File No: NA/710

April 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

OO-tert-butyl O-(2-ethylhexyl) monoperoxycarbonate

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

OO-tert-butyl O-(2-ethylhexyl) monoperoxycarbonate

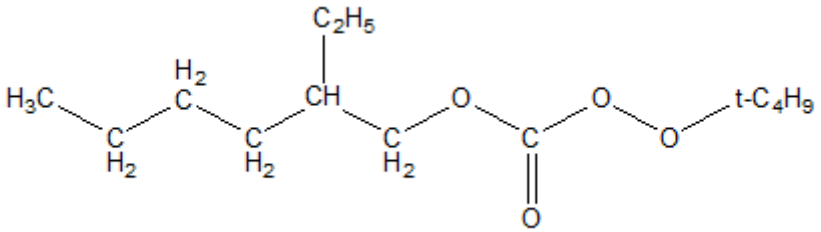
1. APPLICANT

Elf Atochem (Australia) Pty Ltd of 270-280 Hammond Road, DANDENONG SOUTH VICTORIA 3175 has submitted a standard notification statement in support of their application for an assessment certificate for 'OO-tert-butyl O-(2-ethylhexyl) monoperoxycarbonate'.

2. IDENTITY OF THE CHEMICAL

Details on the specific use, import volume and reaction conditions have been exempted from publication in the Full Public Report and the Summary Report.

Chemical Name:	OO-tert-butyl O-(2-ethylhexyl) monoperoxycarbonate
Chemical Abstracts Service (CAS) Registry No.:	34443-12-4
Other Names:	Carbonperoxoic acid, OO-(1,1-dimethylethyl) O-(2-ethylhexyl) ester
Marketing Names:	LUPEROX TBEC, LUPERSOL TBEC
Molecular Formula:	$C_{13}H_{26}O_4$
Structural Formula:	



Molecular Weight:	246.3
Method of Detection and Determination:	Fourier Transform InfraRed (FTIR)
Spectral Data:	IR Major absorbance peaks (approximate): 3 000, 2 900, 2 800, 1 600, 1 400, 1 300 1 200 cm^{-1}

Comments on Chemical Identity

The notified chemical is an organic peroxide which decomposes to free radicals under appropriate conditions. In the present case, the chemical is expected to decompose to a variety of free radicals which may include such species such as the t-butoxy radical [$(CH3)_3CO\bullet$], and the resultant free radicals are effective initiators for the polymerisation of olefins, for example in the production of polyethylene and polystyrene. The decomposition is promoted by elevated temperatures, and for the intended use in production of addition polymers, an ambient reaction temperature of 50 to 100°C was indicated in the notification. The radicals are consumed in the reactions, and become incorporated into the polymer, probably at the ends of the polymer chains.

Apart from thermally initiated decomposition, organic peroxides are inherently thermodynamically unstable, and their rapid decomposition (sometimes explosively) is initiated by a variety of compounds, including ferrous ions, which are ubiquitous in industrial and natural environments.

The company provided an infrared spectrum, which serves to identify the notified chemical.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Light yellow liquid with fruity odour.
Boiling Point:	< -60°C
Specific Gravity at 25°C:	0.927
Vapour Pressure at 20°C:	0.133 kPa (estimated, see comments below)
Water Solubility at 25°C:	2.6 mg/L (estimated, see comments below)
Particle Size:	Not applicable to the liquid
Partition Co-efficient (n-octanol/water):	Log Kow = 4.66 (estimated, see comments below)
Hydrolysis as a Function of pH:	Not determined
Adsorption/Desorption at 20°C:	Log Koc = 3.62 (estimated, see comments below)

Dissociation Constant:	Not determined
Flash Point:	104°C (open cup)
Flammability Limits:	Upper and lower explosive limit not determined as vapour pressure is negligible
Autoignition Temperature:	>75°C
Explosive Properties:	Unstable – see comments below
Reactivity/Stability:	Activation energy 131.8 kJ/mole

Comments on Physico-Chemical Properties

All the physico-chemical data provided was derived from model calculations using the ECOSAR program (US EPA) through appropriate Quantitative Structure Activity Relationships (QSAR's). The assessment accepts 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 K_{ow} and Log K_{oc} are in accord with the high hydrocarbon content of the new chemical. These data indicate that if the notified chemical was stable, it would partition into oil and fat, and if released to soil would bind to and become associated 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 (atm) x Molecular weight (g/mole)/Water solubility (g/L)

The notified chemical contains a peroxycarbonate linkage which could be susceptible to hydrolysis. However, the peroxide group is highly reactive, and in an aqueous environment the chemical would be more likely to decompose to t-butanol, 2-ethyl hexanol and carbon dioxide through reactions of the peroxide group rather than undergo hydrolytic cleavage.

