File No: NA/835

January 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

t-amyl peroxyoctoate (Luperox 575)

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Director
Chemicals Notification and Assessment

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t-amyl peroxyoctoate (Luperox 575)

1. APPLICANT

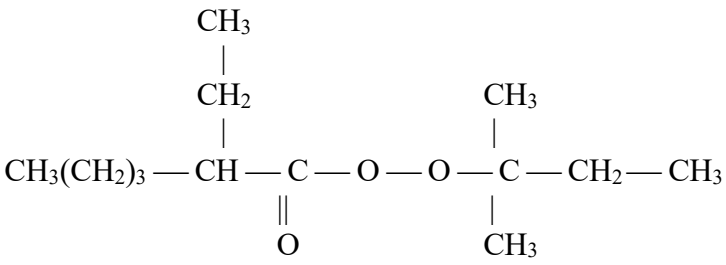
Atofina (Australia) Pty Ltd (ACN No. 000 330 772) of 270 – 280 Hammond Rd DANDENONG SOUTH VIC 3175 has submitted a standard notification statement in support of their application for an assessment certificate for Luperox 575.

2. IDENTITY OF THE CHEMICAL

The chemical impurities, exact use and details of exact import volume have been exempted from publication in the Full Public Report and the Summary Report.

Chemical Name:	hexaneperoxoic acid, 2-ethyl-, 1,1-dimethylpropyl ester
Chemical Abstracts Service (CAS) Registry No.:	686-31-7
Other Names:	t-amyl peroxyoctoate t-amyl peroxy(2-ethylhexanoate)
Marketing Name:	Luperox 575 Lupersol 575
Molecular Formula:	$C_{13}H_{26}O_3$

Structural Formula:



Molecular Weight:	230.35
Method of Detection and Determination:	Infrared (IR) spectroscopy.

Spectral Data: An IR spectrum was provided.

3. PHYSICAL AND CHEMICAL PROPERTIES

The following data were contained in a report using computer modelling or in a product Material Safety Data Sheet (MSDS).

Appearance at 20°C & 101.3 kPa:	Clear liquid.
Freezing Point:	< -80°C
Specific Gravity:	0.9028 at 25°C
Vapour Pressure:	0.88 kPa at 15°C (estimated – see notes below).
Water Solubility:	Estimated at 2.4mg/L at 25°C (estimated – see notes below).
Partition Co-efficient (n-octanol/water):	Calculated log K_{ow} = 4.8 (see notes below).
Particle Size:	Not relevant.
Hydrolysis as a Function of pH:	Calculated $T_{1/2}$ at pH 7.0 = 8.3 days. Calculated $T_{1/2}$ at pH 8.0 = 19.8 hours
Adsorption/Desorption:	Calculated logK_{oc} = 3.4.
Dissociation Constant:	Not determined – see notes below.
Henry's Law Constant:	H = 83 300 Pa.m^3/mole, log H = 4.92 (calculated, see notes below.)
Flash Point:	71°C
Flammability Limits:	Not determined.
Autoignition Temperature:	> 45°C
Explosive Properties:	The self accelerating decomposition temperature is 45°C.
Reactivity/Stability:	Unstable. Half-life = 16 hours.

3.1 Comments on Physico-Chemical Properties

All the physico-chemical data provided were derived from model calculations using the ECOSAR program via appropriate Quantitative Structure Activity Relationships (QSARs).

While measured data would have been preferable, it is appreciated that due to the unstable nature of the compound accurate measurement of these properties would be difficult.

The estimated low water solubility and high values for log P_{ow} and log K_{oc} are in accord with the high hydrocarbon content of the notified chemical. These data indicate that if the compound were stable, it would partition into oil and fat, and if released to soil would bind to and associate with the organic component of soils and sediments.

The Henry's law constant was calculated from the (estimated) vapour pressure and water solubility using the relation –

H = Vapour pressure (Pa) X Molecular weight (g/mol)/ Water solubility (g/L).

The large estimated value of H indicates that the compound would volatilise from water if released in solution.

The compound contains a peroxycarbonate linkage which could be susceptible to hydrolysis. However, the peroxide group itself is highly reactive, and in an aqueous environment the chemical would be more likely to decompose to t-amyl alcohol and 2-ethyl hexanol with concomitant evolution of O_2 through reactions of the peroxide group rather than undergo hydrolytic cleavage.

