transported by road to a distributor's warehouse where the drums will be unloaded and stored in an approved store until required by the customer.

Occupational exposure is unlikely during transport, unloading the container, warehousing and delivery to the manufacturer, as the drums remain sealed until required for use in the manufacturing process. Exposure is expected to occur only in the event of an accident or leaking packaging.

Cleaning products
There is a potential for limited worker exposure during manufacture of the cleaning formulation. As the notified chemical is a liquid with a very low vapour pressure the most likely route of exposure is skin contact, although accidental ocular contact may

occur. The formulation process is an automatically controlled batch process which takes place in a closed vessel, with automatic addition of components. The finished product is transferred to storage tanks, prior to automatic packaging into plastic containers. Dermal exposure may occur during transfer of the notified chemical from drums to process feed tanks; and when formulated product is sampled by the operator and tested in the laboratory. Some exposure to the notified chemical may also occur during cleaning and maintenance of equipment.

Cleaners may be exposed to the notified chemical as part (< 20%) of the end use cleaning formulation. As the final product is a semi-solid gel and the notified chemical has a very low vapour pressure, the main route of exposure is expected to be dermal. Accidental ocular contact may also occur. Exposure to the notified chemical as part of the cleaning formulation may be frequent and prolonged for this group of workers.

Industrial Coatings

The notified chemical may also be used in the future as a component of paints and coatings in Australia. The notifier has stated that specific details about the use of the notified chemical in these applications are not available at this stage. However, the notifier states that the potential exposure routes during manufacture would be similar to those described above for formulation of the cleaning product, principally dermal and ocular contact, and to a lesser degree by inhalation.

Industrial coatings will potentially contain 1 to 20% of solvents such as the notified chemical. Paints containing the notified chemical may be applied using spraying equipment, rollers and brushes.

Occupational exposure to the notified polymer would be greatest during spray application of paints, using a non-automated spray system. In this situation inhalational, dermal and ocular exposure may occur. Application of paints using a fully automated spray booth would result in minimal worker exposure. Dermal exposure to the notified polymer may occur during application of paints using a roller or brush. Inhalational exposure is not expected to occur during application with a roller or brush, although drips and splashes into the eyes may occur during painting. Should contact occur during application, the paint is likely to remain on the exposed surface for some time, hence prolonging exposure. The notified chemical is expected to slowly evaporate as the paint or coating dries, hence inhalation exposure may occur if ventilation is inadequate at this stage.

The notifier states that the number of people who may be exposed and the potential period of exposure can not be assessed at this stage, as the potential market size is not known.

Inks

The notified chemical may also be used as a component of ink formulations for industrial printing processes, ball point and felt point pens, as well as stamp pads.

The details of formulation processes and customers are not known at this stage, although the notifier states that worker exposure during ink formulation processes is also expected to be similar to those described for cleaning products. The notified

chemical may make up 1 to 25% of the final ink product.

In a typical industrial printing operation, workers involved in printing processes may be dermally exposed to ink containing the notified chemical when decanting drums of ink into a reservoir on a printing machine. Splashing may also cause accidental ocular contact. The ink is then automatically fed to a printing device. Potential inhalation exposure may occur during the drying of the printed material, but this should be minimised by controlled drying of the printed product.

Any occupational exposure to the notified chemical as a component of ball point or stamp pad ink is expected to be minimal, due to the small amounts of ink in use at any one time.

Once again, as the potential market size is not known, further details on occupational exposure to the notified chemical as a component of ink products are not available at this stage.

7. PUBLIC EXPOSURE

The notified chemical will be imported and become a component of a surface cleaning product designed for use by the public for the maintenance of hard surfaces in domestic and commercial environments. The notifier estimates that eventually the formulated product will be in use in approximately 400 000 locations or households. Of this number, approximately 360 000 (90%) will be domestic users. The potential exposure of the public to the notified chemical is therefore high, with the principle route of exposure expected to be skin contact. The proportion of the notified chemical in the cleaning product is low (< 20% (w/w)) and the recommendation to wear gloves when using the product may limit skin contact with the notified chemical. The notified chemical may be used in the future in paints and inks, at concentrations of up to 25%.

In the event of a transport accident the likelihood of significant dispersion of the notified chemical from bulk shipments is low, given its packaging in steel drums within steel shipping containers, and its low vapour pressure.

The potential for public exposure during the manufacture of products containing the notified chemical is low.