The notified chemical contains no acidic of basic groups, so the dissociation constant is not relevant.

The notified chemical is an organic peroxide and is unstable. Exposure to heat, flames, sparks, ignition sources and contamination will increase its instability and contact with strong acids, alkalis, oxidisers and reducing agents will cause violent reactions. The decomposition products of the notified chemical are flammable. The self accelerating decomposition temperature is measured at 75°C.

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* (FORS, 1998).

4. PURITY OF THE CHEMICAL

Degree of Purity: >95%

Hazardous Impurities:

Chemical name:	2-ethyl hexanol
CAS No.:	104-76-7
Weight percentage:	1-3%
Toxic properties:	Moderate eye and skin irritant. (Gangolli, 1999)
Chemical name:	Isobutanol
CAS No.:	75-65-0
Weight percentage:	0-0.1%
Toxic properties:	R11: Highly flammable; R20: Harmful by inhalation (NOHSC, 1999b)
Chemical name:	t-butyl hydroperoxide
CAS No.:	75-91-2
Weight percentage:	0-0.5%
Toxic properties:	Harmful by inhalation, in contact with skin and if swallowed; Moderate to severe skin irritant; Severe eye irritant; *In vitro* clastogen in Chinese Hamster Ovary cells. (Gangolli, 1999)
Chemical name:	Hydrolyzable chlorides
Weight percentage:	0-0.1%
Chemical name:	Unidentified impurities
Weight percentage:	1-2%

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

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical will not be manufactured in Australia, but will be imported by sea in 25 L polyethylene jerry cans and delivered to the customer site. The notified chemical will be used as an initiator in the production of addition polymers at the customers plant in Victoria.

The estimated import volume of the notified chemical is less than 50 tonnes per annum over the next five years.

The notified chemical has been in use in Australia during 1999 under a NICNAS Commercial Evaluation permit granted under section 21G of the Act.

6. OCCUPATIONAL EXPOSURE

Transport and Storage
The notified chemical will be imported in 25 L polyethylene jerry cans. Transportation will be in accordance with the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (FORS, 1998). Occupational exposure is not expected except in the event of a spill.

At the customer site the storage and handling of the notified chemical is in accordance with AS2714-1993 *The Storage and Handling of Hazardous Materials – Class 5.2 Substances* (*Organic Peroxides)* (Standards Australia, 1993).

Polymerisation Reaction: (five Reactor Operators; less than 10 minutes/day, 200 days/year)
The reactor operator manually pours the full contents of the jerry cans (notified chemical) into water contained in a "slurry" tank fitted with an agitator. The emptied containers are thoroughly rinsed with water and the rinsings poured into the slurry tank. The container is then perforated and disposed of into a hazardous waste bin. Smaller volumes are poured into a dedicated plastic bucket on weigh scales and charged to the slurry tank. The notifier indicated that spillages during pouring are unlikely as the material is poured slowly from a narrow opening into a much larger opening on the slurry tank or bucket. The plastic bucket is then thoroughly rinsed with water and the rinsings poured into the slurry tank. Charging takes approximately five minutes per batch. Less than five batches may be charged per day.

The notified chemical/water mixture is agitated and pumped via a closed pipeline into the sealed reactor, containing other polymerisation ingredients (50 to 100°C). The reactor is then heated to the polymerisation initiation temperature (50 to 100°C). During the initial stages of polymerisation the reactor contents are examined for bead size; operators use a long handled scoop to collect 25 mL samples via a sampling port on the top of the reactor. The notified chemical is present at less than 1%. The sample hole is open to atmosphere for

approximately one minute each time.

Local exhaust ventilation is positioned at the reactor sample point. The notifier states that personal respiratory protection equipment is not normally required during sampling.

The notified chemical is decomposed and consumed during the polymeristaion process, so there are no further implications for occupational exposure.