The compound contains no acidic or basic groups, so dissociation constant data are not relevant.

4. PURITY OF THE CHEMICAL

Degree of Purity:	minimum of 95%
Hazardous Impurities:	< 4.1%. No impurities at a concentration which would render the notified chemical hazardous.
Non-hazardous Impurities (> 1% by weight):	None.
Additives/Adjuvants:	None.

5. USE, VOLUME AND FORMULATION

The notified chemical will be used as a polymerisation initiator. It will be used at a level of 0.5 – 2% by weight in reactions with monomers and will be imported in 15.6 kg polyethylene closed head cube carboy containers. Less than 10 tonnes per annum are to be imported for the first 5 years.

6. OCCUPATIONAL EXPOSURE

Transport and Storage

The notified chemical will be imported by the notifier and delivered to a single customer on a just in time basis in the desired quantity for the batch size to be manufactured. The chemical is classified as a Dangerous Good and is assigned UN No. 3115, Organic Peroxide, Type D, Liquid, Class 5.2, and is required to be stored below 10°C and transported in accordance with the ADG code. Exposure of workers during transport and storage is only likely to occur in the event of accidental spillage.

Laboratory Testing

Quantities of 20 – 200 grams will be weighed out in glassware and added to batches of 4 – 10 kg for testing in a fume hood. Laboratory staff (3) working 8 hours per day, 10 days per year wear a laboratory coat, safety shoes, safety glasses and rubber gloves when conducting tests.

Resin Manufacture

Nine workers working 8 hours per day, 20 days per year manually add the notified chemical in a full pack size with solvent to a sealed weigh vessel under local exhaust ventilation. The solvent is used to rinse the container so that little residue remains. The weigh vessel is used to charge the main reactor which is filled under local exhaust ventilation. The solvent and notified chemical feeds to the main reactor are conducted over several hours. The notified chemical is of low volatility and this, coupled with the use of fume extraction should preclude inhalation exposure. Nevertheless, the notifier states that respiratory protection is normally worn during resin manufacture. Dermal exposure of workers is possible during transfer operations. Workers wear overalls, safety boots, goggles and gloves to prevent exposure while handling the notified chemical. Once the reaction is complete, the notified chemical becomes incorporated into the polymer and the polymer solution is discharged to bulk storage tanks or to 200 L drums.

Workers handling the notified chemical are experienced at handling other organic peroxides.

After polymerisation, the notified chemical is chemically bonded to long polymer chains and becomes an integral part of the polymer. The polymers will ultimately be used in the manufacture of metal coatings.

7. PUBLIC EXPOSURE

The notified chemical, resin solution and final paint products will be used in industry only. The public will come into contact with the notified chemical only after the paint products have been applied to substrates where a coating film is formed in which the notified chemical is incorporated. The notified chemical will not be available for absorption when incorporated into the films and public exposure should be negligible.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Minimal release during charging of the slurry tank is expected, and any spills and splashes of the compound would most likely be diluted with water and combined with the overall liquid waste stream within the plant.

It was indicated in the submission that the polymerisation reactor is a refluxing vessel – presumably allowing for complete vapour return to the reactor. This and other engineering controls would minimise releases of gases and vapours to the atmosphere during the polymerisation process.

Apart from accidents, very little release of the chemical is expected during addition to the reaction vessel and during the polymerisation process. Since the chemical decomposes to free radicals during the process, no release of the chemical with the final product is expected. Further, the free radicals are themselves incorporated into the polymer, so little release of decomposition products is expected.

The notifier indicated that the reaction batch sizes are arranged to require multiples of a full container load of notified chemical (15.6 kg), so that little unused compound remains in the emptied carboys. Further, small quantities of residual material are washed out of the containers with solvent and added to the reactor. Consequently very little of the notified chemical is likely to be released with disposal of the emptied carboys into landfill.

A small amount of the notified chemical from development laboratories may be released with other plant industrial waste effluent to the municipal sewer, possibly after pre-treatment.

8.2 Fate

All of the notified chemical is consumed during resin manufacture and becomes incorporated into the polymer chains. Except in the case of accident there is little likelihood of release of the chemical, but if this were to occur the chemical is expected to rapidly decompose through rupture of the peroxide bonds. The decomposition products would most likely be carbon dioxide and the two alcohol species indicated above. Rapid decomposition of organic peroxides is effectively catalysed through ferrous ions, which are invariably present in soils and natural waters.