8. ENVIRONMENTAL EXPOSURE

Release

The notifiers claim that most of this chemical will be disposed of through use, primarily by discharge to the water segment and a small quantity by evaporation to the atmosphere. Environmental exposure from residues of the chemical remaining in drums is expected to be extremely small, relative to use. Empty drums will be reconditioned and recycled by drum reconditioning companies, or alternatively salvaged as scrap metal. It is claimed that the import drums have high

reconditioning value.

Cleaning Products
During formulation and clean-up, waste chemical may be discharged to an on-site waste water treatment plant or to the sewer. Losses should be minimised due to the highly automated formulation and packaging processes. The notifiers claim that losses by evaporation will be minimal due to the low vapour pressure of the notified chemical.

During use as a domestic and commercial surface cleaning product, rinse water containing the notified chemical will be discharged to the sewer. The notifiers have anticipated that discharges from sewage treatment systems will be eventually to marine waters (ocean outfall) and to a lesser amount fresh water (river outfall). Product packaging (recyclable PET plastic dispensers) will either be sent for recycling or disposed of to landfill. The notifiers did not supply details of expected residues remaining in the dispensers, but again environmental exposure from this is expected to be low compared with that through use.

Paints, Coatings and Printing Inks
Small quantities of waste arising from the formulation process, ie clean-up and minor spillages during handling, will be discharged into a waste water treatment system or trade waste sewer system. When the notified chemical is formulated into coatings, etc, it is mainly absorbed into the resin. Quality assurance samples may be discharged into a trade waste sewer or incinerated.

Paints and coatings are usually applied in a ventilated booth or work area before oven curing. The notifiers did not detail the application methods expected, but it is assumed that application will be mainly by spray. During such use the notifiers expect that the notified chemical will be slowly released directly to the atmosphere as the applied film sets and hardens. During use as an ink the notifiers expect that the notified chemical will be released via evaporation directly to the atmosphere as it dries. A small quantity of waste is expected to be generated from equipment and work area clean-up, which is expected to be discharged to the sewer or buried in a trade waste or general waste landfill.

Use as an architectural paint could see the coating applied in the open environment. Here, the notified chemical is also expected to evaporate to atmosphere as the paint/coating dries. Inks containing the notified chemical would not be made available to the general public. However, if the chemical is used in the inks for ballpoint and felt tip pens, then there is the potential for use by the general public. However, the pens are designed to securely contain the inks and only release a very small amount of ink when used.

It is expected that empty packaging from paint, coating and ink will be disposed of to either trade waste or municipal waste landfills. The notified chemical will either evaporate to the atmosphere as the coating or ink dries, or otherwise remain with the product inside the container.

Fate

When the notified chemical is used as a component of a cleaning product the chemical is likely to be discharged to sewer, where it will be treated at the sewage treatment plant before discharge via outfall to the aquatic environment. Here it is likely to remain in the aquatic compartment, with only a very minor amount likely to be adsorbed to sludge or evaporated to air. A Mackay Level 1 Fugacity Model (4) has been performed, using the supplied physical and chemical data and 0.001 kPa (0.01 mm Hg) as the vapour pressure. This indicated that the majority (99.6%) will remain in the aqueous compartment. It should be noted that this level of the Mackay model is an equilibrium, steady state system, assuming no movement of the chemical between the various environmental compartments (eg air, water, soil, sediment) (5).

The notifiers expect the evaporated notified chemical to be stable in the troposphere, not subject to photolysis or hydrolysis. It should be washed from the atmosphere following precipitation. The notified chemical would then be dispersed over land and water bodies where it will slowly degrade. It is claimed by the notifiers that its use in paints, coating and inks is only prospective at this time, and it is expected that such products would be used in mainly metropolitan areas where rainfall is more regular and not a “once in a year” event. They do not expect the notified chemical to contribute to smog formation, ozone depletion or global warming. The notified chemical does not contain the halogens required for ozone depletion in the stratosphere. The notified chemical is water soluble and has a relatively low vapour pressure. Therefore, the notified chemical is not expected to persist in the atmosphere long enough to undergo significant photochemical reaction leading to smog formation.

Products of incineration will include water and oxides of carbon.

