File No: STD/1295

May 2008

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Z-85

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

TABLE OF CONTENTS

FULL PUBLIC REPORT

Z-85

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Lubrizol International Inc. (ABN 52 073 495 603)
28 River Street
SILVERWATER NSW 2128

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, Other Names, CAS Number, Molecular and Structural Formulae, Molecular Weight, Spectral Data, Impurities, Purity, Use Details, Import Volume, Details of analogue (for toxicology)

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Dissociation constant, Flammability limits, Acute inhalation toxicity, Induction of germ cell damage, Bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
No

NOTIFICATION IN OTHER COUNTRIES
USA

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Z-85

OTHER NAME(S)
OS220148B
564C-24502E

ANALYTICAL DATA
Reference NMR, IR, HPLC,UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 80%

HAZARDOUS/NON HAZARDOUS IMPURITIES

Chemical Name	Triester derivatives		
CAS No.	Not assigned	*Weight %*	< 10%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Pale amber coloured solid block with a tan coloured liquid.

Property	Value	Data Source/Justification
Melting Point/Freezing Point	39°C	Measured
Boiling Point	382°C at 101.3 kPa	Measured
Density	963 kg/m^3 at 20 ± 0.5°C	Measured
Vapour Pressure	1.2 x 10^{-5} kPa at 25°C	Measured
Water Solubility	< 2.6 x 10^{-4} g/L at 20°C	Measured
Hydrolysis as a Function of pH	Half-lives of 15.8 days at pH 8 and 158 days at pH 7	Estimated
Partition Coefficient (n-octanol/water)	log Pow > 9.4	Measured (temperature not specified)
Adsorption/Desorption	log K_{oc} > 5.63	Measured (temperature not specified)
Dissociation Constant	Not determined	No dissociable functionality
Flash Point	174 ± 2°C at 102.22 kPa	Measured
Flammability	Not predicted to be highly flammable	Estimated based on chemical structure and low vapour pressure.
Autoignition Temperature	366 ± 5°C	Measured
Explosive Properties	Not predicted to be explosive	Estimated based on chemical structure and oxygen balance.
Oxidising Properties	Not predicted to be an oxidising agent.	Estimated based on chemical structure.

DISCUSSION OF PROPERTIES
The notified chemical is insoluble in water, hydrophobic and non-volatile. It is not expected to pose a physical hazard.

For full details of tests on physical and chemical properties, please refer to Appendix A.

Reactivity
There are no known hazardous decomposition products or incompatibility with other substances. The notified chemical is expected to be stable under normal environmental conditions.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported in the neat form (> 80%) or within a lubricant additive package at a concentration of < 20% for reformulation into engine oil products.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 100	< 100	< 100	< 100	< 100

PORT OF ENTRY
Western Australia, Queensland and Victoria

IDENTITY OF MANUFACTURER/RECIPIENTS
Lubrizol International Inc.
28 River Street
Silverwater NSW 2128

TRANSPORTATION AND PACKAGING
The notified chemical will be imported by sea as a neat substance (> 80%) or as a component of a product (< 20%) in 205 L steel drums or 20 MT iso-containers. It will be transported by road or rail from wharf to customer sites for further formulation.

USE
The notified chemical is a lubricant additive for use in engine oils at concentrations of < 5%. Engine oils containing the notified chemical will be used in vehicle manufacturing, mechanical workshops and by members of the public for DIT use.

OPERATION DESCRIPTION

Reformulation of concentrate product
The notified chemical may be imported neat (at > 80%) and transported to the reformulation site where it will be pumped into a storage tank or extracted by suction until use. It will then be pumped using sufficient pressure directly into the blend vessel using an automated procedure. The pipes will be cleaned between transfers using a device known as a 'pig', which is magnetic and involves minimal human exposure. After production, concentrated product containing the notified chemical at < 20% will typically be loaded into isocontainers or drums directly from the blend vessel. These containers will then be stored unopened in a covered warehouse until they are shipped to customers for further blending into the final product.

Blending of engine oil products
At customer blending sites, the concentrate product containing the notified chemical at < 20% will be formulated into engine oil products by mixing with oil and other additives. It will be either decanted from drums or isocontainers into a trough from which it will be pumped into a blend tank, or pumped directly into the blend tank. Blend facilities are expected to be fully automated closed systems.

After blending, the engine oil products containing the notified chemical will be packaged into containers ranging from 1 to 205 L. The packaging facility will usually be located near the blending operation area and the transfer of product to the packaging is expected to be fully automated.

Sampling from blend vessels may take place during the blending process at the reformulation of concentrate product stage or in the blending of engine oil products. A plant operator would open a valve in the vessel and fill a small container for testing.