Control Measures
The notifier indicated that workers charging the reactor or cleaning up spills, wear impervious rubber or PVC gloves and chemical splash goggles or full face shield in addition to their normal overalls, long-sleeved shirt, safety boots and hard hat, to prevent eye and skin contact. Personal respiratory protection equipment is not normally required.

Education and Training
All workers receive education and training in company and regulatory requirements, dangerous goods transport, storage and handling, hazard identification, incident reporting and investigation, interpretation of MSDS and labels, risk assessment, monitoring, control measures, emergency response, selection, use and maintenance of personnel protective equipment, personal hygiene practices and health surveillance.

Adverse Health Effects Reporting
The user company reports no adverse health effects from the use of organic peroxides both in Australia or overseas.

7. PUBLIC EXPOSURE

There is limited potential for exposure of the public to the notified chemical. The notified chemical is used in a sealed reactor and all of the notified chemical is expected to be consumed during reaction. Environmental sources of the notified chemical are also unlikely because release of the chemical is expected to be very low and the notified chemical is likely to be rapidly decomposed.

8. ENVIRONMENTAL EXPOSURE

Release

Minimal release during charging of the slurry tank is expected, and any spills and splashes of the notified chemical would most likely be diluted with water and combined with the overall liquid waste stream within the plant. The notifier indicated that overall liquid waste generated from the plant that will use the chemical is 12.3 ML per annum, which is comprehensively treated before being released into the Melbourne (City West) sewer system. Any spillage of the notified chemical would be substantially diluted before discharge. Also, the compound is highly reactive and would very likely be decomposed to 2-ethyl hexanol and t-butanol prior to release to sewer.

Submitted information[1] indicated that the slurry preparation tank is a closed vessel with a vapour return line to the reactor vapour space. This and other engineering controls minimise releases of gases and vapours to the atmosphere.

Apart from accidents, very little release of the chemical is expected during addition to the slurry tank 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 incorporated into the polymer, so little release of decomposition products is expected.

Fate

All of the notified chemical is consumed during polymerisation and becomes incorporated into the polymer chains. There is little likelihood of release of the chemical, except in the case of accidents, when chemical would be expected to be rapidly decomposed through rupture of the peroxide bonds. The decomposition products would most likely be carbon dioxide and the two alcohol species indicated above. It should be appreciated that the rapid decomposition of organic peroxides is effectively catalysed through ferrous ions, which are invariably present in soils and natural waters. The decomposition products are likely to be decomposed through photodegradation reactions with atmospheric hydroxy radicals.

The high Log K_{oc} indicates that chemical accidentally released to soil would become bound to the organic component. The notified chemical is unlikely to be mobile in the soil compartment and would decompose rapidly through reaction of the peroxide group.

Small neutral compounds with high Log K_{ow} and low water solubility have potential for bioaccumulation (Connell, 1990). Consequently, the notified chemical could potentially bioaccumulate if it persisted in the environment. However, the inherent instability of the chemical indicates it is not persistent so bioaccumulation is very unlikely.

The notifier supplied some calculated data on biodegradation rates, indicating 50% probability of rapid biodegradation with a half life of approximately 3.5 days. However, these calculations are appropriate to the peroxy compound itself, and as indicated above this compound is expected to rapidly degrade through chemical processes to t-butanol and 2-ethylhexanol.

[1] Works Approval Application for new plant (March 1998) submitted by the customer to the Victorian EPA.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of OO-tert-butyl O-(2-ethylhexyl) monoperoxycarbonate

Test	*Species*	*Outcome*	*Reference*
Acute oral toxicity	Rat	LD_{50}>5 000 mg/kg	(Food and Drug Research Laboratories Inc, 1985c)
Acute dermal toxicity	Rat	LD_{50}>2 000 mg/kg	(Food and Drug Research Laboratories Inc, 1985a)
Skin irritation	Rabbit	Slightly irritating	(MB Research Laboratories, 1999b)
Eye irritation	Rabbit	Very slightly irritating	(Food and Drug Research Laboratories Inc, 1985b)
Skin sensitisation	Guinea pig	Non-sensitising	(Centre International de Toxicologie, 1999)

9.1.1 Oral Toxicity (Food and Drug Research Laboratories Inc, 1985c)

Species/strain:	Rat/Sprague-Dawley.
Number/sex of animals:	5/sex.
Observation period:	15 days.
Method of administration:	5 000 mg/kg body weight by gavage
Test method:	EPA Health Effects Test Guidelines (August, 1982).
Mortality:	No deaths were recorded over the observation period.
Clinical observations:	There were no signs of systemic toxicity.
Morphological findings:	No abnormalities were detected.
Comment:	There were no adverse effects on bodyweight gain over the observation period.
LD_{50}:	> 5 000 mg/kg.
Result:	The notified chemical was of very low acute oral toxicity in rats.