The chemical was determined to be ultimately biodegradable, being degraded by 93% within 28 days, in the Modified Zahn-Wellens Test for Inherent Biodegradability [OECD TG 302B (6)]. The chemical was also tested for its ready biodegradability (with pre-exposed inoculum[1]) in the Modified Sturm Test [OECD TG 301B (6)]. To develop a broader understanding of the biodegradability of a compound, environmentally relevant results may be obtained by operating this Test Guideline with inoculum pre-adapted to the compound (6). Here biodegradation was not sufficient for the notified chemical to be classified as readily biodegradable with pre-adaptation of inoculum, with only 21.5% and 24.3% degradation observed for the 10 and 20 mg/L concentrations respectively. Because degradation started after day 20 and no plateau was reached at day 28, it was decided to prolong the test period. After an additional period of 9 days, biodegradation had increased to 32% and 31%, respectively.

[1] The micro-organisms present in the inoculum were pre-exposed to the test substance in an adaptation test. During a period of 18 days exposure, a sample of fresh active sludge was started with the addition of 10.0 mg of the notified chemical per litre, followed by addition of 20.2 mg after seven days and 11.5 mg again at day eleven. This pre-exposed sample was mixed with fresh active sludge and used for inoculation of the test media which were prepared for the Modified Sturm Test.

Considering these results, it is expected that the notified chemical would not be highly persistent and should undergo substantial biodegradation in the environment. The notified chemical's high water solubility will limit its bioavailability and hence bioaccumulation (7).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of trialkylene glycol ether

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} = 2 800 mg/kg (combined sexes)	(8)
acute dermal toxicity	rat	LD_{50} > 2 000 mg/kg	(9)
skin irritation	rabbit	slight irritant	(10)
eye irritation	rabbit	slight irritant	(11)
skin sensitisation	guinea pig	non-sensitising	(12)

9.1.1 Oral Toxicity (8)

Species/strain: rat/Wistar

Number/sex of animals: 15/sex

Observation period: 14 days

Method of administration: gavage; based on the toxicity observed in a dose range finding investigation, the following treatment regimen was selected:

Dose (mg/kg)	*Number Treated M/F*
2 400	5/5
3 200	5/5
4 200	5/5

Clinical observations: major signs of toxicity were lethargy, ataxia, convulsions, tremors and unreactiveness; for surviving animals these symptoms were reversible; from day 2 onward no further clinical signs were observed for the remainder of observation period

Mortality: all deaths occurred within 24 hours of dosing; see table on next page for details:

Dose mg/kg	*Mortality (males)*	*Mortality (females)*
2 400	1/5	2/5
3 200	2/5	4/5
4 200	5/5	5/5

Morphological findings: bloody nose, bloody eye encrustation, red patches in the glandular part of the stomach and in the pancreas, petechiae of the stomach and the thymus, bloody contents or haemorrhage of the small intestine, haemothorax and dark red lungs were observed at necropsy

Test method: similar to OECD guidelines (6)

LD_{50} (combined sexes): 2 800 mg/kg

Result: the notified chemical was of low acute toxicity in rats

9.1.2 Dermal Toxicity (9)

Species/strain: rat/Wistar

Number/sex of animals: 5/sex

Observation period: 14 days

Method of administration: single dermal application of 2 000 mg/kg test substance; site was covered by occlusive dressing for 25 hours; remaining substance was removed using tap water

Clinical observations: none

Mortality: none

Morphological findings: none

Test method: similar to OECD guidelines (6)

LD_{50}: > 2 000 mg/kg

Result: the notified chemical was of low acute dermal toxicity in rats

9.1.3 Inhalation Toxicity

Not performed. The notifier states that, as the vapour pressure of the notified chemical is very low, there is little expectation of adverse health effects arising from the inhalation of the notified chemical under normal conditions, taking into consideration the low toxicity by other routes of exposure.

9.1.4 Skin Irritation (10)

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3 female
Observation period:	7 days
Method of administration:	0.5 mL of the test substance was applied to a 6 cm^2 intact dorsal skin site and the skin was covered by gauze and semi-occlusive dressing for 4 hours; remaining test substance was removed with water after dressing removed; observations made at 45 minutes, 1, 2, 3 and 7 days after removal of dressing and scored according to the method of Draize (13)
Draize scores (13) (see attachment 1 for Draize scales):	all animals had scaly skin at the test site at some time during the observation period all animals developed slight erythema by the 45 minute timepoint; this had cleared by day 7; one animal also showed slight oedema at the 1 and 2 day observation times.
Test method:	similar to OECD guidelines (6)
Result:	the notified chemical was a slight skin irritant in rabbits