End use
Engine oil products containing < 5% of the notified chemical will be used in factories where cars are manufactured, and in mechanical repair garages. For the car manufacturers, engine oil products may be delivered in larger containers such as isocontainers (especially to larger operations). Alternatively, the engine oil products containing the notified chemical may be packaged in smaller containers (1 L or 5 L) for retail sale. The 1 L containers are intended to be used as oil 'top-up', whereas the 5 L containers are usually used during complete oil changes by mechanics or DIY users.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Numbe per siter*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Reformulation of concentrate product			
Transport and storage	2-3	1-3	4-6
Plant operator	2-3	< 1	50
Maintain/clean	2-3	2-4	10-20
Plant operator - sampling	1	<1	100
Blending of engine oil products			
Plant operator	2-3	< 1	50
Maintain/clean	2-3	2-4	10-20
Packaging	2-8	2-4	50
End user	1-3	2-4	Typically < 20

EXPOSURE DETAILS

Transport and Storage
Exposure to the notified chemical (up to > 80%) during transport or storage is unlikely except in the case of accidental spillage or breach of packaging.

Reformulation of concentrate product
Dermal exposure to the neat notified chemical (> 80%) is possible when plant operators are connecting and disconnecting pump lines to storage tanks or blending vessels, as it is possible that residues may be present on equipment used. Dermal and ocular exposure is also possible from spills and splashes. The opportunity also exists for dermal exposure (< 20%) when cleaning up spills or leaks and during maintenance of the blend vessel. It is expected that negligible exposure will occur during the fully automatic and closed blending process. However, maintenance is not expected to occur frequently as residue in the blending vessel will be used for the next blend. No exposure is expected during transfer of the concentrate product containing the notified chemical (< 20%) to packaging as this will be carried out using automated processes. In all cases where there is potential for exposure, workers are expected to wear gloves, goggles and a long sleeved shirt as minimum personal protective equipment (PPE). Inhalation exposure is expected to be negligible given the very low vapour pressure of the notified chemical (1.2×10^{-5} kPa). The potential for aerosol generation is not expected to be significant given the viscosity of the engine oil products. In addition, blending and packaging facilities are expected to be well ventilated.

Blending of engine oil products
The potential for dermal and ocular exposure to the notified chemical during blending of the final product is expected to be similar to that described above for reformulation of the concentrate product. However, the concentration of the notified chemical will be < 20% prior to blending and < 5% in the final product. The notifier states, however, that the concentrate containing the notified chemical (< 20%) may be decanted into a trough prior to blending. In these circumstances there is increased potential for dermal and ocular exposure from spills, drips and splashes. In all cases where there is potential for exposure workers are expected to wear gloves, goggles and a long sleeved shirt as minimum PPE to limit exposure.

Sampling
At blending facilities for the concentrate product and the final product, samples will be taken from blend vessels during the blending process. Dermal exposure may occur when a plant operator will open a valve and fill a small container. To minimise exposure the plant operator will wear gloves, goggles and a long sleeved shirt as minimum PPE.

End use
Filling of engine oil products will occur at car manufacturers and at workshops by mechanics. At car manufacturers, formulated oil containing the notified chemical will be transferred mechanically from drums to vehicle engines using a dip-pipe and pump. There is potential for dermal exposure from drips, spills and splashes during the connection and disconnection of the dip-pipe and pump as well as from handling automotive components contaminated with the engine oil. The notifier states that while workers are not expected to encounter ocular exposure, appropriate PPE to be worn to minimise any potential dermal and ocular exposure.

Professional users such as mechanics, may experience dermal and ocular exposure to final products containing < 5% of the notified chemical when adding the products to automobiles and other machinery. Dermal exposure may be significant if good hygiene practices are not followed during these procedures. Exposure would be minimised by the use of gloves, goggles and a long sleeved shirt.

6.1.2. Public exposure
DIY users may experience dermal and ocular exposure to final products containing < 5% of the notified chemical when adding the products to automobiles and other machinery. Exposure would be minimised if users wear gloves, goggles and a long sleeved shirt. Overall, public exposure is expected to be limited due to its infrequent use, assuming that most consumers do not change their own engine oil.

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical or on a structurally related analogue are summarised in the table below. The notifier stated that the rat acute oral LD_{50} of the analogue chemical was > 2,500 mg/kg – similar to that of the notified chemical. In addition, the differences between the two chemicals were analysed in relation to their expected physicochemical properties and toxicological profiles. The two chemicals were found to be sufficiently similar for assessment by analogy. The details of the toxicological investigations can be found in Appendix B.

