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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME
(NICNAS)

FULL PUBLIC REPORT

Durasyn 164X

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health and Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment, Water, Heritage and the Arts.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

This Full Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

Street Address:	334 - 336 Illawarra Road MARRICKVILLE NSW 2204, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Amochem Pty Ltd (ABN 48 095 713 269)
40 Myrna Road, STRATHFIELD NSW 2135

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Chemical Name, CAS Number, Other Names, Molecular Formula, Structural Formula, Molecular Weight, Spectral Data, Purity, Identity and % weight of toxic or hazardous impurities, Identity of non-hazardous impurities, Identity and % weight of additives/adjuvants, Import Volume, Identity of Reformulating Sites

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Water Solubility, Hydrolysis As A Function of pH, Adsorption/Desorption, Flammability, Autoignition Temperature, Explosive Properties, Reactivity, Acute Oral Toxicity, Acute Dermal Toxicity, Acute Inhalation Toxicity, Skin Irritation, Eye Irritation, Skin Sensitisation, Introduction of Point Mutations, Induction of Germ Cell Damage, Chromosome Damage, Acute Fish Toxicity, Acute Daphnia Toxicity, Acute Algal Toxicity, Bioaccumulation

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA (2007), Canada (2008)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Durasyn 164X
Alpha olefin oligomers, hydrogenated

ANALYTICAL DATA
Reference Proton NMR, Carbon NMR and FTIR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 90%

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported in 200 L closed-head steel drums or shipped in bulk in iso-containers.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	30 - 100	30 - 100	30 - 100	30 - 100	30 - 100

USE
The proposed use of the notified chemical is as a base fluid for the blending of fully formulated synthetic automotive and industrial lubricants, including the formulation of automotive crankcase (motor) oils, transmission fluids, and industrial gear oils at 5-90% of the product. The finished lubricants will be used in industrial, commercial and consumer applications.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
Amochem Pty Ltd
40 Myrna Road
Strathfield NSW 2135

TRANSPORTATION AND PACKAGING
The notified chemical will be transported by ship in either 200 L robust UN approved steel drums, in bulk iso-containers or in 1000 L totes (IBCs). Based on expected volumes and package sizes, the notified chemical is expected to be primarily transported from the dockside to the customer or contract warehouse via trucks, but rail transport may be possible. The notified chemical is then stored until required for despatch to customers. The notified chemical will be distributed to numerous blending premises around Australia, with the number of blending sites expected to be between 6 and 15. The finished lubricant may be packaged in drums (200 L) or bottles (1 L or bigger). Packaging into bottles is usually automated.

The product is not classified as a dangerous good for transport, therefore there are no special storage or transport requirements.

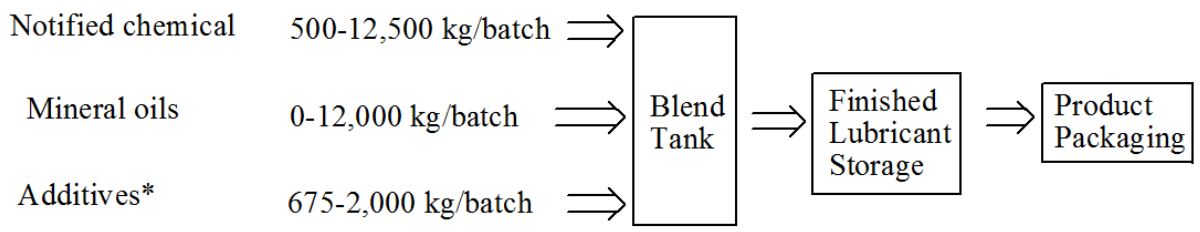
5.2. Operation description
Formulation of lubricants will occur at blending facilities of major lubricant manufacturers.

The notifier does not formulate lubricants and will only provide the notified chemical (i.e., the PAO (Polyalphaolefins) base fluid) to these manufacturers. However, there are certain steps that characterise all operations used to blend full synthetic oils (where only PAO or other synthetic fluids are used as the base fluid) or partial synthetic oils (where mixtures of PAO and mineral oil are used).

Blending occurs in an enclosed blending vessel ("kettle") with appropriate nitrogen blanketing, overflow protection, and vapour capture. The notified PAO is pumped from an appropriate storage tank, via hard piping, into the blending kettle where it is heated to 65°C (± 5°C).

The blended lubricant is pumped via hard piping to a finished lubricant storage tank for subsequent packaging.

Lubricant Blending Operation Process Flow Diagram – Automotive or Industrial



*Additives can include one or more of the following – viscosity index improvers, dispersants, antioxidants, corrosion inhibitors, anti-wear additives, pour point depressants, and anti-foaming agents.

The diagram shows typical quantities of components used per batch in a closed blending operation for the preparation of automotive or industrial lubricants. The scale of operation may vary significantly depending on the size of the company preparing the finished lubricant. Depending on the end-use application of the lubricant, variance on either the high or low end of these ranges could occur.

Summary of use of Durasyn 164X			
Type of use	Automotive crankcase oils	Industrial gear oils	Transmission oils
Percentage of market (%)	50	30	20
Concentration range (%)	5-50	50-90	50-80
Distribution			
Commercial outlets (%)	80	10	80
Industrial plants (%)	10	85	10
Consumers (%)	10	5	10

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Transport and Storage	10 – 30	30 minutes/day	100 days per year
Sampling	5 – 30	30 minutes/day	50 days per year
Maintenance	10 – 20	3 hours/day	20 days per year
Blending operations	5 – 30	8 hours/day	200 days per year
Cleaning	5 – 30	30 minutes/day	200 days per year
Industrial end users	high	1hr/day	50 days per year

Exposure Details

Dockside and Transport

Occupational exposure is not expected except in the case of a spill. Typical PPE worn by workers would be industrial standard overalls, eye protection and rubber /PVC gloves.

Blending

While the blending of lubricants is a highly automated and enclosed process, there is some potential for exposure of workers involved in blending operations using the notified chemical. However, typical blending facilities are designed to minimise exposures to employees and are generally well ventilated and have accidental spill containment and wastewater treatment systems in place.

Except for the collection of process samples for quality control and bottle filling, all handling of notified chemical is expected to be through closed piping.

Occupational exposure is possible in the event of a spill. Skin contact is possible by accidental contact with drips. Eye contact with the notified chemical may occur from leaks or splashes. Inhalation of the notified chemical is possible if heating causes volatilisation however considering the enclosed nature of the blending operation this is not likely to be significant. Ventilation systems are in place to guard against this possibility of aerosols being formed.

Potential exposures during activities such as sampling will be controlled and be of short duration. Protective equipment to be worn during periods where exposures are likely to occur includes impervious gloves and work clothing, and eye protection. Respiratory protection will be worn if there is potential inhalation exposure.

Use

Dermal exposure may occur during commercial and industrial applications. Respiratory exposure is also possible, however is not expected to occur under normal operating conditions. Skin exposure is normally very low, given that the lubricants are normally applied via pumping systems thereby minimising skin contact during application.

5.4. Release

RELEASE OF CHEMICAL AT SITE

No estimates have been provided for the likely quantity of notified chemical released during reformulation, repackaging and use, though such releases are likely to be low.

Waste produced will typically be collected for incineration. Blending and pumping equipment is typically cleaned with lubricating oil that can be recycled into future blends or captured for incineration.

Commercial and consumer products containing the notified chemical may be ultimately disposed of through used oil recycling facilities or household hazardous waste sites. Incineration would still be the expected method of disposing of this material.

Any waste of the notified chemical or products containing the notified chemical would be in liquid form. Quantities of waste will vary depending upon customers' use patterns and are thus difficult to predict.

Bottles are typically never re-used in consumer product blending and filling operations. Empty bottles are expected to be disposed of through municipal household waste collection facilities.

For industrial users, drums and iso-containers may be re-used. The drum or iso-container is first steam cleaned and any wastewater containing the notified chemical is expected to be sent to on-site wastewater treatment facility. Facilities would contain an API (American Petroleum Institute) oil and water separator and it is expected that no more than 5% of the waste chemical will be emulsified in the water. The wastewater is further treated with pond aeration and sand filtration before being released to sewer. Given the low solubility of the notified chemical, it is likely that it will be present in the treated water only in very small quantities. The remaining oily portion of the waste is sent to an incinerator.

Accidental spills at the blending facilities will be contained by plant barriers. The facilities have concrete floors that allow the spilled product to be sucked up with the remaining waste product, ending up in the wastewater treatment facilities. It is likely this will be sent for incineration.

Accidental spills during transport and use will be contained to prevent contamination of soil, surface water and groundwater. The liquid will be adsorbed onto suitable material, and where feasible, contaminated soil removed. These will then be disposed in accordance with local regulations. This is outlined in the Material Safety Data Sheet (MSDS).

RELEASE OF CHEMICAL FROM USE

The used lubricant products containing the notified chemical are typically incinerated or sent to used oil recyclers. The only potential for release to the environment is by individual car owners and owners of equipment who do their own oil changes and do not use correct methods for disposal of used oil.