9.1.5 Eye Irritation (11)

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	14 days
Method of administration:	0.1 mL of the test material was placed in the conjunctival sac of the right eye of each animal; left eye served as control

Draize scores (13) of unirrigated eyes:

	Time after instillation									
Animal	***1 day***		***2 days***		***3 days***		***7 days***		***14 days***	
Cornea	there were no corneal effects in any animals at any time point									
Iris	rabbit number 1 had a Draize score of 1 for iridial effects at the 1 day timepoint; all other scores for iridial effects were zero									
Conjunctiva	***r[a]***	***c[b]***	***r[a]***	***c[b]***	***r[a]***	***c[b]***	***r[a]***	***c[b]***	***r[a]***	***c[b]***
1	2	1	2	1	1	0	1	0	0	0
2	1	2	1	0	1	0	0	0	0	0
3	1	1	1	1	1	1	1	0	0	0

[1] see Attachment 1 for Draize scales
[a] redness [b] chemosis

Fluorescein application: application of fluorescein approximately 24 hours after instillation indicated the following:
rabbit 1 - approximately 52% of the corneal epithelium affected by treatment
rabbit 2 - approximately 2% of the corneal epithelium affected by treatment.
rabbit 3 - no fluorescein retention at this time point

there was no fluorescein retention in any animals at the day three examination

Test method: similar to OECD guidelines (6)

Result: the notified chemical was a slight eye irritant in rabbits

9.1.6 Skin Sensitisation (12)

Species/strain: guinea pig/Dunkin-Hartley

Number of animals: 30 female

Induction procedure: 6 hour occluded application of 0.5 mL of undiluted test substance on days 0, 2, 4, 7, 9, 11, 14, 16, 18; excess material was removed from the skin after each application

Challenge procedure: 6 hour occluded application of 0.5 mL of undiluted test substance; excess material was removed from the skin after application

Challenge outcome:

	Test animals		Control animals	
Challenge concentration	**24 hours***	**48 hours***	**24 hours**	**48 hours**
100%	0/20**	0/20	0/10	0/10

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

Test method: similar to OECD guidelines (6)

Result: the notified chemical was not a skin sensitiser in guinea pigs

9.2 Repeated Dose Toxicity

9.2.1 28 day gavage toxicity study (14)

Species/strain: rat/Fischer 344

Number/sex of animals: 20/sex; all groups (control, low, mid and high dose) 5/sex

Method of administration: gavage; vehicle was corn oil

Dose/Study duration: test material administered daily for a total of 28 days:

control: 0 mg/kg/day
low dose: 100 mg/kg/day
mid dose: 350 mg/kg/day
high dose: 1 000 mg/kg/day

all animals were sacrificed at the end of the treatment period

Clinical observations: pronounced lethargy and shallow respiration, which subsided within four hours of dosing, was noted in animals from the high dose group on test days one through three; these animals adapted to the treatment regimen and appeared clinically normal by test day four; one high dose female was lethargic on test day 15

Clinical chemistry/Haematology: a statistically significant increase in platelet counts was observed in males and females in the high dose group

Histopathology:	a dose-related increase in absolute and relative liver weights was observed in male and female rats in the mid and high dose groups; this observation was accompanied by histopathologic changes of increased hepatocellular size and altered staining in males and females in the high dose group; altered staining of hepatocytes was also noted in males from the mid dose group; no evidence of a treatment-related degenerative change accompanied these hepatic effects; the hypertrophy was attributed to metabolism of the test material a statistical difference in absolute and relative adrenal weights was noted in both sexes in the mid and high dose groups; there were not any accompanying gross or histopathological changes in the adrenal glands absolute kidney weights for low and high dose animals were increased; relative kidney weights for both sexes at the high dose levels were also increased and there were no accompanying gross, histopathological or clinical biochemical changes; the weights were also within the range of historical control values
Test method:	similar to OECD guidelines (6)
Result:	the findings of this 28 day oral repeat dose toxicity study indicate that treatment of rats with the notified chemical at mid and high dose levels induces a number of hepatic changes, which were attributed to metabolism of the test material, but could be considered to be of some toxicological significance

9.2.2 13 week Drinking Water Toxicity Study (15)