9.1.2 Dermal Toxicity (Food and Drug Research Laboratories Inc, 1985a)

Species/strain:	Rabbit/New Zealand White.
Number/sex of animals:	5/sex.
Observation period:	15 days.
Method of administration:	A single dose of 2 000 mg/kg of test substance was applied under occlusive conditions to the shorn dorsal skin of each animal for a period of 24 hours.
Test method:	EPA Health Effects Test Guidelines (August, 1982).
Mortality:	No deaths were recorded over the observation period.
Clinical observations:	Anorexia, diarrheoa, nasal discharge or soft stools was reported in some male and female rabbits.
Morphological findings:	No abnormalities were detected.
Comment:	There were no adverse effects on bodyweight gain over the observation period.
LD_{50}:	> 2 000 mg/kg.
Result:	The notified chemical was of low dermal toxicity in rats.

9.1.3 Inhalation Toxicity

Claims were made and accepted for a waiver to the Schedule requirement for an acute inhalation study. The notifier stated that an inhalation toxicity study was not conducted because of the negligible vapour pressure of the notified chemical, in addition to it being a viscous liquid at room temperature and potential for inhalation toxicity due to aerosols is considered to be insignificant.

9.1.4 Skin Irritation (MB Research Laboratories, 1999b)

Species/strain:	Rabbit/New Zealand white
Number/sex of animals:	3 females
Observation period:	7 days
Method of administration:	A dose of 0.5 ml of test substance placed on the dorsal surface of each animal under semi-occlusive conditions. After 24 hours, the test substance was removed by gentle washing, prior to scoring for dermal reactions.
Test method:	OECD TG 404

Draize scores:

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

[a] see Attachment 1 for Draize scales. *flaking skin.

Mean scores (24, 48, 72 hour observation) for individual animals

Erythema: 1, 2, 0.33;
Oedema: 0.33, 1.33, 0.

Comment:

One animal had slight erythema and barely perceptible oedema on day 7. There were no abnormal physical signs noted during the observation period. One animal lost weight at the 72 hour scoring interval. All other body weights were normal.

Result:

The notified chemical was slightly irritating to the skin of rabbits

9.1.5 Eye Irritation (Food and Drug Research Laboratories Inc, 1985b)

Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	6 (sex not specified)
Observation period:	3 days
Method of administration:	A single ocular dose of 0.1 mL of test substance instilled into one eye of each animal; The other eye served as control.
Test method:	FDA (21 CFR Part 58; 16 CFR 1500; FDRL Standard Operating procedures)
Comment:	One animal had conjunctival redness and discharge (score =1 in both cases) while another had a similar grade of redness without discharge at the 24 hour observation period
Result:	The notified chemical was very slightly irritating to the eyes of rabbits.

9.1.6 Skin Sensitisation (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:	<u>Test Animals</u> 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. <u>Control Animals</u> 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 notified chemical was considered non-sensitising to the skin of guinea pigs.

9.2 Repeated Dose Toxicity (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 (Pharmakon Research International, 1989)

Strains:	*Salmonella typhimurium* TA1535, TA1537, TA1538, TA98 and TA100
Metabolic activation:	6% rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors
Concentration range:	All concentrations were tested in triplicate. Experiment 1: with and without S9 0, 167, 500, 1 670, 5 000, 7 500, 10 000 μg/plate. Experiment 2: with S9 0, 5, 16.7, 50, 167, 500 1 000 and 1 670 μg/plate.
Test method:	OECD TG 471; US EPA Federal register (Vol. 48, No. 230, November 29, 1983)
Comment:	Experiment 1: The test substance was insoluble at concentrations ≥ 1670 μg/plate. There was evidence of toxicity at 10 000 μg/plate without S9 and at doses of ≥ 500 and/or 1670 μg/plate with S9. There were statistically significant increases in mutant colonies, to approximately 3.0-, 1.8- and 3.6-fold control values in TA1537, TA98 and TA100, respectively, at doses of 167 and/or 500 μg/plate with S9. Experiment 2: Toxicity was again observed at doses of ≥ 500 μg/plate.