The majority of the spent lubricant products containing the notified chemical collected at commercial outlets, such as automotive fleets, trucking firms, and servicing companies, or by industrial users will be incinerated or sent to used oil recyclers. When incinerated, the notified chemical will form water vapour and oxides of carbon. Therefore, the potential for release of the notified chemical to the environment is low from these sources. A small amount may be released to the environment through spills and leaks, with these likely to be widely dispersed. If the notified chemical is washed off road surfaces, it is expected to adsorb to adjacent soils and sediments. A sizeable release of the notified chemical to the aqueous environment is possible (*e.g.,* ship wreck), though unlikely.

There is also likely to be some disposal of the lubricant products to landfill from users who do their own oil changes and from empty containers, which are likely to be disposed of *via* landfill. The fate of oils sent to landfill is not clear, but it is thought that they may slowly migrate through the soil with some adsorption depending on the chemical nature of the hydrocarbon and the soil content. The notified chemical is likely to adsorb strongly to soil and unlikely to leach into the aquatic compartment. However, it may float on surface water with the potential to physically foul aquatic organisms.

A survey by the Australian Institute of Petroleum (AIP 1995) indicates that of the annual sales of automotive engine oils in Australia, some 60% are potentially recoverable (i.e., not burnt in the engines during use). This report also indicates that around 86% of oil changes take place in specialised automotive service centres, where

old oil drained from crankcases could be expected to be disposed of responsibly - either to oil recycling or incineration. The remaining 14% are removed by "do it yourself" (DIY) enthusiasts, and in these cases some of the used oil would be either incinerated, left at transfer stations where it is again likely to be recycled, or deposited into landfill. A recent report estimated that DIY activities account for between 7 to 10% of the unaccounted used oil (Meinhardt 2002). The notifier estimated up to 10% of the lubricant will be used by consumers.

According to a survey tracing the fate of used lubricating oil in Australia (Snow 1997) only around 20% of used oil removed by enthusiasts is collected for recycling, approximately 25% is buried or disposed to landfill, 5% is disposed of into stormwater drains and the remaining 50% unaccounted for.

Consequently, assuming that oil removed by professional mechanics is disposed of appropriately (i.e., sent for recycling or possibly burning as workshop heating oil), negligible release of the notified chemical should result from these professional activities. During recycling it is expected that most of the chemical will decompose and any remainder will report to the asphalt portion.

Assuming that 14% (14.0 tonnes based on 100 tonne maximum usage) of the used oil is removed by the DIY enthusiasts it is possible to have 20% (2.8 tonnes) collected for recycling, 25% (3.5 tonnes) buried or disposed to landfill, 5% (700 kg) disposed into stormwater drains and 50% (7 tonnes) unaccounted for.

Since gear oil and transmission fluid changes are likely to be carried out by specialists, and will be disposed of more appropriately, an amount less than 1% of the total import volume of the notified chemical could be expected to enter the aquatic environment via disposal into the storm water system. Since the use of the lubricating oils will occur throughout Australia, all releases resulting from use or disposal of used oil will be very diffuse, and release of the notified chemical in high concentrations is very unlikely except as a result of transport accidents.

The notified chemical is not expected to bioaccumulate as it is at least inherently biodegradable. The notified chemical also has low water solubility which would reduce the availability of the notified chemical to the aquatic compartment, thus reducing the bioaccumulation potential.

5.5. Disposal

Any waste produced will typically be collected for incineration. Blending and pumping equipment is typically cleaned with lubricating oil (not the notified chemical) that can be recycled into future blends or captured for incineration. Commercial and consumer products containing the notified chemical may be ultimately disposed of through used oil recycling facilities or household hazardous waste sites. Incineration would still be the expected method of disposing of this material. Bottles are typically never re-used in consumer product and blending and filling operations. Empty bottles are expected to be disposed of through household hazardous waste facilities. For industrial users, drums and iso-containers may be re-used. The drum or iso-container is first steam cleaned and any wastewater containing the notified chemical is expected to be sent to on-site wastewater treatment facility.

5.6. Public exposure

It is expected that during transport, storage, blending and industrial use, exposure of the general public to the notified chemical will be minimal, except in the event of an accidental spill.

Up to 10% of finished lubricants (containing max 90% of the notified chemical) will reach the public retail market, where they will be used to replace or top-up automotive lubricants, for example, engine and gearbox oils. Consequently, there is likely to be intermittent dermal exposure, with the potential for accidental eye, oral and inhalation exposure.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Colourless liquid with characteristic odour

Melting Point/Freezing Point Approximately -56ºC (pour point)

Method	ASTM D-97 "Standard Test Method for Pour Point of Petroleum Products"
REMARKS	Range from -51ºC to -60ºC
Test Facility	INEOS Belgium (2007) and Dixie Services Inc. North America (2007)

Boiling Point 365.6 – 580.5°C at 101.3 kPa (with decomposition)

Method ASTM D-2887 "Standard Test Method for Boiling Range Distribution of Petroleum Fractions by Gas Chromatography"
Remarks Samples were run by a GC simulated distillation variation of ASTM D-2887.
Test Facility INEOS Belgium (2007) and Dixie Services Inc. North America (2007)

Density 829 kg/m^3 at 15.6°C

Method ASTM D-4052 "Standard Test Method for Density and Relative Density of Liquids by Digital Density Meter"
Test Facility INEOS Belgium (2007) and Dixie Services Inc. North America (2007)

Vapour Pressure 1.3×10^{-8} kPa at 20°C

Method ASTM D-2879 "Standard Test Method for Vapour Pressure Temperature Relationship and Initial Decomposition Temperature of Liquids by Isoteniscope"
Test Facility Texas Oil Tech Laboratory (2007) and INEOS North America (2007)

Water Solubility < 6.1 mg/L at 20°C

Method OECD TG 105 Water Solubility.
Remarks Flask Method was used for determination of solubility of an analogue chemical (DURASYN 223), which is expected to have a greater water solubility than the notified chemical. The result was based on total organic carbon (TOC) analysis.
Test Facility Investigative Science Incorporated (2006)

Viscosity 18.5 cSt at 40°C
4.11 cSt at 100°C

Method ASTD D-445 Standard Test Method for kinematic Viscosity of Transparent and Opaque Liquids
Test Facility Phoenix Chemical Laboratory (2006)

Hydrolysis as a Function of pH Not determined

Remarks On the basis of the evidence presented, it is reasonable to conclude that the notified chemical will not be susceptible to hydrolysis and, as such, conducting hydrolysis testing is not warranted. It can be concluded that hydrolysis will not be a significant degradation pathway for the notified chemical in the environment.

Partition Coefficient (n-octanol/water) log Pow at 20°C = 11.99-13.96.

METHOD OECD TG 117 Partition Coefficient (n-octanol/water), HPLC Method.
EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks After attempted determination by the HPLC method showed the notified chemical did not elute, the partition coefficient of the notified chemical was modelled using KOWWIN modelling software (PRTL, 2006) and was estimated to range from 11.99 to 13.96.
TEST FACILITY PTRL West Inc (2006)

Adsorption/Desorption log K_{oc} = > 4.96 at 20°C (K_{oc} > 91200) (based on log Koc = 0.81 log K_{ow} + 0.10)

METHOD Estimation.
Remarks The estimation of minimum soil adsorption coefficients (K_{oc}) for the notified chemical was based on an empirically derived relationship between the K_{oc} and the octanol-water partition coefficient (K_{ow}) for "predominantly hydrophobic" chemicals. Based on these values, the notified chemical is predicted to be immobile in soil, under environmentally relevant conditions.

Dissociation Constant Not tested

Remarks As the notified chemicals do not contain any ionisable groups, it is not expected that they will dissociate throughout the environmentally relevant range of pH 4-9.

Particle Size Not applicable to liquids.

Flash Point 206-216ºC (pressure unspecified)

Method ASTM D-93 "Standard Test Method for Flash and Fire Points by Pensky-Martens Closed Cup Tester"
Test Facility INEOS Belgium (2007)

Flammability Limits Lower explosive limit of 0.23% at 250°C (DURASYN 223)

Method ASTM E 681-98 "Standard Test Method for Concentration Limits of Flammability of Chemicals (vapours and Gases)"
Remarks The analogue chemical (DURASYN 223) with slightly lower molecular weight was not volatile enough under the conditions of the test (at up to 250°C incoming air temperature) to determine upper flammability limits. No ignition was obtained at the temperature specified in ASTM E 681-98.
Test Facility Texas Oiltech Laboratories, Inc. (2006)

Autoignition Temperature > 348.8ºC

Method ASTM E659 Standard Test Method for Autoignition Temperature of Liquid Chemicals
Remarks Based on an analogue chemical (DURASYN 223) with lower molecular weight.
Test Facility Phoenix Chemical Laboratory (2006)

Explosive Properties Not tested

Remarks Using the approach outlined by "Bretherick's Handbook of Reactive Chemical Hazards" (Bretherick, 1990), the notified chemical is not expected to show any explosive tendencies. An examination of the structures of the notified chemical shows that it does not contain groups that are expected to cause or enhance explosibility.

Reactivity Not expected to be reactive in use.

Remarks In general, the notified chemical is not designed or expected to be reactive in use. This is confirmed by the structure of the notified chemical.