Species/strain:	rat/Fischer 344
Number/sex of animals:	60/sex; control and high dose groups: 20/sex low and mid dose groups: 10/sex
Method of administration:	drinking water
Dose/Study duration::	test material administered for a total of 13 weeks:

	control: 0 mg/kg/day low dose: 100 mg/kg/day mid dose: 350 mg/kg/day high dose: 1 000 mg/kg/day
	all animals were sacrificed at the end of the treatment period, with the exception of 10 animals from control and high dose groups, which were maintained for an additional 4 week recovery period before sacrifice
Clinical observations:	dose-related decreases in water consumption, attributed to reduced water palatability, occurred in males and females at all dose levels; decreased water consumption in high-dose males and females was associated with decreased feed consumption and body weight gain; feed consumption and body weight growth were not affected at the low and mid dose levels
Urinalysis	increases in urine specific gravity and protein content were noted for animals in the mid and high dose groups; these changes attributed to lower water consumption in these animals and were largely reversed at the end of the treatment free period
Clinical chemistry/Haematology	there were a number of minor, but statistically significant changes in haematological and clinical biochemical parameters; these included decreased red blood cell count, decreased haemoglobin concentration, decreased haematocrit, white blood cell or platelet counts in animals of the high dose group; these changes fell with the range of historical control values
Histopathology:	**Organ weights** statistically significant increases in absolute and/or relative liver weights were observed in males of all treatment groups, and females of the mid and high dose groups; absolute and relative kidney weights were significantly increased in males and females from the high dose groups, and females from the mid dose group; these changes were thought to be treatment-related
	the organ weights of hearts in females and

	adrenals in males from the high dose group were also significantly different to control values; these changes were not associated with histopathological alterations **Histopathology** high dose animals showed liver effects which consisted of an increase in the size of hepatocytes, which was accompanied by altered staining of the cytoplasm; no evidence of a treatment-related degenerative change accompanied these hepatic effects; these effects were thought to be related to metabolism of the test substance and changes were reversed at the end of the 4 week recovery period a slight increase in the severity of renal tubular degeneration was noted in males from the high dose group; the rate of incidence of this effect had decreased in the recovery group
Test method:	similar to OECD guidelines (6)
Result:	treatment of rats with a high dose (1 000 mg/kg/day) of the notified chemical for a period of 13 weeks induced changes in haematological parameters indicative of haemolytic effects and metabolic changes in the liver of males and females; slight changes were also noted in the kidneys of males of the high dose group

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (16)

Strains:	*Salmonella typhimurium* TA 1535, TA 1537, TA 98 and TA 100
Concentration range:	5, 15.8, 50, 158, 500, 1 580 and 5 000 μg/plate assay was performed as two independent experiments; vehicle was DMSO; assays were carried out in the presence and absence of rat liver S9 fraction
Test method:	similar to OECD guidelines (6)

Result:	the notified chemical was not mutagenic in the bacterial strains tested in the presence or absence of metabolic activation provided by rat liver S9 fraction; concurrent positive controls demonstrated the sensitivity of the assay

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (17)

Species/strain:	mouse/CD-1 (ICR) BR
Number and sex of animals:	25/sex
Doses:	187.5, 625 and 1 875 mg/kg; vehicle was corn oil; animals were sacrificed 24, 48 or 72 hours after treatment
Method of administration:	gavage
Comments	one negative control and two males in the high dose group died before scheduled necropsy
Test method:	similar to OECD guidelines (6)
Result:	the notified chemical did not induce micronuclei in mouse bone marrow cells when orally administered at concentrations up to and including the maximum tolerated dose

9.4 Overall Assessment of Toxicological Data

The combined oral LD_{50} for both sexes for the notified chemical was found to be 2 800 mg/kg in rats and the dermal LD_{50} was found to be greater than 2 000 mg/kg in a limit test in the same species. Inhalational toxicity studies were not performed. The notified chemical was a slight skin and eye irritant in rabbits, and was found not to be a skin sensitiser in guinea pigs.

Repeat dose oral toxicity studies were carried out using two methods of administration; gavage (28 day study) and drinking water (13 week study). Effects on the liver were noted in both studies, and were thought to be due to metabolic adaptation. Minor, but statistically significant haematological changes indicative of haemolysis of red blood cells were seen in animals in the high dose group (1 000 mg/kg/day) in the 13 week study. A slight increase of the severity of renal tubular degeneration was also noted in the kidneys of males in the high dose group of the 13 week study.