Statistically significant increases in mutant colonies, to approximately 1.8- and 2.2-fold those of the control values, were observed in TA98 and TA100, respectively, at doses up to 500 μg/plate.

All strain-specific positive control mutagens responded appropriately.

Result: The notified chemical was considered to be mutagenic under the conditions of the assay.

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (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 notified chemical 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 the notified chemical) and hydrogen peroxide to produce DNA damage (8-OH-dG formation), Ha-*ras* mutations and sustained epidermal hyperplasia and dermal cellularity. The notified chemical at 0, 10, 100 or 200 µmol was applied topically, twice weekly for 4 weeks to Virgin Senecar female mice (10 animals per dose group for histological investigations and 5 mice per group each for DNA damage and Ha-*ras* mutation induction). The notified chemical 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 demonstrated very low acute oral toxicity and low dermal toxicity in rats (LD_{50} > 5 000 mg/kg and LD_{50} > 2 000 mg/kg, respectively). No inhalation toxicity study was conducted because of the low vapour pressure of the notified chemical and, being a viscous liquid at room temperature, there is little potential for inhalation of aerosols.

In a skin irritation study with three rabbits, there was evidence of erythema and oedema, which was more persistent in one of the animals, still being present to a very slight extent at day 7. The notified chemical was therefore considered to be a slight skin irritant, but the mean scores for skin lesions were below the threshold for classifying the notified chemical as an irritant. In an eye irritation study, very slight conjunctival redness seen in a small number of animals had resolved by 48 hours and, on this basis, the notified chemical was considered to be a very slight irritant to the rabbit eye.

A skin sensitisation study 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, the notified chemical was not considered to have sensitising potential.

A 28-day repeated dose study in rats 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.

There was evidence of *in vitro* mutagenic activity in *Salmonella typhimurium.* In the first experiment (with and without S9), there were statistically significant increases in mutant colonies, to approximately 3.0-, 1.8- and 3.6-fold control values in TA1537, TA98 and TA100, respectively, at doses of 167 and/or 500 μg/plate with S9. In a repeat experiment (with S9), statistically significant increases in mutant colonies, to approximately 1.8- and 2.2-fold those of the control values, were observed in TA98 and TA100, respectively, at doses up to 500 μg/plate. The *in vitro* mutagenic activity, however, was not reproduced in the *in vivo* mouse micronucleus assay, where the notified chemical failed to induce a statistically significant increase in the number of micronucleated polychromatic erythrocytes. There was therefore insufficient evidence to classify the notified chemical as a mutagen.

The notified chemical was investigated in a four week repeat dose dermal study for its ability to produce DNA damage and sustained epidermal hyperplasia in mouse skin. The notified chemical increased dermal cellularity but the cell types increased 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.

Hazard Classification:
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* (NOHSC, 1999a).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No ecotoxicity studies were performed. The unstable nature of the compound would have made the acquisition of reliable toxicity data difficult. However, the notifier did provide some estimated toxicity data for fish and daphnia. This data was calculated using QSAR and is tabulated below.

Calculated Ecotoxicity Data:

Test	*Species*	*Results (Nominal)*
Acute Toxicity	Fish	LC_{50} (96 h) = 0.84 mg/L
Acute Toxicity	Daphnia	LC_{50} (48 h) = 0.76 mg/L

The calculations were based on the (calculated) value of Log K_{ow} using the ECOSAR program through the relations –

Log LC_{50} (96 h) = -3.037 + 0.122 Log Kow for fish, and
Log LC_{50} (48 h) = -0.575 - 0.415 Log Kow for daphnia,

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

These data indicate that the new compound is likely to be highly toxic to fish and invertebrates, and although no estimates were provided, could also be expected to be toxic to algae. However, as discussed above the high reactivity of the peroxide group dictates rapid decomposition of the compound in natural waters, and consequently the chemical would not persist in the environment. This will mitigate the potential toxicity.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

If any of the notified chemical were released to the soil or water compartment as a consequence of accidental spills, it would be adsorbed by the soil but would rapidly decompose to carbon dioxide, t-butanol and 2-ethylhexanol, or possibly 2-ethylhexyl carbonic acid.