The notifier provided a draft summary test report on the aerobic biodegradation in a closed bottle test (OECD TG 301 D) for a close structural analogue of the compound ie. t-butylperoxy 2-ethylhexyl carbonate (TBEC), which was previously assessed as NA/710. The test material appears to be ultimately biodegradable. This biodegradation test is probably more representative of that for an equimolar mixture of t-butyl alcohol and 2-ethyl hexanol rather than of the initial test compound itself, since this is expected to degrade quickly to these two alcohols.

The high estimated value for log K_{oc} indicates that chemical released to the soil as a result of spill or accident would become bound to the organic component of the soil. The notified chemical is unlikely to be mobile in the soil compartment, and is expected to decompose rapidly through reaction of the peroxide group.

Small neutral compounds with high log P_{ow} values and low water solubility have a potential

for bioaccumulation (Connell, 1989), so the notified chemical could potentially bioaccumulate if it persisted in the environment. However, the inherent instability of the chemical indicates a very short lifetime in the environment, and so bioaccumulation is considered unlikely.

The notified chemical is volatile and has a high Henry's law constant. Therefore, it is possible on release to water that some of the chemical would enter the atmospheric compartment. In this situation it would decompose through photo-degradation reactions with atmospheric hydroxy radicals. The notifier indicated that the overall rate constant for reaction of the notified chemical with these radicals is 8×10^{-12} cm^3/mol/sec. Taking the average concentration of the OH radicals as 1.5×10^6 radicals/cm^3, the atmospheric half life is around 16 hours.

9. EVALUATION OF TOXICOLOGICAL DATA

Skin sensitisation, repeated dose toxicity and chromosomal damage studies were not available for the notified chemical. However, these studies have been conducted with the analogue TBEC notified as NA/710 and extracts from the Full Public Report for this chemical are reproduced below in the relevant sections.

9.1 Acute Toxicity

Summary of the acute toxicity of t-amyl peroxyoctoate

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 5 000 mg/kg	(Reagan, Becci & Parent, 1981a)
acute dermal toxicity	rabbit	LD_{50} > 2 000 mg/kg	(Reagan, Becci & Parent, 1981b)
skin irritation	rabbit	Slight to moderate irritant	(Reagan, Becci & Parent, 1981c)
eye irritation	rabbit	Not irritant	(Reagan, Becci & Parent, 1981d)

9.1.1 Oral Toxicity (Reagan, Becci & Parent, 1981a)

Species/strain: Rat/Sprague-Dawley

Number/sex of animals: 5/sex

Observation period: 14 days

Method of administration: Oral (gavage) at a dose of 5g/kg body weight.

Test method: OECD TG 401

Mortality: None.

Clinical observations:	Ataxia, decreased activity, soft stool, wet yellow belly and diarrhea on days 1 and 2.
Morphological findings:	Not given.
LD_{50}:	> 5 000 mg/kg
Result:	The notified chemical was of very low acute oral toxicity in rats.

9.1.2 Dermal Toxicity (Reagan, Becci & Parent, 1981b)

Species/strain:	Rabbit/New Zealand White (NZW).
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Under occlusive dressing for 24 hours at a dose of 2g/kg on abraded and intact skin.
Test method:	Similar to OECD TG 402.
Mortality:	One animal died on day 7.
Clinical observations:	From day 11 scattered observations of diarrhea, soft stool and loss of appetite.
Morphological findings:	None given.
LD_{50}:	> 2 000 mg/kg
Result:	the notified chemical was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

Not provided.

9.1.4 Skin Irritation (Reagan, Becci & Parent, 1981c)

Species/strain:	Rabbit/NZW
Number/sex of animals:	6/males.
Observation period:	72 hours.

Method of administration: 0.5 mL of the test substance under occlusive dressing for 24 hours on intact and abraded skin.

Test method: Similar to OECD TG 404.

Draize scores for animals with intact skin:

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

[a] see Attachment 1 for Draize scales

Comment: Readings were only reported for the 24 and 72 hour time points, therefore, calculation of mean scores was not meaningful.