Endpoint	*Test substance*	*Result and Assessment Conclusion*
Rat, acute oral toxicity	Notified chemical	LD50 > 2000 mg/kg bw low toxicity
Rat, acute dermal toxicity	Analogue	LD50 > 2000 mg/kg bw low toxicity
Rabbit, skin irritation	Analogue	slightly irritating
Rabbit, eye irritation	Analogue	severely irritating
Mouse, skin sensitisation – Local lymph node assay	Analogue	no evidence
Rat, repeat dose oral toxicity – 28 days.	Analogue	NOAEL = 1000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	Notified chemical	non mutagenic
Genotoxicity – in vitro chromosome aberration	Analogue	non genotoxic

Toxicokinetics, metabolism and distribution.
Absorption through the skin is unlikely given the high log Pow (> 9.4). However, the high log Pow value and low molecular weight suggest absorption may occur through the gastrointestinal tract. The systemic effects observed in the repeat dose toxicity study on the analogue chemical indicate that absorption may occur via this route, although its extent is unknown.

Acute toxicity.
The notified chemical and its analogue were both of low acute oral toxicity and the analogue was of low acute dermal toxicity. Toxicity via inhalation is likely to be low based on the low vapour pressure and low oral toxicity of the notified chemical.

Irritation and Sensitisation.
An acceptable analogue of the notified chemical was found to be severely irritating to the eyes based on a Rabbit Enucleated Eye Test (REET). The REET was performed in place of an *in vivo* acute eye irritation/corrosion test because the analogue chemical was suspected to be strongly irritating and/or corrosive. Treatment of enucleated rabbit eyes with the analogue chemical for 10 secs yielded the following effects: corneal opacity, sloughing, corneal swelling and fluorescein uptake. Based on these effects the analogue chemical was considered to have the potential to cause severe ocular irritation and therefore an *in vivo* study was not performed due to animal welfare concerns. The notified chemical, based on its similarity to the analogue, is expected to be severely irritating to the eye.

An acceptable analogue of the notified chemical was found to be slightly irritating to the skin. The analogue had pH = 1 indicating the potential for severe irritation or corrosion. Therefore, as a pre-screening test, the Transcutaneous Electrical Resistance (TER) Assay was performed. After treatment with the analogue chemical, the electrical conductivity across rat skin did not increase significantly indicating that it was unlikely to be corrosive. Further tests were conducted *in vivo* in rabbits, with a single application of the analogue chemical applied using a semi-occluded dressing. No adverse reactions were observed upon application of the analogue chemical for 3 minutes and 1 hour. However, after application for 4 hrs, well-defined erythema was observed in two animals persisting in one to 48 hrs. Very slight oedema was observed in two animals persisting in one to 48 hrs. Slight desquamation was also observed in two animals, 7 days after treatment. Therefore, the analogue of the notified chemical is considered to be slightly irritating to skin, but these effects were not sufficient for the analogue to be classified according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC: 1008 (2004)]. Based on its similarity to the analogue, the notified chemical can be expected to be slightly irritating to skin.

The notified chemical is not expected to be sensitising, as there was no evidence of skin sensitisation in a mouse local lymph node assay (LLNA) on an acceptable analogue of the notified chemical at concentrations up to 25%.

Repeated Dose Toxicity.
In the 28-day repeat dose oral toxicity study on an acceptable analogue of the notified chemical, increased liver weights and centrilobular hepatocyte enlargement were observed in males and females treated with 1000 mg/kg bw/day. As no necrotic or inflammatory changes were observed, these effects were considered to be adaptive changes.

Treatment-related increases in kidney weights were observed in males treated with 1000 mg/kg bw/day ($p<0.05$). Globular eosinophilic depositions were found in the tubular epithelium of males dosed at 150 and 1000 mg/kg bw/day. These effects were considered to be male-rat specific changes, typical of a hydrocarbon nephropathy that does not occur in female rats and other species. These effects were not considered to be relevant to human health evaluation.

The No Observed Adverse Effect Level (NOAEL) for the notified chemical is expected to be 1000 mg/kg bw/day, based on the absence of observed adverse effects at this dose level in a study on the analogue chemical.

Mutagenicity.
The notified chemical was found to be non-mutagenic in a bacterial reverse mutation test. An analogue of the notified chemical showed no evidence of clastogenicity to human lymphocytes *in vitro*, either with or without metabolic activation. Based on these results, the notified chemical is not suspected to be a mutagen or carcinogen.

Classification
The REET was conducted according to Good Laboratory Practices (GLP) and the notified chemical can be reasonably expected to produce severe eye irritation *in vivo*. In its most recent *Manual of Decisions*, the European Chemicals Bureau (ECB) states that a positive result in the REET is sufficient for classification with *R41 Risk of serious damage to eyes* (ECB, 2006).

Therefore, the notified chemical should be considered as though classified as:

R41 - Risk of serious damage to eyes

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Based on the available data, the notified chemical may cause severe eye damage and therefore scenarios involving ocular exposure are of greatest concern. The concentration cut-off levels for mixtures containing severe eye irritants are ≥ 10% for classification as R41 and ≥ 5% to < 10% for classification as R36 (NOHSC, 2004). These cut-off levels would apply to the notified chemical as imported (> 75%) and in the reformulated concentrate product (< 20%) but not in the final engine oil product (< 5%).