7. TOXICOLOGICAL INVESTIGATIONS

The studies below were based on analogue chemicals that are considered likely to have similar toxicological characteristics to the notified chemical.

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 > 5000 mg/kg bw (4 studies)	low toxicity
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rat, acute inhalation LC50 < 5.1 mg/L/1 hour	harmful
Rabbit, skin irritation (3 studies)	slightly irritating
Rabbit, skin irritation	moderately irritating (based on 24 hour exposure)
Rabbit, eye irritation (4 studies)	slightly irritating
Guinea pig, skin sensitisation – adjuvant test.	limited evidence of sensitisation
Guinea pig, skin sensitisation – adjuvant test (2 studies)	no evidence of sensitisation
Rat, repeat dose/developmental toxicity – 91 days.	NOEL = 500 mg/kg bw/day
Genotoxicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosomal aberrations in human lymphocytes	non genotoxic
Genotoxicity – in vitro mammalian cell gene mutation test	equivocal
Genotoxicity – in vivo mouse micronucleus test	non genotoxic

7.1. Acute toxicity – oral

7.1.1 Analogue chemical 1

TEST SUBSTANCE — Analogue chemical 1

METHOD — Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).

Species/Strain — Rat/Sprague-Dawley derived, albino rats

Vehicle — Undiluted

Remarks - Method — The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5000	0

LD50 — > 5000 mg/kg bw

Signs of Toxicity — Clinical changes observed during the observation period are as follows:

1. Transient mild depression
2. Oil hair coats

All animals appeared grossly normal by the fifth post-dosage day.

Effects in Organs — Cross necropsies performed at the end of the study revealed in one rat:

1. Yellow-brown spot on the stomach lining

No other gross pathological findings were seen.

Remarks - Results — No deaths occurred during the observation period.

CONCLUSION — The analogue chemical is of low toxicity via the oral route.

TEST FACILITY — Hill Top Biolabs (1998a)

7.1.2 Analogue chemical 2

TEST SUBSTANCE — Analogue chemical 2

METHOD — Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).

Species/Strain — Rat/Sprague-Dawley derived, albino rats

Vehicle	Undiluted
Remarks - Method	The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5000	0

LD50	> 5000 mg/kg bw
Signs of Toxicity	Clinical changes observed during the observation period are as follows: 1. Mild transitory depression 2. Oily and/or scruffy hair coats All animals appeared grossly normal by the third or fourth post-dosage day.
Effects in Organs	Cross necropsies performed at the end of the study revealed in one rat: 1. Small spleen 2. Stomach lining appeared thickened and filled with clear liquid containing a bright yellow substance No other gross pathological findings were seen.
Remarks - Results	No deaths occurred during the observation period.

CONCLUSION The analogue chemical is of low toxicity via the oral route.

TEST FACILITY Hill Top Biolabs (1998b)

7.1.3 Analogue chemical 3

TEST SUBSTANCE Analogue chemical 3

METHOD Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).

Species/Strain	Rat/Sprague-Dawley derived, albino rats
Vehicle	Undiluted
Remarks - Method	The protocol was followed with a deviation. a. One male rat dosed on this acute oral study weighted 178 grams which is slightly below the specified weight range in the protocol. This deviation did not compromise any aspect of this study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5000	0

LD50	> 5000 mg/kg bw
Signs of Toxicity	Clinical changes observed during the observation period are as follows: 1. Mild depression 2. Scruffy hair coats 3. Oily and/or scruffy hair These signs persisted through the third or fourth post-dosage days after which the animals appeared grossly normal.
Effects in Organs	The gross necropsies performed at the end of the study revealed no gross pathological changes.
Remarks - Results	No deaths occurred during the observation period.

CONCLUSION The analogue chemical is of low toxicity via the oral route.

TEST FACILITY Hill Top Biolabs (1998c)

7.1.4 Analogue chemical 4

TEST SUBSTANCE	Analogue chemical 4
METHOD	Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).
Species/Strain	Rat/Sprague-Dawley derived, albino rats
Vehicle	Undiluted
Remarks - Method	The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5000	0

LD50	> 5000 mg/kg bw
Signs of Toxicity	Clinical changes observed during the observation period are as follows: 1. Transient mild depression 2. Oily hair coats These oily hair coats were observed on the day of dosing and persisted through the third post-dosage day after which the rats appeared grossly normal.
Effects in Organs	Gross necropsies performed at the end of the study revealed no gross pathological changes.
Remarks - Results	No deaths occurred during the observation period.
CONCLUSION	The analogue chemical is of low toxicity via the oral route.
TEST FACILITY	Hill Top Biolabs (1998d)

7.2. Acute toxicity – dermal

TEST SUBSTANCE	DURASYN 125
METHOD	OECD TG 402 Acute Dermal Toxicity. U.S. EPA Health Effects Guidelines, OPPTS 870.1200 (1998)
Species/Strain	Rat/Sprague-Dawley derived, albino
Vehicle	Undiluted
Type of dressing	Occlusive
Remarks - Method	The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	There were no signs of gross toxicity, dermal irritation, adverse pharmacological effects, or abnormal behaviour.
Signs of Toxicity - Systemic	
Effects in Organs	No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.
Remarks - Results	All animals survived, gained body weight, and appeared active and health during the study (Although the report was not signed by the main investigator, the data provided corresponds with the overall toxicological profile of these compounds and is considered to be relevant).
CONCLUSION	The analogue chemical is of low toxicity via the dermal route.

TEST FACILITY	Product Safety Laboratories (2006)

7.3. Acute toxicity – inhalation

TEST SUBSTANCE	Analogue chemical 3
METHOD	U.S. Environmental Protection Agency. Toxic Substance Control Act Test Guidelines (40 CFR Part 798). Official Journal of the European Communities, Council Directive 67/548/EEC and all subsequent adaptations.
Species/Strain	Rat/Sprague-Dawley CD
Vehicle	None.
Method of Exposure	Whole-body exposure
Exposure Period	1 hour
Physical Form	Liquid aerosol
Particle Size	1.9 μm ± 1.8%
Remarks - Method	No deviations from protocol noted.

RESULTS
In the study, a group of 10 CD rats (5/sex) were exposed to an aerosol of analogue chemical 3 at 5170 mg/m^3 (maximum practical concentration) for 1 hour. A control group (5/sex) was similarly exposed to room air only. The animals were observed for 14 days after exposure.

The average aerosol particle size was 1.9 μm with a standard deviation of 1.8. Only one treated female survived during the study and other treated animals died or were sacrificed on days 1 - 3 after exposure. Clinical signs of toxicity included reduced activity, partly closed eyes, hunched back, lateral prostration, increased respiratory rate, laboured and irregular breathing, and muzzle and abdominal staining. The surviving female was clinically normal by day 9. No clinical signs were observed in the controls.

Gross pathological examination revealed an increased incidence of fluid in the trachea, uncollapsed lungs and discolouration of the lungs in animals that died during the study and increased lung and trachea weights in the surviving female. Microscopical examination showed acute pneumonia and/or haemorrhage in the lungs, and slight focal or multifocal degeneration and/or necrosis of the epithelium of the nasal septum in the treated animals. The surviving female had mild interstitial pneumonia of a chronic nature and slight focal hyperplasia of the respiratory epithelium. Myocardial degeneration and/or fibrosis were also observed in this animal and was considered possibly related to the treatment.

CONCLUSION	The analogue chemical is harmful via inhalation.
TEST FACILITY	Bio-Research Laboratories (1994)

7.4. Irritation – skin

7.4.1 Analogue chemical 1

TEST SUBSTANCE	Analogue chemical 1
METHOD	US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 M, 3 F
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	0.42	2	> 24 hours	0
Oedema	0	0	-	-

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results: The Primary Irritation Index was found to be 0.5 based on erythema and oedema. No evidence of tissue damage was found.

CONCLUSION: The analogue chemical is slightly irritating to the skin.

TEST FACILITY: Hill Top Biolabs (1988e)

7.4.2 Analogue chemical 2

TEST SUBSTANCE: Analogue chemical 2

METHOD: US 16 CFR 1500 Hazardous Substances Labelling Act.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 6 F
- Vehicle: None
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive.
- Remarks - Method: Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	0.67	3	> 72 hours	1
Oedema	0.42	2	> 24 hours	0

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results: The Primary Irritation Index was found to be 1.3 based on erythema and oedema. No evidence of tissue damage was found.

CONCLUSION: The analogue chemical is slightly irritating to the skin.

TEST FACILITY: Hill Top Biolabs (1988f)

7.4.3 Analogue chemical 3

TEST SUBSTANCE: Analogue chemical 3

METHOD: US 16 CFR 1500 Hazardous Substances Labelling Act.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 6 F
- Vehicle: None
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive.
- Remarks - Method: Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	2	3	> 72 hours	3
Oedema	1	2	> 72 hours	1

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results: The Primary Irritation Index was found to be 3.1 based on erythema and oedema. No evidence of tissue damage was found.

CONCLUSION: The analogue chemical is moderately irritating to the skin.