Result: The notified chemical was slightly to moderately irritating to the skin of rabbits.

9.1.5 Eye Irritation (Reagan, Becci & Parent, 1981d)

Species/strain: Rabbit/NZW

Number/sex of animals: 3/sex.

Observation period: 72 hours.

Method of administration: 0.1 mL into the conjunctival sac of 1 eye; the untreated eye served as control.

Test method: Similar to OECD TG 405.

Result: No Draize scores above zero were recorded in any animal at any time point for conjunctival, corneal or iridal effects. The notified chemical was not irritating to the eyes of rabbits.

9.1.6 Skin Sensitisation (TBEC) (Centre International de Toxicologie, 1999)

Species/strain: Guinea pig/Hartley Crl: (HA)BR

Number of animals: 10/sex (treated group); 5/sex (control group)

Induction procedure:

- *Test Animals*

Day 1:
Three pairs of intradermal injections (0.1 mL) into the dorsal skin of the scapular region:

- Freund's complete adjuvant (FCA) 1:1 in saline;
- test substance at 10% w/w in corn oil;
- test substance at 10% w/w in a 1:1 mixture of FCA and saline.

Day 7:
The same region received a topical application of sodium lauryl sulfate in vaseline (10%, w/w) to induce local irritation.

Day 8:
The undiluted test substance (0.5mL) was applied to the same test site for 48 hours under occlusive dressing.

- *Control Animals*

Treated as above but omitting the test substance.

Challenge procedure:

Day 22:
Animals were challenged with undiluted test substance (0.5mL) on the right flank, under occlusive dressing for 24 hours.

Day 33:
Animals were rechallenged with 50% (w/w) test substance in corn oil (0.5 mL), on the left flank.

Test method:

OECD TG 406; Magnusson and Kligman Maximisation Method

Comment:

No clinical signs or deaths were noted during the study.

At 24 hours after the first challenge application, 4/10 control and 8/20 test animals had signs of very slight erythema. There was also well-defined erythema in 1/10 control and 4/20 test animals. Most reactions were associated with dry skin and persisted at the 48-hour reading.

At rechallenge, 3/10 control and 8/20 test animals had signs of very slight erythema 24 hours after patch removal. There was well-defined erythema in one control animal and in 5/20 test animals, with few of these reactions persisting at 48 hours.

The similarity of incidence and severity of reactions in both

control and test animals suggested an irritant effect, rather than a delayed contact hypersensitivity reaction.

Result: The test substance was non-sensitising to the skin of guinea pigs.

9.2 Repeated Dose Toxicity (TBEC) (MB Research Laboratories, 1999a)

Species/strain: Rat/Wistar albino

Number/sex of animals: 5/sex/group

Method of administration: Oral (gavage) at a volume of 2 mL/kg.

Dose/Study duration: Doses of 0, 150, 550 or 1 000 mg/kg of test substance in vehicle (mineral oil) were administered daily for 28 days (with the exception of day 20, due to insufficient quantity of test substance).

Test method: OECD TG 407

Clinical observations:
The deaths of two females at 550 mg/kg/day and two females at 1 000 mg/kg/day during the study were attributed to inadvertent gavage accidents, and not to toxic effects of the test substance. Other clinical signs were considered to be minor and were commonly distributed throughout all groups. There were no significant differences in food consumption and Functional Observational Battery results between groups.

Clinical chemistry/Haematology
The only haematological parameter that was significantly different (decreased) between treated and control groups was the mean haemoglobin concentration of males in the 1 000 mg/kg group.

Significant differences in clinical chemistry parameters between the groups were noted with chloride, glucose, albumin and total protein concentrations, but were considered to be irrelevant because of a lack of a dose-response effect.

Organ weights and organ/body weight ratios:
There were no significant differences in organ weights between groups, but significantly larger liver/body weight ratios were seen in females dosed at 1 000 mg/kg, compared with control females.

Histopathology:
Treatment-related microscopic changes were in the stomach of male and female animals dosed at 1 000 and 550 mg/kg/day, in a dose-related manner. These changes consisted of moderate to marked thickening of the squamous mucosa of the non-glandular areas due to increased hyperplasia and hyperkeratosis of the epithelial mucosa. There was also an extreme acute inflammation involving both the mucosa and submucosa of the non-glandular area with oedema and mostly polymorphonuclear inflammatory cell infiltrations. At 1 000 mg/kg/day, one male had oedema/inflammation in the mucosa and submucosa of

the glandular area. Focal necrosis (erosions) of the superficial epithelium in the non-glandular area was also observed.