Transport and warehouse workers and plant operators involved in reformulation of the concentrate product would be at a high risk of eye damage, if ocular exposure to the notified chemical occurred during handling of the imported neat form (> 75%). Maintenance workers and plant operators would also be at risk of eye damage if ocular exposure to the notified chemical (< 20%) occurred during cleaning of reformulation equipment or during handling of the concentrate product prior to blending into the final product.

Workers involved in blending of the final product and maintenance of the blending equipment may also be at risk of eye irritation. However, the risk posed to these workers is considered to be lower given the lower concentration of the notified chemical in these products (< 5%).

In all worker activities, the risk of eye damage or irritation would be minimised by the use of recommended eye/face protection at all times.
Given the low severity of observed effects in the rabbit test, and given the anticipated use of gloves and a long sleeved shirt to minimise exposure to the skin, the risk of skin irritation to dermally exposed workers is not considered to be unacceptable.

6.3.2. Public health

The risk to the public is not considered unacceptable assuming that most consumers do not change their own engine oil. For DIY users changing their own engine oil containing the notified chemical, there is a risk of adverse eye effects resulting from ocular exposure during the draining of used engine oil. However, the risk is not considered unacceptable, given that draining of engine oil is an infrequent event and the concentration of the notified chemical in the engine oil is < 5%.

There is also potential for skin irritation in DIY users exposed to splashes, drips and spills of engine oils containing the notified chemical when changing their own engine oil. The risk is not considered to be unacceptable given the limited adverse effects observed in the skin irritation study, the infrequent handling of engine oil containing the notified chemical and the low concentration of the notified chemical in engine oil products (< 5%).

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

At the blending facilities, release during the highly automated blending process is not expected. The equipment used will be cleaned with oil and these washings will be used in the formulation of the next batch or another oil blend. In these situations release would occur through accidental spills, which would be recycled or collected for incineration. Any of the notified chemical remaining in the import containers, expected to be < 1% of the contents, which is equivalent to up to 1000 kg of the notified chemical, would be washed out and recycled or collected for incineration.

RELEASE OF CHEMICAL FROM USE

Some minor, diffuse exposure will result from spills during addition to and removal of oil from vehicles. Around 86% of oil changes take place in specialised automotive service centres, where release of the notified chemical from professional activities should be disposed of appropriately. The remaining 14% will be removed by DIY enthusiasts. The DIY proportion of oil changes could potentially lead to improper disposal of used oil (55%) to soils or sediments and stormwater drains.

RELEASE OF CHEMICAL FROM DISPOSAL

Iso-containers and drums should be sent for cleaning and reconditioning by a licensed company. The resultant washings from such companies are typically passed to an on site waste treatment facility and any waste sludge is typically incinerated.

Used oil, drained from crankcases at specialised automotive service centres is expected to be disposed of either to oil recycling centres or to incineration.

A survey tracing the fate of used lubricating oil in Australia (Snow, 1997) found that only around 20% of used oil removed by enthusiasts is collected for recycling, approximately 25% is buried or disposed of in landfill, 5% (700 kg of the notified chemical) is disposed of into stormwater drains and the remaining 50% is used in treating fence posts, killing grass and weeds or disposed of in other ways.

7.1.2 Environmental fate

The notified chemical is expected to float and spread following accidental introduction into aquatic environments, with adsorption to sediment the major fate process.

For the details of the environmental fate studies please refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

A worst case estimated PEC might be calculated if it is assumed that 0.7% of the notified chemical (maximum 700 kg) is released into stormwater drains in a single metropolitan area with a geographical footprint of 500 km^2 and an average annual rainfall of 500 mm, all of which drains to stormwater. 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 x 10^6 m^3, the resultant PEC is approximately 2.8 µg/L. It should be stressed that this result is a worst case scenario, as in reality releases of the notified chemical would be more diffuse and at lower levels.

7.2. Environmental effects assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Test substance*	*Result*	*Assessment Conclusion*
Fish Toxicity	Analogue	96-hr LC50 > 0.78 mg/L	Not toxic to *Onchorhynchus mykiss* up to the limit of water solubility (time-weighted mean concentration).
Daphnia Toxicity	Notified chemical	EC50 > 82 mg/L of WAF Acute	Some toxicity to *Daphnia magna* up to the limit of the water solubility.
	Analogue	21-day EC50 > 0.1 mg/L Chronic	Toxic to *Daphnia magna*.
Algal Toxicity	Analogue	EC50 > 0.55 mg/L	Not toxic to algae to the limit of its water solubility.
Inhibition of Bacterial Respiration	Analogue	EC50 > 1000 mg/L	Not considered harmful to bacterial respiration.

The notified chemical shows some toxicity to *Daphnia* up to the limit of its water solubility.