TEST FACILITY: Hill Top Biolabs (1988g)

7.4.4 Analogue chemical 4

TEST SUBSTANCE: Analogue chemical 4

METHOD: US 16 CFR 1500 Hazardous Substances Labelling Act.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3 F, 3 M
- Vehicle: None
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive.
- Remarks - Method: Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	0.42	1	> 24 hours	0
Oedema	0.17	1	> 24 hours	0

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results: The Primary Irritation Index was found to be 0.5 based on erythema and oedema. No evidence of tissue damage was found.

CONCLUSION: The analogue chemical is slightly irritating to the skin.

TEST FACILITY: Hill Top Biolabs (1988h)

7.5. Irritation – eye

7.5.1 Analogue chemical 1

TEST SUBSTANCE: Analogue chemical 1

METHOD: US 16 CFR 1500 Hazardous Substances Labelling Act.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3 F, 3 M
- Observation Period: 72 hours
- Remarks - Method: No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0.61	1	> 72 hours	1
Conjunctiva: chemosis	0.28	1	> 72 hours	1
Conjunctiva: discharge	0	0	-	
Corneal opacity	0	0	-	
Iridial inflammation	0	0	-	

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results The eyes of five rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 4.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY Hill Top Biolabs (1988i)

7.5.2 Analogue chemical 2

TEST SUBSTANCE Analogue chemical 2

METHOD US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain Rabbit/New Zealand White
Number of Animals 6 F
Observation Period 72 hours
Remarks - Method No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0.17	1	> 72 hours	1
Conjunctiva: chemosis	0	0	-	0
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results The eyes of two of the rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 2.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY Hill Top Biolabs (1988j)

7.5.3 Analogue chemical 3

TEST SUBSTANCE Analogue chemical 3

METHOD US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain Rabbit/New Zealand White
Number of Animals 6 F
Observation Period 72 hours
Remarks - Method No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0.67	1	> 72 hours	1
Conjunctiva: chemosis	0.33	2	> 72 hours	1
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results The eyes of all the rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 6.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY Hill Top Biolabs (1988k)

7.5.4 Analogue chemical 4

TEST SUBSTANCE Analogue chemical 4

METHOD US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 F, 3 M
Observation Period 72 hours
Remarks - Method No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0.50	1	> 72 hours	1
Conjunctiva: chemosis	0.22	1	> 72 hours	1
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results The eyes of three rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 4.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY Hill Top Biolabs (1988k)

7.6. Skin sensitisation

7.6.1 Analogue chemical 1

TEST SUBSTANCE Analogue chemical 1

METHOD OECD TG 406 Skin Sensitisation - <Maximisation Test>.
EC Directive 96/54/EC B.6 Skin Sensitisation - < Maximisation Test >.
EPA Subdivision F, Series 81-6, Dermal Sensitisation. 1984.
Japanese Ministry of Agriculture Forestry and Fisheries, 59 NohSan No. 4200. 1985.
Species/Strain Guinea pig/Dunkin-Hartley
PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: < 1%
topical: 100%

MAIN STUDY

Number of Animals	Test Group: 20	Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: 10% topical: 25-100%	
Signs of Irritation	Slight erythema in one control animal at the intradermal induction site. Slight erythema in most animals after topical induction.	
CHALLENGE PHASE		
1st challenge	topical: 100%	
2nd challenge	topical: 50%, 100%	

Remarks - Method No deviations from protocol noted.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	100%	2/20	1/20	1/20	0/20
	50%	-	-	0/20	0/20
Control Group	100%	0/10	0/10	0/10	0/10
	50%			0/10	0/10

Remarks - Results

Challenge
Positive responses were noted in 2/20 of the test group animals at 24 h after patch removal, lasting to 48 h after patch removal in 1 animal. There were no positive responses noted in Control group animals.
Rechallenge
A positive response was noted in 1/20 of the test group animals challenged with 100% of the analogue chemical, at 24 h after patch removal only.
In this study, only one (5%) positive response was noted in the test group at the 48 h challenge observation. If the one response seen at challenge was a true sensitisation response, this animal would have been expected to respond in the same way at rechallenge; no such response was noted in this animal at rechallenge. It is known that the chemical is a mild irritant and is thought to be responsible for the reactions.
No clinical signs, other than skin reactions at the test sites, were noted.

CONCLUSION There was limited evidence of reactions indicative of skin sensitisation to the analogue chemical under the conditions of the test.

TEST FACILITY Inveresk Research (1997a)

7.6.2 Analogue chemical 2

TEST SUBSTANCE Analogue chemical 2

METHOD Magnusson and Kligman (1969)

Species/Strain	Guinea pig/Dunkin-Hartley	
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 5% topical: 100%	
MAIN STUDY		
Number of Animals	Test Group: 20	Control Group: 20
INDUCTION PHASE	Induction Concentration: intradermal: 5% topical: 100%	
Signs of Irritation	None.	

CHALLENGE PHASE	
1st challenge	topical: 100%
2nd challenge	None.
Remarks - Method	No deviations from protocol noted.

RESULTS

Remarks - Results	No animals in either the control or test article treated groups exhibited positive signs of erythema.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the analogue chemical under the conditions of the test.
TEST FACILITY	Pharmakon Research International (1992a)

7.6.3 Analogue chemical 3

TEST SUBSTANCE	Analogue chemical 3
METHOD	Magnusson and Kligman (1969)
Species/Strain	Guinea pig/Dunkin-Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: slight erythema at 0.5% topical: slight erythema at 10% in 1/4 animals.
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 20
INDUCTION PHASE	Induction Concentration: intradermal: 5% topical: 10%
Signs of Irritation	None noted.
CHALLENGE PHASE	
1st challenge	topical: 10%
2nd challenge	None.
Remarks - Method	No deviations from protocol noted.

RESULTS

Remarks - Results	No animals in either the control or test article treated groups exhibited positive signs of erythema.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the analogue chemical under the conditions of the test.
TEST FACILITY	Pharmakon Research International (1992b)

7.7. Repeat dose toxicity

7.7.1 Analogue chemical 1: 91- day toxicity study with in utero exposure phase (range finding study)

TEST SUBSTANCE	Analogue chemical 1
METHOD	In-house protocol (not specified)
Species/Strain	Rat/Sprague-Dawley
Route of Administration	Oral – gavage
Exposure Information	Exposure: From gestation day 0 to lactation day 20. Dose regimen: 7 days per week Pregnant females only were treated. All F0 females in groups 2 and 3, 3 females from groups 1 and 4 and 1 female from group 5 were euthanised and necropsied following lactation. Females from groups 4 and 5 were

	dosed for a total of 91 days. Ten F1 pups/sex/group were selected for a 21-day study phase initiated on postpartum day 22 and continued through postpartum day 42.
Vehicle	PEG 400
Remarks - Method	No deviations from protocol were noted.

RESULTS

Dose mg/kg bw/day	*Number and Sex of Animals*	*Mortality*
0 (control)	6 F	0
100	6 F	0
500	6 F	0
1000	6 F	0
2000	6 F	0

Mortality and Time to Death

F0

Two females which failed to deliver were euthanised on post-breeding day 25.

F1

There was no effect of treatment on pup viability. A slightly greater male to female ratio of pups in group 5 on lactation day 0 was of unknown significance.

Clinical Observations

F0

A range of clinical observations was recorded as minor and likely to be due the vehicle. None were attributed to the test article. However, clinical signs are more apparent in high dose animals. No significant changes in body weights or body weight gain due to treatment were found during gestation, lactation or those dosed for 91 days.

There were no test article related effects on length of gestation, parturition or lactation.

F1

A number of incidental clinical findings were noted but were not related to the test article.

Effects in Organs

F0

There were no macroscopic or microscopic observations which were test article related.

F1

No test article related macroscopic or microscopic findings were noted.

Remarks – Results

None.

CONCLUSION

No significant maternal or developmental toxicity occurred with analogue chemical 1 at dosage levels up to 2000 mg/kg bw/day and indicated levels of 100, 500 and 1000 mg/kg bw/day for the main study.

TEST FACILITY Springborn Laboratories, Inc. (1995)

7.7.2 Analogue chemical 2: 91- day toxicity study with in utero exposure phase (main study)

TEST SUBSTANCE	Analogue chemical 1
METHOD	In-house protocol (not specified)
Species/Strain	Rat/Sprague-Dawley
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week Both males and females were dosed four weeks prior to mating. For the males, dosing continued until scheduled euthanasia (at the end of the breeding period). For the females dosing continued through gestation and through lactation day 20 or until euthanasia for females without evidence of mating and/or failure to deliver. Dams that delivered and weaned their offspring were euthanised on lactation day 21.
Vehicle	PEG 400
Remarks - Method	Minor deviations from protocol were noted but appeared to be unlikely to affect the outcome of the study.

RESULTS

Group	*Number and Sex of Animals*		*Dose mg/kg bw/day*	*Mortality*	
	F0	F1		F0	F1
I (control)	30/sex	20/sex	0	1 female	
II (low dose)	30/sex	20/sex	100	5 females	1 female
III (mid dose)	30/sex	20/sex	500	7 females	1 male
IV (high dose)	30/sex	20/sex	1000	3 females	1 male

Mortality and Time to Death

F0

One control female was euthanised as moribund during an incomplete delivery and one low dose female died accidentally. Four low dose, seven mid dose and three high dose females were euthanised post breeding day 25 after they produced no evidence of littering. One high dose female was euthanised due to total litter loss.