Treatment-related microscopic changes were noted in the kidneys of male animals dosed with 1 000 and 550 mg/kg/day. These appeared in a dose-related manner and consisted of an increase in Mallory-Heidenhain staining of the kidney which was due to the presence of hyaline droplets in the cortical tubular epithelial cells.

Animals dosed at 150 mg/kg/day had no treatment-related microscopic changes in any organs or tissues.

Comment:
The pathological changes noted in the stomach of males and females dosed at 1 000 and 550 mg/kg/day were considered to be biologically relevant and treatment-related. The kidney pathology noted in male rats was not considered to be relevant to human exposure because the enzyme system responsible for hyaline droplet formation is unique to the male rat. No treatment related changes were observed at 150 mg/kg/day.

Result:
The no observed adverse effect level (NOAEL) is established at 150 mg/kg/day based on the lack of significant test substance related effects or toxicity at this dose.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Haddouk, 1999)

Strains:	TA 1535, TA 1537, TA98, TA100 and TA 102.
Metabolic activation:	Rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors.
Concentration range:	<u>Without S9 mix</u> Experiments 1 and 2: 156.25, 312.5, 625, 1 250 and 2 500 µg/plate <u>With S9 mix</u> Experiment 1: 156.25, 312.5, 625, 1 250 and 2 500 µg/plate for strains TA 1535, TA 100 and TA 102, 78.125, 156.25, 312.5, 625 and 1 250 µg/plate for strains TA 1537 and TA 98. Experiment 2: 312.5, 625, 1 250, 2 500 and 3 125 µg/plate for strains

	TA 1535, TA 100 and TA 102, 312.5, 625, 750, 1 250 and 1 500 μg/plate for strains TA 1537 and TA 98
Test method:	OECD TG 471
Comment:	The test substance was toxic at some dose levels and the doses chosen for the various strains and conditions reflected this. No increase in the number of revertants above background was observed without S9 mix in any strain. With S9 mix in strain TA 98 a non-reproducible 2-fold increase in the number of revertants occurred at the top dose. This increase is not considered significant. In strain TA 102, an increase of approximately 2-fold in the number of revertants per plate was observed from a dose level of 312.5 μg/plate in experiment 1. Although not conclusive, this weak mutagenic activity was confirmed in the second experiment which involved a preincubation step. The maximum level of revertants was 5 times the spontaneous level and the numbers of induced mutants were 506, 924, 728, 1167 and 688 at dose levels of 312.5, 625, 1250, 2500 and 3125 μg/plate, respectively.
Result:	The notified chemical was mutagenic under the conditions of the test.

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (TBEC) (BioReliance, 1999)

Species/strain:	Mouse/ICR
Number and sex of animals:	5/sex/group
Doses:	Animals were dosed with 0, 300, 600 or 1 200 mg/kg of test substance dissolved in corn oil, at a constant volume of 20 mL/kg.
Method of administration:	Animals were dosed by intraperitoneal injection. Sampling times were 24 and 48 hours post-administration.
Test method:	OECD TG 474
Comment:	No mortality occurred at any dose level during the course of the study. Following administration of the test substance, lethargy, piloerection and diarrhoea was evidenced in all test animals.

Reduction of 2 to 20% in the ratio of polychromatic erythrocytes to total erythrocytes was observed in some of the test groups, suggesting toxicity of the test substance to the bone marrow cells.

The number of micronucleated polychromatic erythrocytes per 2 000 polychromatic erythrocytes in the test-substance-treated groups was not statistically increased relative to respective controls, regardless of sex, dose level or sampling time.

All criteria for a valid test were met.

Result: The test substance was not considered to be clastogenic in mouse bone marrow cells *in vivo*, under the conditions of the assay.