The alcohols are volatile and once released to the air compartment would decompose through reaction with hydroxyl radicals to produce water and carbon dioxide.

Although the notified chemical is likely to be highly toxic to aquatic organisms, in the unlikely event of release into the water compartment it is expected to undergo rapid decomposition catalysed by traces of ferrous/ferric ions, to t-butanol and 2-ethylhexanol. These two compounds are at worst slightly toxic to aquatic organisms (Vershuer, 1996) with the LC_{50} for 2-ethylhexanol against rainbow trout cited as 32-37 mg/L. In any case, it is unlikely that the compounds would reach significant concentrations in the environment from breakdown of the notified chemical. Also, the compounds would decompose in air through reaction with hydroxyl radicals.

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

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

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical is of very low acute oral and low acute dermal toxicity in rats. It is not a skin sensitiser, but it is a very slight eye and slight skin irritant. Acute inhalation studies were not carried out on the basis that the notified chemical has low vapour pressure and is a viscous liquid and therefore unlikely to present as a significant inhalation hazard.

In a repeat dose oral toxicity study in rats, treatment related changes to the stomach mucosa were observed at 1 000 and 550 mg/kg/day. The NOAEL is 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 no genotoxic activity was observed *in vivo* in a mouse micronucleus test.

The notified chemical was investigated in a four week repeat dose dermal study for its ability to produce DNA damage and sustained epidermal hyperplasia in mouse skin. The notified chemical 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.

The notifier states that the notified chemical is in use in Europe and the USA with no adverse health effects reported. Furthermore, no adverse effects have been reported during its use in Australia under a Commercial Evaluation permit.

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* (NOHSC, 1999a).

The notified chemical is classified as a Dangerous Good - Organic Peroxide - Class 8.2 under the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (FORS, 1998). 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* (FORS, 1998). During import and transport of the notified polymer, there is unlikely to be any worker exposure, except in the event of a spill. The small pack sizes (25 kg) and transport regulations would minimise the likelihood of exposure. In addition, drivers of vehicles of dangerous goods are trained in

emergency procedures. Exposure after a spill of organic peroxide would be controlled by the emergency procedures described in the *Initial Emergency Response Guide Number 32* (Standards Australia, 1997).

The notifier states that the storage and handling of the notified chemical and other organic peroxides used at customer sites is in accordance with AS2714-1993 *The Storage and Handling of Hazardous materials – Class 5.2 Substances (Organic Peroxides)* (Standards Australia, 1993). During its use as an initiator in the production of addition polymers, inhalation exposure to the notified chemical is expected to be negligible, because of the low volatility, low frequency and duration of exposure opportunities, during charging and reactor sampling, in addition to local exhaust ventilation. Skin and eye contact and therefore the risk of irritation will be minimised by the wearing of safety goggles, long PVC or rubber gloves and protective clothing. Under the described conditions of use and regulations on the storage, handling and transport of organic peroxides and worker education and training, the risk of adverse health effects from occupational exposure to the notified chemical is expected to be negligible.

Public Health
The notified chemical will be used in a sealed reactor, will not be available to the public, is not expected to be present in finished products and environmental releases of the notified chemical are expected to be very low. Therefore, there is negligible potential for public exposure to the notified chemical arising from its use as an initiator in polymerisation reactions. Based on the toxicity profile and use pattern of the notified chemical, it is considered that the notified chemical will not pose a significant hazard to public health.

13. RECOMMENDATIONS

To minimise occupational exposure to OO-tert-butyl O-(2-ethylhexyl) monoperoxycarbonate 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;

- Good personal hygiene should be practised to minimise the potential for ingestion;
- 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* (FORS, 1998).

If the conditions of use are varied, greater exposure of the public to the product may occur. In such circumstances, further information may be required to assess the hazards to public health.

14. MATERIAL SAFETY DATA SHEET

The MSDS for OO-tert-butyl O-(2-ethylhexyl) monoperoxycarbonate 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

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.
		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