F1

There were no apparent test article effects on pup viability, live litter size, mean pups per litter and male to female ratio. One male in each of the mid and high dose groups and 1 low dose female were found dead on days 94, 54 and 27, respectively.

Clinical Observations

F0

A range of clinical observations was recorded as minor and likely to be due the vehicle. None were attributed to the test article.

No changes in body weights or body weight gain due to treatment was found for F0 males. For the females the only observation related to treatment was a significant decrease in body weight gain for high dose females.

The only treatment related changes to food consumption were in high dose females over days 1 – 7 and 7 – 14 of lactation. These changes were significant in g/animal/day but not when calculated as g/kg/day.

There were no test article related effects on fertility, length of gestation, pregnancy status, parturition or lactation.

F1

A number of incidental clinical findings were noted but were not related to the test article. Significant increases in body weight in high dose animals were noted in males over weeks 11 and 12 and in females over weeks 3 to 4 but were not ascribed to the test article. Food consumption decreased in mid dose females over weeks 6 to 7, in the low, mid and high dose groups over weeks 12 to 13 and in the low and mid dose groups over weeks 13 to 14. These changes were not considered to be biologically significant due to a lack of dose response or an abnormally increased control value.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
F1

Clinical Chemistry: No test article related changes.
Haematology: Elevated prothrombin time in high dose males; no dose related changes in females.

Effects in Organs
F0

None of the macroscopic observations in the F0 males were test article related.

None of the macroscopic findings for the euthanised females could be ascribed to the test article or the vehicle.

F1

No test article related macroscopic or microscopic findings were noted.

Remarks – Results
Treatment of F0 rats with analogue 1 at the designated dosage levels did not produce significant organ toxicity or effects on fertility nor did the F1 pups exhibit toxic effects during the parturition and lactation phases. In the F1 rats during the 91-day toxicity phase no organ toxicity could be attributed to the test article. A significant increase in prothrombin time in high dose males was not considered to be biologically meaningful as it did not correlate with a decrease in platelets, gross necropsy or microscopic findings.

CONCLUSION
A Lowest Observed Adverse Effect Level (LOAEL) of 1000 mg/kg/d due to the clinical signs prevalent in the high dose females that indicate stress (unkempt appearance) and the loss of the entire litter in one high dose female. A No Observed Effect Level (NOEL) of 500 mg/kg/d is set based on effects seen at the higher level.

TEST FACILITY	Springborn Laboratories (1994)

7.8. Genotoxicity – bacteria

TEST SUBSTANCE	Analogue chemical 1
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100; *Escherichia coli WP2uvr*A.
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction.
Concentration Range in Main Test	a) With metabolic activation: 0, 156.25, 312.5, 625, 1250, 2500, 5000 µg/plate b) Without metabolic activation: 0, 156.25, 312.5, 625, 1250, 2500, 5000 µg/plate
Vehicle	Sorbitan stearate and polysorbate 60.
Remarks - Method	No deviations from protocol noted.

RESULTS

Remarks - Results	No evidence of cytotoxicity was noted at any concentrations. Some precipitates were noted at 5000 µg/plate. No toxicity was noted in a preliminary test on the basis of a consistent number of spontaneous mutant colonies in TA100 up to 5000 µg/plate. Negative controls were within acceptable limits and positive controls demonstrated the sensitivity of the test. No sign of increase in revertant colonies in any test strains, with or without metabolic activation.
CONCLUSION	The analogue chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Inveresk Research (1997b)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE	Analogue chemical 5
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test. EC Directive 92/69/EC B.10 Mutagenicity - In vitro Mammalian Chromosome Aberration Test.
Cell Type/Cell Line	Human lymphocytes
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction
Vehicle	Ethanol
Remarks - Method	No deviations from protocol noted.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	39, 78.1, 156.25, 312.5, 625, 1250*, 2500*, 5000*	4 hr	20 hr
Test 2	625, 1250*, 2500*, 5000**	4 hr	20, 44 hr
Present			
Test 1	39, 78.1, 156.25, 312.5, 625, 1250*, 2500*, 5000*	4 hr	20 hr
Test 2	625, 1250*, 2500*, 5000**	4 hr	20, 44 hr

*Cultures selected for metaphase analysis. ** Cultures selected for metaphase analysis at both harvest times

RESULTS

Remarks - Results	The negative controls were within historical limits and the positive controls demonstrated the sensitivity of the test. In test 2 one of the positive control cultures was negative due to excessive toxicity but this did not negate the conclusions of the experiment.
CONCLUSION	The analogue chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.
TEST FACILITY	Safepharm Laboratories Limited (1995a)

7.10. Genotoxicity – in vitro

TEST SUBSTANCE	Analogue chemical 5
METHOD	OECD TG 476 In vitro Mammalian Cell Gene Mutation Test. EC Directive 2000/32/EC B.17 Mutagenicity - In vitro Mammalian Cell Gene Mutation Test.
Cell Type/Cell Line	Chinese Hamster Ovary cells
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction
Vehicle	Ethanol

Remarks - Method: Two protocol deviations were described, that were considered by the study author to have no effect on the validity of the test results: the activated portion of test 1 was lost due to contamination and was repeated; in the confirmatory assay the number of cells seeded in the solvent control and all the test substance-treated cultures, except for one replicate at the highest concentration of 5000 µg/mL, was less than 2×10^5 cells/plate.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	313, 625, 1250, 2500, 5000	4 hrs	8 days	7 days
Test 2	313, 625, 1250, 2500, 5000	"	"	"
Present				
Test 1	313, 625, 1250, 2500, 5000	"	"	"
Test 2	313, 625, 1250, 2500, 5000	"	"	"

RESULTS

Remarks - Results: The first trial exhibited no differences in relative cloning efficiencies (RCEs) without metabolic activation. Contamination of cells conducted with metabolic activation invalidated the results and therefore this portion of the study was re-initiated. An increase in the number of mutants at 625 µg/ml was observed as compared to the control with metabolic activation. During the confirmatory trial, this increase in mutants was not observed at the same dose level, but at 2500 µg/ml. As there was no dose relationship and the number of mutants fell within the historical laboratory number, the test article utilised in the study was concluded to be non mutagenic. The positive control (with activation) had a range of average number of mutants per dose from approximately 200-400, while the analogue chemical had an average number of mutants of 8-9. Overall, the mutagenic potential of analogue chemical in this study was inconclusive.

CONCLUSION: Under the study conditions, the mutagenic potential of the analogue chemical, was equivocal.

TEST FACILITY: Sitek Research Laboratories (2001)

7.11. Genotoxicity – in vivo

TEST SUBSTANCE: Analogue chemical 6

METHOD: OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
EC Directive 84/449/EC B.12 Mutagenicity - Mammalian Erythrocyte Micronucleus Test.

Species/Strain: Mouse/CD-1
Route of Administration: Oral – gavage
Vehicle: Arachis oil
Remarks - Method: No deviations from protocol noted.

Group	*Number and Sex of Animals for each sacrifice time*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5/sex	0	24, 48, 72 hrs
II (low dose)	5/sex	1250	24, 48, 72 hrs
III (mid dose)	5/sex	2500	24, 48, 72 hrs
IV (high dose)	5/sex	5000	24, 48, 72 hrs
V (positive control, CP)	5/sex	50	24 hrs

CP=cyclophosphamide.

RESULTS

Doses Producing Toxicity	No clinical signs noted.
Genotoxic Effects	There was no indication of toxicity at any dose level.
Remarks - Results	There was no statistically significant increase in micronucleated PCEs in any test group when compared to vehicle control. There were no differences in the PCE/NCE ratio in any dose group as compared to the control. Positive control group showed a marked increase in the incidence of micronucleated polychromatic erythrocytes, confirming the system.

CONCLUSION The analogue chemical was not clastogenic under the conditions of this in vivo mouse micronucleus test..

TEST FACILITY Safepharm Laboratories Limited (1995b)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE Notified chemical

METHOD OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.

Inoculum	Activated sludge
Exposure Period	28 Days
Auxiliary Solvent	None specified
Analytical Monitoring	IC and TOC
Remarks – Method	The sample biodegradability is calculated from the released CO_2 compared to blank and the reference.

RESULTS

Notified chemical		*Sodium benzoate*	
Day	*% degradation*	*Day*	*% degradation*
0	0	0	0
1	6	1	8
2	12	3	13
3	18	6	13
6	49	8	36
8	58	8	36
10	65	10	67
14	65	14	69
16	86	16	87
20	90	20	87
22	90	22	90
24	97	24	95
27	100	27	97
28	104	28	103

Remarks – Results The test substance attained 6% degradation after 1 day and 65% degradation after 10 days thereby satisfying the 10 day window validation criterion. The test substance can therefore be considered to be readily biodegradable under the strict terms and conditions of the OECD Guidelines. The reference degradation indicates guideline criteria were met.