9.4 Induction of Sustained Skin Hyperplasia and DNA Damage (Slaga, 1997)

In support of a claim that the notified chemical does not have the potential to be a skin carcinogen, the notifier provided a copy of a paper by Slaga (1997), describing a pre-screen assay of nine peroxides (including TBEC) and hydrogen peroxide to produce DNA damage (8-OH-dG formation), Ha-*ras* mutations and sustained epidermal hyperplasia and dermal cellularity. TBEC at 0, 10, 100 or 200 µmol was applied topically, twice weekly for 4 weeks to Virgin Sencar female mice (10 animals per dose group for histological investigations and 5 mice per group each for DNA damage and Ha-*ras* mutation induction). TBEC induced dermal cellularity when administered topically, but no significant responses were observed with respect to the other three endpoints. However, dimethylbenz[a]anthracene (10 or 100 nmol), the positive control carcinogen, elicited a positive response for all four endpoints. Increased dermal cellularity, as an isolated finding, was therefore considered to be an insufficient index of carcinogenic potential.

While these results have value in being able to provide an hypothesis for a mechanism of action for specific classes of potential skin carcinogens, they nevertheless need to be regarded with caution for regulatory purposes because the number of chemicals employed in this study do not constitute sufficient data to adequately assess the sensitivity, specificity or accuracy of the assay. Also, several of the endpoints of the assay, particularly 8-OH-dG formation and Ha-*ras* mutations, may be too specific to cover all possibilites of genotoxic damage which may give rise to skin tumours.

9.5 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity in rats (LD_{50} > 5 000 mg/kg) and low acute dermal toxicity in rabbits (LD_{50} > 2 000 mg/kg). According to the Material Safety Data Sheet (MSDS) for the notified chemical, TBEC has a low 4-hour acute inhalation toxicity of 42.2 mg/L in rats. Therefore, the notified chemical is also predicted to exhibit low acute inhalation toxicity in rats. The notified chemical was a slight to moderate skin irritant but was not an eye irritant in rabbits.

A skin sensitisation study using TBEC in guinea pigs resulted in lesions of similar intensity

and severity in both control and test animals after challenge and rechallenge applications. Because these responses were considered to be suggestive of an irritant effect, rather than arising from a delayed contact hypersensitivity reaction, TBEC was not considered to have sensitising potential.

A 28-day repeated dose study in rats using TBEC produced no clinical effects but did produce dose related histopathological changes at 1 000 and 550 mg/kg. The pathological changes were noted in the stomach of male and female animals rats and in the kidneys of male rats only. The pathological changes noted in the stomach are considered to be biologically significant. The kidney pathology noted in male rats was not considered to be relevant to human exposure because the enzyme system responsible for hyaline droplet formation is unique to the male rat. The no observed adverse effect level (NOAEL) is established at 150 mg/kg/day based on the lack of significant test substance related effects or toxicity at this dose.

The notified chemical was mutagenic in bacteria but was not clastogenic in mouse bone marrow cells.

TBEC was investigated in a four week repeat dose dermal study for its ability to produce DNA damage and sustained epidermal hyperplasia in mouse skin. It increased dermal cellularity but the cell types involved were not identified. There was no significant increase in induction of 8-OH-dG, Ha-*ras* mutations or epidermal hyperplasia. It was considered that this finding in isolation is an insufficient index of carcinogenic potential.

Based on the toxicological data provided the notified chemical would not be classified as a hazardous substance under the *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No ecotoxicity studies were performed on the notified chemical. However, toxicity tests for the analogue TBEC using fish and sewage sludge bacteria have been conducted and copies of summary draft reports were supplied by the notifier.

Test	Species	Results (Nominal)
Acute Toxicity against Fish OECD TG 203	Guppy *Poecilia reliculata*	LC_{50} (96 h) = 8.66 mg/L NOEC = 2.1 mg/L
Activated Sludge Respiration Inhibition OECD TG 209	Sewage Bacteria	EC_{50} (30 minutes) = 64 mg/L

Fish

The fish test was conducted using semi-static methodology (48-hour renewal of test media) at 24-25°C over a 96-hour test period. Test media were prepared at nominal concentrations of the test material of 0 (control), 1.0, 2.1, 4.6, 10.0 and 21.0 mg/L using acetone as a co-solvent, and stirring for 24 hours prior to commencement of the tests. The test media so prepared were clear and showed no signs of undissolved material.