The notified chemical was not mutagenic in bacteria and did not induce chromosome damage in mouse bone marrow cells *in vivo.*

Based on information supplied by the notifier, trialkylene glycol ether would not be classified as hazardous according to *The Approved Criteria for Classifying Hazardous Substances* (18).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies have been supplied by the notifiers. The fish and water flea tests were carried out to OECD Test Methods. The algal toxicity test is based on the OECD Test Guideline 201 (6).

Test	***Species***	***Results***
acute toxicity semi-static, nominal [OECD TG 203]	guppy (*Poecilia reticulata*)	96 hour LC_{50} = 564 mg/L NOEC = 180 mg/L
acute immobilisation static, nominal [OECD TG 202]	water flea (*Daphnia magna*)	48 hour NOEC = 1 000 mg/L
level of phytotoxicity static, measured	green alga (*Selenastrum capricornutum)*	*Cell Count/mL* 5 day EC_{50} = 265 mg/L 5 day NOEC = 22.3 mg/L *Cell Volume* 5 day EC_{50} = 351 mg/L 5 day NOEC = 22.3 mg/L

Exposure to the notified chemical for 24 hours resulted in the death of all fish at the concentration of 1 000 mg/L. At a concentration of 320 mg/L effects seen were an increase of pigmentation, hyperreactivity and total inhibition of swimming ability. The notifiers concluded that the notified chemical shows toxicity to the guppy at concentrations higher than 180 mg/L after 96 hours exposure. However, the results still indicate that the notified chemical is practically non-toxic to the guppy.

Based on the results of the range finding study, the water fleas were only exposed to the one test concentration of 1 000 mg/L. No significant immobilisation was observed after 48 hours of exposure. Therefore, the results indicate that the notified chemical is practically non-toxic to the water flea.

The notifiers claim that the test methodology to determine the toxicity of the notified chemical to green algae, which is based on OECD TG 201 (6), was recommended by the United States Environment Protection Agency. The method and results of this test are acceptable, and the notified chemical can be classed as practically non-toxic to algae. However, it should be noted that algae begin to exhibit unspecified[2] toxic effects from 22.3 mg/L (the NOEC), which was the second lowest concentration tested.

[2] Toxic effects were unspecified other than measured as a reduction in mean total cell volume and mean total cell counts per millilitre.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The majority of the notified chemical will be disposed of to sewer through use in cleaning products. Here it is expected to pass through the treatment process relatively unchanged. The notifiers provided a scenario where each of the households in the Malabar Catchment Area (Sydney, NSW) used the contents of a product pack on the same day. A similar scenario has been calculated for a small hypothetical country town. The predicted environmental concentrations (PECs) of the notified chemical (assuming no biodegradation or removal) are outlined below.

Calculation Factor	*City - Malabar Catchment*	*Country Town (Hypothetical)*
amount of notified chemical entering sewer per day	1 986 kg	45 kg
volume of effluent at STP	455 ML	1 ML
concentration in effluent at STP	4.36 mg/L	45 mg/L
dilution factor in receiving waters	1:10 (ocean outfall)	1:2 (river outfall)
PEC in receiving waters	0.44 mg/L	22.5 mg/L
safety factor for exposure to most sensitive aquatic organism, algae (5 day EC_{50} = 265 mg/L)	600	12

Noting that these calculations represent a worst case, the PECs show that the concentrations of notified chemical entering the aquatic environment due to use in cleaning products should be well below those of environmental concern. For instance, if the dilution factor for effluent from the country STP was decreased, ie there was no natural creek flow besides the discharged effluent, the safety factor will still be 6. (It should be noted this is example is an extreme worst case situation.) While the notified chemical should remain in the aquatic compartment (4), it should not persist as it will be further diluted and degraded with time.

Use of the notified chemical in paints, coatings and printing inks should not pose any significant environmental hazard. As the chemical dries, it will evaporate from the product, entering the atmosphere where it will be widely dispersed. The notifiers claim that alkylene glycol ethers are stable in the troposphere, not subject to degradation under the influence of UV light, and do not react with atmospheric oxygen or nitrogen. It is not expected that the notified chemical will contribute to ozone depletion, smog formation or global warming. The chemical should not persist in the atmosphere being washed out by precipitation. Dispersed at extremely low concentrations over land and water bodies, the chemical should degrade.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The occupational health risk posed to transport workers is low, as exposure during transport, handling in warehouses or stores will only occur in the event of a spill. In

addition, the notified chemical is not a dangerous good for transport by road, rail, sea or air and is not expected to pose a significant health hazard if acute exposure occurs.