7.2.1 Predicted No-Effect Concentration

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
21 day EC50 (Daphnia Chronic from Analogue)	> 0.10	mg/L
Assessment Factor	50.00	
Mitigation Factor	1.00	
PNEC:	> 2.0	µg/L

7.3. Environmental risk assessment

Insert the Risk Quotient Table (PEC/PNEC)

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	2.8	> 2.0	< 1.4
Q - Ocean	0.28	> 2.0	< 0.14

Based on the data from an acceptable analogue of the notified chemical, the calculated Q - River is just above the acceptable threshold (1.0), which could indicate a potential risk to the river compartment. However, the calculated result would be very much a worst-case scenario, and in reality most of the notified chemical would be readily absorbed by the sludge deposit as the result of its high absorption/desorption (log K_{oc} 5.63). The practical Q-River would thus be predicted to be lower than 1.0, which means the actual risk of the notified chemical to river compartment would not be unacceptable.

The notified chemical is not considered to pose an unacceptable risk to ocean environment based on the Q - ocean.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

A Rabbit Enucleated Eye Test (REET) was performed on an acceptable analogue of the notified chemical. The REET was performed in place of an in vivo acute eye irritation/corrosion test because the analogue chemical was suspected to be strongly irritating and/or corrosive.

The REET is conducted according to Good Laboratory Practices (GLP) and the test results can be reasonably expected to produce severe eye irritation *in vivo*. In addition, the European Chemicals Bureau (ECB) believes that a positive result in the REET is sufficient for classification with R41 Risk of serious damage to eyes (ECB, 2006). Therefore, the notified chemical should be considered as though it is classified as:

R41 - Risk of serious damage to eyes

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***
Environment	Acute Category 2 Chronic Category 2	Toxic to aquatic life Toxic to aquatic life with long lasting effects.
Human Health	Category 1	Danger: Causes serious eye damage

Human health risk assessment

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

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

Environmental risk assessment

On the basis of the PEC/PNEC ratio and the reported use pattern, the notified chemical is not considered to pose a risk to the environment.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Employers should implement the following safe work practices:
  - *Eyewash stations should be maintained at all sites where the notified chemical (as introduced and in the reformulated concentrate) is handled.*

- The Office of the ASCC, Department of Employment and Workplace Relations (DEWR), should consider the following health hazard classification for the notified chemical:
  - *R41 May cause serious eye damage*

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - *≥10%: R41 May cause serious damage to eyes*
  - *5%≤ conc ≤10%: R36 Irritating to eyes*

CONTROL MEASURES
Occupational Health and Safety

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational risk to the notified chemical as introduced (> 75%) and in the reformulated concentrate containing the notified chemical (< 20%):
  - *Eye/face protection.*

  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.

Disposal

- The notified chemical should be disposed of by incineration or to landfill.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
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(1) of the Act; if

- the notified chemical is used in products for sale to the public at concentrations ≥ 5%.

or

(2) Under Section 64(2) of the Act; if

- the function or use of the chemical has changed from lubricant additive for use in engine oils, or is likely to change significantly;
- the amount of chemical being introduced has increased from 100 tonnes 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.

Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point 39°C

Method	OECD TG 102 Melting Point/Melting Range.
Remarks	The DSC method was employed
Test Facility	Safepharm (2007a)

Boiling Point 382°C at 101.3 kPa

Method	OECD TG 103 Boiling Point.
Remarks	The DSC method was employed. The notified chemical bubbled from 220°C and changed to a light brown colour from about 280°C. This observation is possibly indicative of decomposition.
Test Facility	Safepharm (2007a)

Density 963 kg/m^3 at 20 ± 0.5°C

Method	OECD TG 109 Density of Liquids and Solids.
Remarks	Pycnometer method.
Test Facility	Safepharm (2007a)

Vapour Pressure 1.2 x 10^{-5} kPa at 25°C

Method	OECD TG 104 Vapour Pressure.
Remarks	Determined with a vapour pressure balance between 23-33°C.
Test Facility	Safepharm (2007b)

Water Solubility < 2.60 x 10^{-4} g/L at 20°C

Method	OECD TG 105 Water Solubility.
Remarks	Determined using the Flask Method. HPLC used for concentration analysis. No peaks of test material were detected in definitive tests with HPLC, indicating very low water solubility of the test chemical. Using chemical estimation software WSKOWWIN, version 1.41, © 2000 US Environmental Protection Agency, the test material has a predicted water solubility of 4.197 x 10^{-6} mg/L.
Test Facility	Safepharm (2007a)

Hydrolysis as a Function of pH Half-lives of 15.8 days at pH 8 and 158 days at pH 7