No fish mortality was observed over the 96-day period at 1.0 and 2.1 mg/L whereas 100% mortality was observed after 72 hours exposure to 21 mg/L. No sub lethal behavioural or physical effects were observed. The oxygen concentration was usually > 60% saturation, except for the nominal 10.0 mg/L where it was slightly lower. The actual concentrations of the test compound were apparently measured, although these were not reported in the summary report provided. The data were analysed to provide the 96-hour LC_{50} value of 8.66 mg/L and No Observed Effect Concentration (NOEC) of 2.1 mg/L.

These results suggest that the notified chemical is moderately toxic to guppies.

Sewage bacteria

The test on respiration inhibition of sewage bacteria by TBEC was apparently conducted by coating silica gel with a known amount of test material dissolved in dichloromethane, and allowing the solvent to evaporate. Different weights of the "loaded" silica gel were then added to aliquots of the sewage inoculum to provide nominal concentrations of the test substance (range not indicated in the summary report). The inoculum containing the silica gel was aerated for 30 minutes and the rate of oxygen uptake in each test system measured and compared with that in a system containing no test compound (ie. no loaded silica). The results of this test were analysed to provide an EC_{50} (ie. the nominal concentration of test material producing 50% inhibition of respiration compared with the control) of 64 mg/L with 95% confidence limits 15.7-117.0 mg/L. There appeared to be a high degree of uncertainty in respect of the test substance concentration and it was stated in the report that "Test compound does not remain in solution", although no further elaboration was offered.

The results indicate that the compound exhibits some toxic effects on the respiration of sewage bacteria.

QSAR Estimated toxicities

The notifier also supplied some estimated toxicities based on QSAR for the notified chemical. The calculations were based on the calculated value of log P_{ow} using the ECOSAR program through the relations appropriate for peroxyacids/peroxides as follows:

Acute toxicity against fish
$\log LC_{50}$ (96 h) = -3.037 + 0.122 $\log P_{ow}$,

and

Acute toxicity against *daphnia*
$\log LC_{50}$ (48 h) = -0.575 - 0.415 $\log P_{ow}$,

with the derived LC_{50} values expressed as mmole/L.

Using the QSAR estimated value for log P_{ow} of 4.8, the equations estimate 96-hour LC_{50} for fish (species not specified) as 0.81 mg/L and the 48-hour LC_{50} against *daphnia* as 0.62 mg/L.

In so far as the fish toxicity estimate can be compared with that actually measured for the guppy (LC_{50} = 8.6 mg/L), the agreement is within an order of magnitude. In respect of this, the QSAR estimates for toxicity are critically dependent on the value of log P_{ow} used, and since this was itself estimated through a QSAR, agreement between the estimated and measured results of an order of magnitude is reasonable.

A chronic 14-day toxicity estimate for fish was also calculated as 1.13 mg/L.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

If any of the notified chemical were released to the soil or water compartments as a consequence of accidental spills, it would be adsorbed by the soil. However, the compound would be rapidly decomposed to carbon dioxide, t-amyl alcohol and 2-ethyl hexanol, or possibly a carboxylic acid derived from 2-ethyl hexanol. These alcohols are volatile and once released to the air compartment would be decomposed through reaction with hydroxyl radicals, producing water and carbon dioxide.

Although likely to be toxic to aquatic organisms (LC_{50} against guppy measured as 8.6 mg/L) and slightly toxic to sewage bacteria (EC_{50} determined as 64 mg/L), the notified chemical if released into the water compartment (considered unlikely), is expected to undergo rapid decomposition to t-amyl alcohol and 2-ethyl hexanol catalysed by traces of ferrous/ferric ions. These two compounds are at worst slightly toxic to aquatic organisms (Verschueren, 1996) with the LC_{50} for 2-ethyl hexanol against rainbow trout cited as 32-37 mg/L. It is unlikely that they would reach significant concentrations in the environment as a result of breakdown of the notified chemical. Also they are slightly volatile and once released to the air compartment would decompose through reaction with hydroxyl radicals.

While the notified chemical may have potential for bioaccumulation, it is not expected to persist in the environment, so the possibility for bioaccumulation will be reduced.

The environmental hazard from the notified chemical is considered to be small when it is used as a catalyst for emulsion polymerisation in the manner indicated by the notifier.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment

The notified chemical is of very low acute oral and low acute dermal toxicity in rats and rabbits, respectively. The analogue TBEC exhibited low acute inhalation toxicity in rats (4-hour LC_{50} = 42.2 mg/L) according to the MSDS for the notified chemical. It is not an eye irritant but is slight to moderate skin irritant in rabbits. TBEC is not a skin sensitiser in guinea pigs.