CONCLUSION	The test substance is readily biodegradable.
TEST FACILITY	SafePharm Laboratories Ltd, Derbyshire UK (2008)

8.1.2. Bioaccumulation

Not expected to bioaccumulate, since the test substance is readily biodegradable. Release to the aquatic compartment is also expected to be low.

8.2. Ecotoxicological investigations

Results are available for several related analogues of the notified substance.

Considering the range of structures, molecular weights and lack of water solubility, it can be concluded the results are relevant to the notified chemical.

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Durasyn 223
METHOD	OECD TG 203 Fish, Acute Toxicity Test - Static EC Directive 92/69/EEC C.1 Acute Toxicity for Fish - static
Species	*Brachydanio rerio*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	TOC analysis
Remarks – Method	The test substance was prepared as a Water Accommodated Fraction (WAF) due to its expected low water solubility. The test substance was tested for toxicity towards fish only up to the limit of its water solubility. For this purpose a suspension of the test substance was prepared to 10 g in 1 L of drinking water. The notified chemical was introduced into the dilution water whilst shaking. Shaking was further continued for further 24 h at room temperature. Thereafter the suspension was filtered through a filter paper. The pH of the elute was not corrected.
RESULTS	Under the conditions used for the test no toxic effect of Durasyn 223 to the fish was observed.

Water extract -Test substance (g/L)	*Number of Fish*	*Mortality*			
		24h	*48h*	*72h*	*96h*
0 (control)	7	0	0	0	0
10	7	0	0	0	0

LC50	> 1000 mg/L WAF nominal at 96 hours.
NOEC	1000 mg/L WAF nominal at 96 hours.
Remarks – Results	All organisms of the control and the treatment at 1000 mg/L survived the 96 h WAF toxicity test. The levels of substance were analysed by IR, which indicated the water soluble fraction was stable over time.
CONCLUSION	The test substance is considered to be non toxic to *Brachydanio rerio* up to the limit of its water solubility.
TEST FACILITY	Institut Fresenius, Chemische und Biologische Laboratorien GmBH (1997).

8.2.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Analogue chemical 6
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test - Static EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	TOC analysis
Remarks – Method	In the range finding study *Daphnia magna* were exposed to a series of 100 and 1000 mg/L Water Accommodated Fractions of the test substance at loading rates of 100 and 1000 mg/L. Amounts of test substances (0.20 and 2.00 g) were each separately dispersed onto the surface of 2 L of reconstituted water to give 100 and 1000 mg/L loading rates respectively and then stirred by magnetic stirrer for 24 h prior to the study start, care was taken to avoid vortex formation or gross mixing. Stirring was stopped after 24 hours and the mixture allowed to stand for 1 hour prior to removal of the aqueous phase or Water Accommodated Fraction (WAF) for testing. No vortex was formed during stirring of the test water. During testing, the WAF was observed to be a clear colourless solution at 0, 24 and 48 hours.

RESULTS

Concentration (mg/L)		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control		10	0	0
100		10	0	0
1000		10	0	0

ELR50	> 1000 mg/L WAF at 48 hours
NOEC	1000 mg/L WAF at 48 hours
Remarks – Results	Total organic carbon (TOC) analyses were performed at 0 and 48 h, with no significant change compared to control, though levels were low (0.87-2.77 mg C/L).
CONCLUSION	The test substance is considered to be non-toxic to *Daphnia magna* up to the limit of its water solubility.
TEST FACILITY	Safepharm Laboratories Limited (1995c)

8.2.2.2. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Durasyn 166
METHOD	OECD TG 211 Daphnia sp. Reproduction Test - Static.
Species	*Daphnia magna*
Exposure Period	21 day
Auxiliary Solvent	None
Water Hardness	Total hardness as $CaCO_3$: 160-170 mg/L
Analytical Monitoring	TOC analysis
Remarks – Method	Culture and WAF were prepared in 1900-L batches of fortified well water according to the formula for hard water (U.S. EPA, 1975). Water Accommodated Fractions (WAF) of the loading rate (125 mg/L) were prepared daily at each renewal period by adding 0.539 mL of test

substance directly into 3.5 L of fortified well water in a 4.0 L screw cap glass jar. The mass of test substance (0.4372 g) to be added was based on the experimentally-determined specific gravity of 0.8112 g/L. Prior to the addition of the fortified well water and test substance, a Teflon®-coated stir bar was added to the 4.0 L screw capped glass jar. The screw capped glass jar was then placed on a magnetic stir plate and stirred with no vortex for 48 hours. The WAF was then allowed to settle for 1 hour prior to use. The individual WAFs were drawn off directly into each replicate exposure vessel. A control solution was also prepared following the same procedures outlined except without the addition of the test substance. Analytical measurement of the WAFs was not considered feasible.

At the termination of the study, data obtained on organism survival, reproduction and growth were statistically analysed to identify significant effects. Analyses were performed using the organism response in each replicate vessel. All statistical conclusions were made at the 95% level of certainty except in the case of Shapiro-Wilk's and F-Test for equality of two variances, in which the 99% level of certainty was applied.

The TOXTAT program was used to perform the computations and determine the No-Observed-Effect Loading Rate (NOELR) for survival, reproduction and growth. The NOELR is defined as the highest nominal rate that resulted in no statistically significant difference from the controls.

RESULTS

Below table shows survival of parental daphnids and number of offspring released per female daphnid (*Daphnia magna*) in control during the 21 day static-renewal exposure to Durasyn 166 (equivalent to Durasyn 125).

Day	A	B	C	D	E	F	G	H	I	J	NoADI	% Survival
Total Number of Offspring Released per Daphnid												
21	167	128	162	206	137	215	166	192	196	174	0	100

NoADI = Number of Adult Daphnids Immobilised

Below table shows survival of parental daphnids and number of offspring released per female daphnid (*Daphnia magna*) in the 125 mg/L loading rate during the 21 day static-renewal exposure to Durasyn 166 (equivalent to Durasyn 125).

Day	A	B	C	D	E	F	G	H	I	J	NoADI	% Survival
Total Number of Offspring Released per Daphnid												
21	172	137	157	151	138	141	155	179			2	80

NoADI = Number of Adult Daphnids Immobilised

Below table shows nominal loading retested, daphnid survival and cumulative mean number of offspring released, mean total body length and dry weight of daphnids (*Daphnia magna*) during 21 day static- renewal exposure to Durasyn 166 (equivalent to Durasyn 125).

Test Day 21				
Nominal Loading (mg/L)	**Mean % Survival**	**MNoOR per female (SD)**	**MTBL in mm (SD)**	**MDW in mg (SD)**
Control	100	174(28)	5.15 (0.14)	1.03 (0.14)
125	80	154 (15)	5.20 (0.09)	1.04 (0.11)
NOELR (mg/L)	125	125	125	125

SD = Standard deviation
MNoOR = Mean Number of Offspring Released
MTBL = Mean Total Body Length
MDW = Mean Dry Weight
NOELR = No-Observed-Effect loading Rate

Remarks – Results	Survival, reproduction and growth rate data from chronic exposure of *Daphnia magna* to Durasyn 166 are presented in the three tables above. Following 21 days of exposure, the control Daphnid survival and reproduction (100 % and 174 offspring per female, respectively) met the minimum standard criteria established by OECD Guidelines No 211 (i.e., > 80 % survival, > 60 offspring per female). As demonstrated by the performance of control organisms, the exposure system provided conditions which are appropriate for promoting acceptable survival, reproduction and growth of the test species.
CONCLUSION	Based on the results of this study, 21-day exposure to WAF of nominal loading rate of 125 mg Durasyn 166/L had no adverse effect on the survival, growth and reproduction of daphnids (*Daphnia magna*). The No-Observed-Effect Loading Rate (NOELR) for all biological endpoints was determined to be 125 mg/L. While there were differences in mean percent survival and mean number of offspring, they were not statistically significant.
TEST FACILITY	Springborn Smithers Laboratories U.S.A (2002a)

8.2.2.3. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Durasyn 223
METHOD	OECD TG 211 Daphnia sp. Reproduction Test - Static.
Species	*Daphnia magna*
Exposure Period	21 day
Auxiliary Solvent	None
Water Hardness	Total hardness as $CaCO_3$: 160-170 mg/L
Analytical Monitoring	TOC analysis
Remarks – Method	Culture and WAF were prepared in 1900-L batches of fortified well water according to the formula for hard water (U.S. EPA, 1975). Water Accommodated Fraction (WAF) of the loading rate (125 mg/L) were prepared daily at each renewal period by adding 0.544 mL of test substance directly into 3.5 L of fortified well water in a 4.0 L screw cap glass jar. The mass of test substance (0.4373 g) to be added was based on the experimentally-determined specific gravity of 0.8039 g/L. Prior to the addition of the fortified well water and test substance, a 7 cm Teflon®-coated stir bar was added to the 4.0 L screw capped glass jar. The screw capped glass jar was then placed on a magnetic stir plate and stirred with no vortex for 48 hours. The WAF was then allowed to settle for 1 hour prior to use. The individual WAFs were drawn off directly into each replicate exposure vessel. A control solution was also prepared following the same procedures outlined except without the addition of the test substance. Analytical measurement of the WAFs was not considered feasible. At the termination of the study, data obtained on organism survival, reproduction and growth were statistically analysed to identify significant effects. Analyses were performed using the organism response in each replicate vessel. All statistical conclusions were made at the 95 % level of certainty except in the case of Shapiro-Wilk's and F-Test for equality of two variances, in which the 99 % level of certainty was applied. The TOXTAT program was used to perform the computations and determine the No-Observed-Effect Loading Rate (NOELR) for survival, reproduction and growth. The NOELR is defined as the highest nominal rate that resulted in no statistically significant difference from the

controls.