Method	Estimated using HYDROWIN version 1.67, © 2000 US Environmental Protection Agency.
Remarks	A hydrolysis test could not be conducted according to OECD TG 111 due to the essentially insolubility and complex nature of the notified chemical. Hydrolysis of the notified chemical was therefore, estimated using Episuite computer-based estimation software, indicating hydrolysis could be an important factor under alkaline conditions.
Test Facility	Safepharm (2007a)

Partition Coefficient (n-octanol/water) log Pow > 9.4 (temperature not specified)

Method OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks HPLC Method. The dead time was determined by using Thiourea. The column temperature was set as 30ºC. The partition coefficient has been test as Log Pow > 9.40 because the retention time was longer than that of 1-penyltridecane. High Pow is expected according to the low water solubility of the notified chemical.
Test Facility Safepharm (2007a)

Adsorption/Desorption – screening test log K_{oc} > 5.63

Method OECD TG 121 Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC).
Remarks HPLC screening method was used. The dead time was determined by using formamide. Column temperature was set as 30˚C. Testing was carried out at neutral pH due to the absence of any possible dissociating functional groups in the notified chemical. The retention time of the notified chemical was longer than DDT. High K_{oc} is expected from the high P_{ow} and the low water solubility of the notified chemical.
Test Facility Safepharm (2007a)

Flash Point 174 ± 2ºC at 102.22 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Remarks Closed cup method
Test Facility Safepharm (2007b)

Autoignition Temperature 366 ± 5ºC

Method EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Test Facility Safepharm (2007b)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE Notified chemical

METHOD
- Species/Strain: Rat/Sprague-Dawley
- Vehicle: Arachis oil BP
- Remarks - Method: No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	1 F	2000	0/1
4	4 F	2000	0/4

- LD50: >2000 mg/kg bw
- Signs of Toxicity: There were no signs of systemic toxicity.
- Effects in Organs: There were no remarkable necropsy findings.
- Remarks - Results: None

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

TEST FACILITY SafePharm (2007c)

B.2. Acute toxicity – dermal

TEST SUBSTANCE Acceptable analogue of notified chemical

METHOD
- Species/Strain: Rat/Sprague-Dawley
- Vehicle: Test substance administered as supplied.
- Type of dressing: Semi-occlusive.
- Remarks - Method: No significant protocol deviations.

RESULTS

Number and Sex of Animals	*Dose mg/kg bw*	*Mortality*
5 M	2000	0/5
5 F	2000	0/5

- LD50: >2000 mg/kg bw
- Signs of Toxicity - Local: None
- Signs of Toxicity - Systemic: There were no treatment related clinical signs observed.
- Effects in Organs: There were no treatment related effects observed in organs.
- Remarks - Results: None

CONCLUSION The notified chemical, based on its similarity to the analogue, may be expected to be of low toxicity via the dermal route.

TEST FACILITY Safepharm (2006a)

B.3. Irritation – skin

TEST SUBSTANCE: Acceptable analogue of notified chemical

METHOD

Species/Strain	Rabbit/New Zealand White
Number of Animals	3 (1 M, 2 F)
Vehicle	Test substance administered as supplied
Observation Period	7 days
Type of Dressing	Semi-occlusive.
Remarks - Method	The notified chemical was thought to be corrosive given a pH =1. Therefore before testing *in vivo,* a pre-test (Transcutaneous Electrical Resistance Assay) was conducted on rat skin. This predicted the notified chemical was not corrosive. A stepwise procedure involving 3-min and 1-hr semi-occluded applications of the notified chemical to one rabbit did not produce corrosive effects. Upon seeing no corrosive results after the 1-hr application, a main study involving a 4-hr application was conducted. The three rabbits (1 M, 2 F) used in the main study originated from two different suppliers. This was not considered to have a significant effect on the outcome of the study.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0.33	1.67	1.33	2	72 hrs	0 D
Oedema	0	0.67	0.33	1	48 hrs	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.
D = Slight desquamation

Remarks - Results	After semi-occluded application for 4 hrs, very slight erythema was observed in the male at 24 hrs but was not observed at 48 hrs. Well-defined erythema was observed in the two female rabbits at 24 hrs and persisted in one to 48 hrs. Very slight oedema was observed in two female rabbits at 24 hrs and persisted in one to 48 hrs. 7 days after treatment with the notified chemical, slight desquamation was observed in the two female animals.

CONCLUSION: The notified chemical, based on its similarity to the analogue, may be expected to be slightly irritating to the skin.

TEST FACILITY: Safepharm (2006b)

B.4. Irritation – eye

TEST SUBSTANCE: Acceptable analogue of notified chemical

METHOD: Rabbit Enucleation Eye Test (REET), conducted according to GLP. The Rabbit Enucleation Eye Test was conducted in place of the OECD TG 405 Acute Eye Irritation/Corrosion test.