TBEC in a repeat dose oral toxicity study in rats, exhibited treatment related changes to the stomach mucosa at 1 000 and 550 mg/kg/day. The NOAEL was established at 150

mg/kg/day based on the absence of treatment related effects at this dose.

The notified chemical displayed mutagenic activity in a bacterial reverse mutation assay, but TBEC exhibited no genotoxic activity *in vivo* in a mouse micronucleus test.

TBEC was investigated in a four week repeat dose dermal study for its ability to produce DNA damage and sustained epidermal hyperplasia in mouse skin. It increased dermal cellularity, however, there was no significant increase in induction of 8-OH-dG, Ha-*ras* mutations or epidermal hyperplasia. It was considered that this finding in isolation is an insufficient index of carcinogenic potential.

Based on the data supplied the notified chemical would not be classified as a hazardous substance under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999).

The notified chemical is classified as a Dangerous Good - Organic Peroxide - Class 5.2 under the *Australian Code for the Transport of Dangerous Goods by Road and Rail*. In addition it is subject to Australian Standard AS2714-1993 *The Storage and Handling of Hazardous materials – Class 5.2 Substances (Organic Peroxides)* (Standards Australia, 1993).

Occupational Health and Safety

Transportation of the notified chemical will be in accordance with the *Australian Code for the Transport of Dangerous Goods by Road and Rail*. During import and transport of the notified chemical, there is unlikely to be any worker exposure, except in the event of a spill. In addition, drivers of vehicles of dangerous goods are trained in emergency procedures. Exposure after a spill of organic peroxide would be controlled by using the emergency procedures described in the *Initial Emergency Response Guide Number 32* (Standards Australia, 1997).

The notified chemical is transported to a single customer site for use in a purpose built reactor for the production of acrylic polymers. It is transported to this site on a just in time basis for production of batches using a full pack of the chemical. If there is a delay the chemical will be placed into an existing peroxide store for periods of up to 3 days. Storage is at less than 10°C to avoid self-accelerating decomposition which occurs at 45°C and may generate flammable vapours which could autoignite. For transport and storage workers, this appears to be the main health risk as the chemical is not classified as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999).

Laboratory testing involves small amounts of the notified chemical and reactions are conducted inside a fume hood. Laboratory workers wear laboratory coat, safety shoes, safety glasses and rubber gloves to control exposure and the risk of adverse health effects is low.

The notified chemical is manually added to a weigh vessel which automatically feeds the main reactor. This is performed under local exhaust ventilation so that inhalation exposure is controlled. However, dermal exposure is possible during this addition and during rinsing of the container with solvent. Workers wear overalls, safety boots, goggles and gloves during transfer operations to limit exposure. Therefore, the risk of adverse health effects is low. Once the chemical has been added to the weigh vessel it is in an enclosed system. Exposure

is possible in the event of a runaway reaction in the reactor but a range of engineering controls are in place for this eventuality. The notified chemical in incorporated into a polymer at a maximum concentration of 2% so the health risk for any workers coming into contact with the notified chemical at this stage is negligible.

The polymer produced using the notified chemical is subsequently blended into coatings for use on metal substrates. The health risk to workers coming into contact with the notified chemical in these coatings is no greater than that for the polymer itself, which as noted above is negligible.

Public Health

The notified chemical and any subsequent polymer solutions or paint products will be used in industry only. The public will come in contact with the notified chemical only after paint products have been applied to metal substrates to form a coating film. The notified chemical in the paint film will not be available for absorption and the public health risk is negligible.

13. RECOMMENDATIONS

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

- The storage and handling of the notified chemical and other organic peroxides to be in accordance with Australian Standard 2714-1993 *The Storage and Handling of Hazardous Chemicals and Materials* (Standards Australia, 1993).

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.1 (Standards Australia, 1990); impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia, 1998); all occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994);

- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;

- A copy of the MSDS should be easily accessible to employees.

The transportation of the notified chemical and other organic peroxides to be in accordance with the *Australian Code for the Transport of Dangerous Goods by Road and Rail*.

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, 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

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

16. REFERENCES

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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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