RESULTS

Below table shows survival of parental daphnids and number of offspring released per female daphnid (*Daphnia magna*) in control during the 21 day static-renewal exposure to Durasyn 223.

Day	A	B	C	D	E	F	G	H	I	J	NoADI	% Survival
Total Number of Offspring Released per Daphnid												
21	192	213	216	163	186	142	158	144	153	177	0	100

NoADI = Number of Adult Daphnids Immobilised

Below table shows survival of parental daphnids and number of offspring released per female daphnid (*Daphnia magna*) in the 125 mg/L loading rate during the 21 day static-renewal exposure to Durasyn 223.

Day	A	B	C	D	E	F	G	H	I	J	NoADI	% Survival
Total Number of Offspring Released per Daphnid												
21	172	189	166	200	179		189	150		193	2	80

NoADI = Number of Adult Daphnids Immobilised

Below table shows nominal loading retested, daphnid survival and cumulative mean number of offspring released, mean total body length and dry weight of daphnids (*Daphnia magna*) during 21 day static- renewal exposure to Durasyn 223.

	Test Day 21			
Nominal Loading (mg/L)	**Mean % Survival**	**MNoOR per female (SD)**	**MTBL in mm (SD)**	**MDW in mg (SD)**
Control	100	174(27)	5.13 (0.22)	1.03 (0.14)
125	80	180 (16)	5.25 (0.08)	0.99 (0.06)
NOELR (mg/L)	125	125	125	125

SD = Standard deviation
MNoOR = Mean Number of Offspring Released
MTBL = Mean Total Body Length
MDW = Mean Dry Weight
NOELR = No-Observed-Effect loading Rate

Remarks – Results

Survival, reproduction and growth rate data from chronic exposure of *Daphnia magna* to Durasyn 223 are presented in the three tables above.

Following 21 days of exposure, the control Daphnid survival and reproduction (100% and 174 offspring per female, respectively) met the minimum standard criteria established by OECD Guidelines No 211 (i.e., > 80% survival, > 60 offspring per female). As demonstrated by the performance of control organisms, the exposure system provided conditions which are appropriate for promoting acceptable survival, reproduction and growth of the test species.

CONCLUSION

Based on the results of this study, 21-day exposure to WAF of nominal loading rate of 125 mg Durasyn 223/L had no adverse effect on the survival, growth and reproduction of daphnids (*Daphnia magna*). The No-Observed-Effect Loading Rate (NOELR) for all biological endpoints was determined to be 125 mg/L. While there were differences in mean percent survival, they were not statistically significant.

TEST FACILITY

Springborn Smithers Laboratories U.S.A (2002b)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE

Analogue chemical 6

METHOD	OECD TG 201 Alga, Growth Inhibition Test. EC Directive 92/69/EEC C.3 Algal Inhibition Test.
Species	*Selenastrum capricornutum*
Exposure Period	96 hours
Concentration Range Nominal	1000 mg/L
Auxiliary Solvent	None
Water Hardness	Not measured
Analytical Monitoring	TOC analysis
Remarks – Method	For the purpose of definitive study approximately 24 hours prior to the study start an amount of test substance (4000 mg) was dispensed onto the surface of 2 L of culture medium to give a 2000 mg/L loading rate and stirred for 20 hours. The stirrer rate (rpm) of the magnetic stirrer and the depth of the vortex (approximately 20-25% of the depth of the mixing vessel) was recorded. After 20 hours stirring was stopped and the mixture allowed to stand for 4 hours prior to removal of the aqueous phase or Water Accommodated Fraction (WAF) for testing. An aliquot (300 mL) of the 2000 mg/L loading rate WAF was diluted 50:50 with algal suspension to give a final test concentration of 1000 mg/L loading Water Accommodated Fraction. Total organic carbon (TOC) analyses were performed at 0 and 96 h, with no significant change compared to control, though levels were low (0.53-2.35 mg C/L). The pHs, temperatures, conductivities and dissolved oxygen concentrations were within acceptable levels.

RESULTS

Biomass		Growth	
Nominal (WAF) E_bLR_{50} mg/L at 96 h	Nominal (WAF) NOEC mg/L at 96 h	Nominal (WAF) E_bLR_{50} mg/L at 96 h	Nominal (WAF) NOEC mg/L at 96 h
> 1000	1000	> 1000	1000

Remarks – Results	The 24, 48, 72 and 96 h E_bLR_{50} were > 1000 mg/L when calculated using biomass or growth rate.
CONCLUSION	The results for the test substance showed no effect on growth at a concentration of 1000 mg/L.
TEST FACILITY	Safepharm Laboratories Limited (1995d)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

The notified chemical will be imported and reformulated into lubricant oils at the blending facilities. The used oil and the sludge collected from the on-site wastewater treatment facilities may be incinerated. This will generate water vapour and oxides of carbon and hydrogen. The main environmental exposure is expected to result from inappropriate disposal of waste lubricant product, assuming a worst case scenario of about 14% of oil changes in Australia are performed by DIY enthusiasts.

This disposal is however, widespread across Australia. Most of the improperly released notified chemical due to DIY activities is likely to become associated with soils or sediments, as will the notified chemical released to landfill as container residues. The notified chemical released into the aquatic environment would be expected to become associated with the sediments due to its estimated low water solubility. While some components of the notified chemical are not readily degradable, these can be expected to slowly degrade due to biotic and abiotic processes.

The amount released to stormwater drains (less than 1% of the import volume) can enter the aquatic compartment and could be expected to become associated with suspended organic material (due to the calculated high P_{OW}), settle out into the sediments and eventually be biodegraded.

It is difficult to estimate the Predicted Environmental Concentration (PEC) of the notified chemical released into stormwater drains, which have the potential to directly enter the aquatic environment. However, a worst case estimated PEC might be calculated if it is assumed that all of the notified chemical that is expected to be released into stormwater drains into a single metropolitan area with a geographical footprint of 500 square kilometres and an average annual rainfall of 500 mm. With a maximum annual release into this localised stormwater system of 700 kg and the annual volume of water drained from this region estimated to be approximately 250×10^6 m^3, the resultant PEC is approximately 3 µg/L. It should be stressed that this result is very much a worst case scenario, and that in reality releases of the chemical would be much more diffuse than indicated here, and also at significantly reduced levels.

9.1.2. Environment – effects assessment

Based on the ecotoxicity data provided, the notified chemical is not toxic up to the limit of water solubility where TOC = 0.87-2.77 mg/L. A PNEC could not be calculated based on the TOC value.

9.1.3. Environment – risk characterisation

The notified chemical is not toxic to the aquatic organisms tested up to the limit of its water solubility where the TOC = 0.87-2.77 mg/L. This value allows for at least 3 orders of magnitude safety factor in comparing with the PEC of 3 µg/L. Further, the low water solubility of the notified chemical and its limited release to the aquatic environment (mainly via stormwater drainage) reduce the possibility of sufficient amounts remaining in solution to cause acute toxicity. The notified chemical is expected to become associated with sediments, and biodegradation will further reduce the risk to the aquatic life.

Overall, the environmental risk from the proposed blending and use of the notified chemical is expected to be low.

While the molecular weight < 1000, the notified chemical is not expected to bioaccumulate, since the notified chemical is readily biodegradable. Also, under normal usage, the notified chemical is not expected to enter the aquatic environment and to pose a risk to aquatic organisms.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Inhalation exposure during formulation is not expected to be significant as it is likely to be controlled by general and local exhaust ventilation.

Dermal and ocular exposure during formulation while connecting and disconnecting pumps and lines and to a lesser extent during system cleaning and maintenance is expected to be low given that PPE will be employed in all blending establishments to control dermal and ocular exposure. While the use of couplings and pumps designed to minimise spillage is desirable, the extent of their use by customers for the notified chemical is unknown.

The estimated dermal exposure to the notified chemical, based on EASE model (EASE) using reasonable worst case defaults for particular activity (European Commission, 2003) is as follows:

Activity	*Estimated exposure for activity <mg/day>*	*Estimated exposure for notified chemical <mg/kg bw/day>* *
Manual addition of liquids	420	6
Coupling and decoupling of transfer line	42	0.6
Quality control sampling	21	0.3

* for a 70 kg worker and a 100% dermal absorption factor

For end use of oils or fluids containing the notified chemical estimated exposure can reasonably be described under the above category of "manual addition of liquids" with a similar value.

9.2.2. Public health – exposure assessment

Exposure of the public to the notified chemical will be minimal during transport, storage, blending and industrial use, except in the event of an accidental spill.

Up to 10% of products will be able to be purchased by the public. Of these the most widely used would be expected to be engine oils and exposure will be similar to that described for commercial use of these oils. DIY enthusiasts may experience repeated dermal exposure to these oils containing the notified chemical. Protective gloves may not necessarily be used during applications, however, users should have access to the MSDS of the lubricant.