Species/Strain	Rabbit
Number of Animals	3
Observation Period	240 minutes
Remarks - Method	Five enucleated rabbit eyes were excised and allowed to equilibrate for 30 mins in a Perspex clamp placed within a superfusion chamber. Saline solution was allowed to irrigate the surface of the cornea via a saline drip in the rear of the chamber. The eyes were re-examined after 30 mins of

equilibration to ensure that no signs of irritation resulted from the excision. Corneal thickness was measured using an ultrasonic pachymeter. Any eyes with corneal swelling greater than 10% of the pre-enucleation measurement or stained with fluorescein were discarded.
After inspection proceeding equilibration, three eyes held by Perspex clamps were removed from the superfusion chamber and placed horizontally into a petri dish. 0.1 ml of the notified chemical (undiluted) was applied evenly to the surface of the cornea of three eyes. After ten seconds the notified chemical was washed off using a minimum 20 ml of saline solution.
After treatment, the eyes were returned to the superfusion chamber as per pre-treatment.
The remaining two eyes remained untreated and served as controls.

The thickness of the cornea was measured using an ultrasonic pachymeter pre-enucleation, post-equilibration and 60, 120, 180 and 240 mins following treatment. For each enucleated eye a measurement was made at the optical centre, and at four other locations at the apex of the cornea. A mean value for corneal thickness was calculated based on these four measurements. The corneal thickness for each eye 60, 120, 180 and 240 mins following treatment was used to calculate the percentage change compared with the corneal thickness pre-treatment.
Corneal cloudiness was assessed pre-enucleation, post-equilibration and approximately 60, 120, 180 and 240 mins following treatment. Examination of the eye was assessed using a slit-lamp biomicroscope.
The uptake of fluorescein by the corneal epithelium was assessed pre-enucleation, post-equilibration and approximately 240 mins following treatment using a cobalt blue filter of the split-lamp biomicroscope after application of Fluorescein Sodium drops.

RESULTS

Corneal cloudiness was observed in all test eyes during the study. Cloudiness persisted at the same level at all observation periods.
Sloughing was observed in all test eyes from 120 mins to 240 mins following treatment.
Fluorescein uptake was observed in all test eyes at 240 mins following treatment.
Corneal swelling was observed in all test eyes with a maximum value of 113.9% of the thickness of the cornea post-equilibration.

Remarks - Results

The results of the REET indicated the potential for severe eye irritation. Accordingly, the *in vivo* eye irritation test was considered unnecessary and was not performed in the interests of animal welfare.

CONCLUSION

The notified chemical, based on its similarity to the analogue, may be expected to be severely irritating to the eye.

TEST FACILITY

Safepharm (2006c)

B.5. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE

Acceptable analogue of notified chemical in acetone/olive oil (4:1)

METHOD

OECD TG 429 Skin sensitisation: Local Lymph Node Assay.

Species/Strain

Mouse/CBA/Ca CruBR

Vehicle

Acetone/olive oil (4:1)

Remarks - Method

No significant protocol deviations.
Test concentrations were chosen on the basis of a preliminary screening test. A-Hexylcinnamaldehyde (Tech. 85%) was used as a positive control to test the sensitivity of the strain of mouse.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	2241.76	
5	2236.38	1.00
10	2872.57	1.28
25	5919.70	2.64
Positive Control		
5		3.53
10		5.39
25		8.23

Remarks - Results: No signs of systemic toxicity were noted.
At all concentrations the mean DPM was not significantly different ($p \geq 0.05$) to the vehicle control group. A stimulation index of <3 was recorded for all concentrations tested.

CONCLUSION: There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the analogue chemical. Therefore, the notified chemical, based on its similarity to the analogue, is not expected to be sensitising.

TEST FACILITY: Safepharm (2006d)

B.6. Repeat dose toxicity

TEST SUBSTANCE: Acceptable analogue of the notified chemical

METHOD: OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).

Species/Strain: Rat/Sprague-Dawley Crl:CD (SD) IGS BR
Route of Administration: Oral – gavage
Exposure Information: Total exposure days: 28 days
Dose regimen: 7 days per week
Post-exposure observation period: None
Vehicle: Polyethylene glycol 400
Remarks - Method: No significant protocol deviations.
Dosages were determined by a preliminary 14-day range finding study, in which no mortality or serious toxicity were observed up to 1000 mg/kg bw/day. No urinalysis was performed.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 per sex	0	0
low dose	5 per sex	15	0
mid dose	5 per sex	150	0
high dose	5 per sex	1000	0

Mortality and Time to Death
No mortalities were observed during the study.

Clinical Observations
An increase in salivation was observed up to 10 mins after dosing in all animals dosed at 1000 mg/kg/day and occasionally persisted for up to 1 hour. Occasional staining around the eyes, mouth and fur were also observed at this dose level.

Salivation was also observed in males treated with 150 mg/kg/day up to 10 mins after dosing.

No other significant, treatment-related clinical signs were observed.