The occupational health risk to workers who will be involved in reformulating the notified chemical into cleaning products, inks or paints is predicted to be low. Dermal contact is expected to be the main route of exposure. The relatively low molecular weight of the notified chemical and its physico-chemical properties do not preclude dermal absorption but an acute dermal toxicity study in rats indicates that dermal absorption is unlikely to cause systemic effects. Red blood cell haemolysis is an effect associated with exposure to glycol ethers (19) and prolonged exposure to high doses of the notified chemical (1 000 mg/kg/day) induced minor but statistically significant changes in haematological parameters indicative of haemolysis in rats. However, engineering controls and appropriate use of personal protective equipment (see recommendations section) are expected to limit exposure to the concentrated form of the notified chemical.

Based on the results of a rabbit study the notified chemical may cause slight skin irritation if contact occurs. In addition, prolonged or repeated skin contact may lead to degreasing and drying of the skin. Guinea pig studies indicate that the notified chemical is unlikely to be a skin sensitiser in humans.

If accidental eye contact occurs during reformulation, slight eye irritation may result, but permanent damage is not likely. As discussed in the occupational exposure section, inhalation is not expected to be a significant route of exposure during reformulation, given that the vapour pressure of the notified chemical is very low and it will not be heated above room temperature during the reformulation and packaging processes.

Workers may be exposed to the notified chemical as a component of a number of formulated products. The maximum concentration of the notified chemical in these products is expected to be up to 25%, and exposures are predicted to be primarily dermal in nature. However exposure by inhalation may be possible during spray painting with coatings containing the notified chemical, if sufficient engineering controls and personal protective equipment are not utilised. Accidental ocular exposure to cleaning products, paints and inks may also occur. As the concentration of the notified chemical in end use products is unlikely to exceed 25%, and toxicity tests indicate a low hazard for the chemical, the occupational risk for these workers is also predicted to be low.

There is potential for public exposure to the notified chemical as a component of cleaning products. Accidental ingestion of the notified chemical is unlikely, as the cleaning formulation is a semi-solid (a gel). Inhalation is also an unlikely route of exposure, as the vapour pressure of the notified chemical is very low and the cleaning formulation is used at ambient temperature. The possibility of eye contact is reduced by the physical nature of the formulation of the commercial product, which is a semi-solid, thus reducing the potential for splashing. Eye contact may occur, however, where users inadvertently wipe their eyes or surrounding skin with their hands after or during use of the product. In this situation irritation is likely to be slight and without permanent injury, and readily limited by flushing the eye with water.

Given the low acute toxicity of the notified chemical, its low toxicity in repeat dose studies and the nature of the formulation to be marketed to the public, the risk to the health of users of the cleaning formulation containing the notified chemical is likely to be low.

13. RECOMMENDATIONS

To minimise occupational exposure when handling trialkylene glycol ether in concentrated form, the following guidelines and precautions should be observed:

- industrial clothing which conforms to the specifications detailed in Australian Standard (AS) 2919 (20) and occupational footwear which conforms to Australian and New Zealand Standard (AS/NZS) 2210 (21) should be worn;

- gloves which conform to Australian Standard 2161-1978: *Industrial Safety Gloves and Mittens (excluding Electrical and Medical Gloves)* (22) should be worn if exposure is likely to be repeated or prolonged, to minimise skin drying and defatting;

In addition, the following guidelines and precautions should be observed when handling products containing trialkylene glycol ether:

- if exposure by inhalation is likely (eg when spraying paints containing the notified chemical in a poorly ventilated space) a mask should be selected and fitted which conforms to Australian/New Zealand Standard 1715-1994: *Use and Maintenance of Respiratory Protective Devices* (23) and Australian/New Zealand Standard 1716-1991: *Respiratory Protective Devices* (24);

- Spillage of the notified chemical and products containing it should be avoided, spillages should be cleaned up promptly and put into containers for disposal;

- Good personal hygiene should be practised to minimise the potential for ingestion;

- A copy of the Material Safety Data Sheet (MSDS) should be easily accessible to employees, and adequate information should be easily accessible for end use products containing the notified chemical.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (25).

This MSDS was provided by Dow Chemical (Australia) Limited 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 Dow Chemical (Australia) Limited.

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