9.2.3. Human health – effects assessment

All toxicological data were based on analogue chemicals.

Acute toxicity

The notified chemical is likely to be of low acute oral toxicity (LD50 > 5000 mg/kg bw) and low acute dermal toxicity (LD50 > 2000 mg/kg bw). Inhalation toxicity was high in a study using a liquid aerosol however this is considered to be due to aspiration rather than inherent toxicity. The notified chemical has a higher viscosity than the analogue, reducing the potential of aspiration hazard. However, the data does demonstrates however the potential for significant injury resulting from the inhalation into the respiratory tract.

Irritation and Sensitisation

Skin irritation in a study was reported following 24 hours of exposure. It is expected that the extended timeframe may result in increased irritation as compared to a shorter exposure period. Based on the skin irritation studies available for analogue chemicals 5 and 6 conducted over 4 hours, the notified chemical is likely to be non-irritating or slightly irritating.

Based on eye irritation studies for four analogue chemicals, the notified chemical is likely to be slightly irritating to the eye.

One of three sensitisation studies showed limited evidence of skin sensitisation. Responses were higher at 24 hours than at 48 hours and may have attributed to irritation rather than sensitisation. The two other studies were negative. Overall, the notified chemical is not likely to be sensitising to the skin.

Repeated Dose Toxicity
A preliminary dose range finding study was conducted with an analogue chemical to evaluate dose levels for a definitive toxicity/reproduction study.

Male and female Sprague dawley rats (30/sex/group) were dosed 0, 100, 500 or 1000 mg/kg bw/day, by oral gavage, once daily, for 4 weeks prior to mating and through lactation day 20. Twenty male and female pups/group (the F1 generation) were then dosed commencing on Day 22 of parturition for a total of a minimum of 90 days.

There were no test article related deaths during the study. Some animals were euthanised in all dose groups due to not producing litters. One F0 female in the high dose group was euthanised due to the loss of her entire litter. One F1 male in the 500 and 1000 mg/kg bw/d group and one F1 female in the 100 mg/kg bw/d group were found dead. As these animals had no clinical signs corresponding to toxicity, the deaths of these animals are likely due to gavage error as indicated by the perforated esophagus of the low dose female.

Body weight gain and food consumption were generally comparable to control animals at all dose levels, with the exception of decreased body weight gains in high dose females during week 4. Clinical signs or gross necropsy findings were sporadically manifested throughout the dose groups (F0 and F1) and included, but not limited to, hair loss, soft stools, scabs, unkempt appearance (which was more apparent in high dose F0 females), reddish staining, discharge or fluid, dark material around the eyes, nose and mouth, malalignment, incisor trimming, lacrimation, salivation, urine staining, rales, oily material around the neck, digit swelling, dehydration, mammary swelling, and axillary palpable masses. There were no dose relation or effects that could be correlated to the test substance noted amongst the findings, except for the exception above.

There were no differences in fertility indices (including pup viability, body weights, external observations) in any group as compared to the control group. There were no abnormal macroscopic findings in the pups that were not selected or were found dead prior to necropsy.

At study termination, a slight increase of prothrombin time was noted in F1 high dose males. The toxicological significance of this remains unclear. Although there were some changes in the 500 mg/kg bw/d F1 females (decreased MCHC and prothrombin time and increased erythrocytes and hematocrit), these were considered slight and of no toxicological significance. There were no treatment related biochemical, gross or microscopic histopathology findings.

Minor clinical signs and slight differences in hematology parameters were observed in animals dosed 1000 mg/kg bw/day and no toxicologically significant adverse effects were observed in animals dosed at 500 mg/kg bw/day. Therefore a NOEL of 500 mg/kg bw/d is provided indicating low systemic and reproductive hazard.

Mutagenicity
Analogue chemicals were non mutagenic in bacteria reverse mutation, not genotoxic in chromosomal aberrations in human lymphocytes in vitro, and not genotoxic in mouse micronucleus test in vivo. The mutagenic potential of an analogue chemical in the study of mutagensis in Chinese Hamster Ovary cell in vitro was inconclusive under the study condition. The study contained a confirmatory trial. The test article concentrations ranged from 313 to 5000 μg/ml. The first trial exhibited no differences in relative cloning efficiencies (RCEs) without metabolic activation. Contamination of cells conducted with metabolic activation invalidated the results and therefore this portion of the study was re-initiated. An increase in the number of mutants at 625 μg/ml was observed as compared to the control with metabolic activation. During the confirmatory trial, this increase in mutants was not observed at the same dose level, but at 2500 μg/ml. As there was no dose relationship and the number of mutants fell within the historical laboratory number, the test article utilised in the study was concluded to be non mutagenic. The positive control (with activation) had a range of average number of mutants per dose from approximately 200-400, while analogue chemical 5 had an average number of mutants of 8-9 indicating a lower potential for inducing mutations. Overall, the mutagenic potential of analogue chemical 5 in this study was equivocal.

Overall, the notified chemical is not likely to be genotoxic.

Based on the available data, the notified chemical is not classified as a hazardous substance in accordance with the *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2004).

Based on available data, the notified chemical is not classified as R65 (aspiration hazard). However, the notified chemical should be classified as R65 if it meets viscosity criteria.

9.2.4. Occupational health and safety – risk characterisation

Acute exposure

There is a risk of skin irritation experienced by lubricant blenders and end users as the lubricant contains up to 90% of notified chemical. Dermal exposure is likely to be low due to the highly controlled environment but may occur if the workers do not conform to safe practices. The risk of slight skin irritation will need to be controlled by the use of adequate PPE, particularly impervious gloves and protective clothing. Workers should also avoid eye contact as the notified chemical is slightly irritating to the eyes. Inhalation exposure and risk is likely to be low in the scenarios described.

Repeated dose exposure

Based on a NOEL of 500 mg/kg bw/day, derived from a 91-day rat oral study the margin of exposure (MOE) for various activities are as follows:

Activity	*Estimated exposure for notified chemical <mg/kg bw/day>*	*Margin of Exposure (MOE)*
Manual addition of liquids	6	83
Coupling and decoupling of transfer line	0.6	830
Quality control sampling	0.3	1670

The MOE for blenders under "manual addition of liquids" will be the same as for end users of products containing the notified chemical. MOE greater than or equal to 100 accounting for intra- and inter-species differences are considered acceptable. The above table suggests that the risk of systemic effects may not be acceptable during manual operations, unless workers have appropriate skin and eye protection during blending and end use.

9.2.5. Public health – risk characterisation

The risk to the public from manual addition of products containing the notified chemical (up to 90%) to automobiles or other machinery is considered acceptable as the frequency of use will be limited. The MSDS contains adequate information to warn users regarding the hazards in the lubricant.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

Based on available data, the notified chemical is not classified as R65 (aspiration hazard). However, the notified chemical should be classified as R65 if it meets viscosity criteria.

and

As a comparison only, the classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Aspiration hazard	1	May be fatal if swallowed and enters airways

10.2. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

Under the conditions of the occupational settings described, the notified chemical not considered to pose an unacceptable risk to the health of workers.

10.3.2. Public health

When used in the proposed manner, the notified chemical not considered to pose an unacceptable risk to public health.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was in accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for the notified chemical provided by the notifier was in accordance with the *National Code of Practice for the Labelling of Workplace Substances* (NOHSC 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - Local exhaust ventilation

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Spillage should be avoided; spills should be should be cleaned up promptly with absorbents which should be put into containers for disposal; avoid contact with eyes and skin

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Goggles, chemical resistant gloves, overalls, and protective clothing
  - Respiratory protection, where exposure to aerosol is likely

  Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)], workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Public health

- The following measures should be taken by end users to minimise public exposure to the notified chemical:
  - Avoid skin and eye contact
  - Wear gloves

Environment

- The following measures should be implemented for release of the notified chemical to the environment:
  - If emergency personnel are unavailable, contain spilled material. For small spill add absorbent material, scoop up and place in a sealed, liquid proof container for disposal. For large spills dike spilled material or otherwise contain material to ensure runoff does not reach waterway.

Disposal

- Avoid contact of spilled material and runoff with soil and surface waterways. Consult an environmental professional to determine if local, regional or national regulations would classify spilled or contaminated materials as hazardous waste. Dispose of in accordance with all applicable local and national regulations.

Storage

- Keep container tightly closed. Keep container in a cool, well ventilated area. Empty containers may contain harmful, flammable/combustible or explosive residue or vapours. Do not cut, grind, weld, reuse or dispose of containers unless adequate precautions are taken against these hazards.

Emergency procedures

- Contain spilled material. For small spill add absorbent. Scoop up material in a sealed, liquid-proof container for disposal. For large spills contain material to ensure runoff does not reach waterway.

12.1. Regulatory Obligations

This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from as a base fluid for the blending of fully formulated synthetic automotive and industrial lubricants, or is likely to change significantly;
- the amount of chemical being introduced has increased from 100 tonne per annum, or is likely to increase, significantly;
- if the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

No additional secondary notification conditions are stipulated.

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