Laboratory Findings – Clinical Chemistry, Haematology
There were no treatment-related changes in the haematological parameters assessed.
Females treated at all dose levels showed a statistically significant increase in mean cell haemoglobin ($p<0.05$). However, the significance was minimal in each case ($p<0.05$) and was considered one lower than the expected control value and therefore the increases were considered unrelated to treatment.

Effects in Organs
All animals dosed at 1000 mg/kg bw/day showed increases in liver weights and males in that group also showed increases in kidney weight ($p<0.05$). No treatment-related effects were detected in animals treated in the mid and low dose groups. No macroscopic abnormalities were observed at necropsy.

Histopathology
Centrilobular hepatocyte enlargement was observed in all animals dosed at 1000 mg/kg/day.
Globular accumulations of eosinophilic material were observed in the tubular epithelium of three males dosed at 1000 mg/kg/day and in three males dosed at 150 mg/kg/day.

Remarks – Results
The centrilobular hepatocyte enlargement and increased liver and kidney weights observed in animals dose at 1000 mg/kg bw/day may be considered to be adaptive metabolic responses to treatment with a xenobiotic. The eosinophilic globular accumulations observed in three males at 1000 and 150 mg/kg bw/day were considered to be characteristic of a typical hydrocarbon nephropathy peculiar to the male rat and absent in female rats and other species. Therefore these effects would not be considered relevant to human health.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) for the analogue chemical was established as 1000 mg/kg bw/day in this study, based on the absence of any treatment-related adverse health effects.

The No Observed Effect Level (NOEL) for the analogue chemical was considered to be 150 mg/kg/day for females and 15 mg/kg/day for males.

The notified chemical, based on its similarity to the analogue, is expected to have a NOAEL = 1000 mg/kg.

TEST FACILITY Safepharm (2007d)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test.

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100. *E. coli*: WP2uvrA
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphthoflavone-induced rat liver.
Concentration Range in Main Test	a) With metabolic activation: 50-5000 µg/plate b) Without metabolic activation: 50-5000 µg/plate
Vehicle	Acetone
Remarks - Method	No significant protocol deviations. Plate incorporation method.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	> 5000			
Test 1		> 5000	≥ 1500	Negative
Test 2		> 5000	≥ 1500	Negative

Present	> 5000			
Test 1		> 5000	≥ 1500	Negative
Test 2		> 5000	≥ 1500	Negative

Remarks - Results

CONCLUSION The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY Safepharm (2007e)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE Acceptable analogue of the notified chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain Human
Cell Type/Cell Line Lymphocyte
Metabolic Activation System S9 fraction from phenobarbitone/β-naphthoflavone-induced rat liver.
Vehicle DMSO
Remarks - Method No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 14.61, 29.22*, 58.44*, 87.66*, 116.88, 175.32	4 hrs	20 hrs
Test 2	0*, 7.31, 14.61*, 29.22*, 58.44*, 87.66, 116.88	24 hrs	24 hrs
Present			
Test 1	0*, 58.44, 116.88, 233.75*, 350.63*, 467.5*, 701.25	4 hrs	20 hrs
Test 2	0*, 14.61, 29.22*, 58.44*, 116.88*, 233.75, 467.5	4 hrs	20 hrs

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	>58.44	>87.66	29.22	Negative
Test 2	>58.44	>58.44	233.75	Negative
Present				
Test 1	>233.75	>467.5	58.44	Negative
Test 2		>116.88	58.44	Negative

Remarks - Results In Test 2 with metabolic activation the notified chemical induced small increases in the number of cells with chromosome aberrations. The increases were not considered dose-related. No statistically significant increases in aberrations were noted in the other three test groups.
The notified chemical did not induce a statistically significant increase in the numbers of polyploid cells at any dose level in either of the exposure groups.
All vehicle (solvent) controls had frequencies of cells with aberrations within the range expected for normal human lymphocytes.
All the positive control materials induced statistically significant increases in the frequency of cells with aberrations, indicating the satisfactory performance of the test and of the activity of the metabolising system.

CONCLUSION The analogue chemical was not clastogenic to human lymphocytes cell treated *in vitro* under the conditions of the test. Therefore, the notified

	chemical, based on its similarity to the analogue, is expected to be non-genotoxic.
TEST FACILITY	Safepharm (2007f)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO2 Evolution Test.
Inoculum	Activated Sewage Sludge Micro-organisms
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	DOC was detected using Inorganic Carbon analysis using a Shimadzu TOC-5050A TOC analyser.
Remarks - Method	Activated Sewage Sludge was exposed to 14.4 mg/L (10 mg carbon/L) of the test material for 28 days at 21˚C in darkness for ready biodegradability test. The degradation of the test material was assessed by the determination of carbon dioxide produced. Control test with inoculum, standard test with standard material sodium benzoate, and toxicity control test were conducted for validation purposes.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
6	33	6	41
14	46	14	65
22	61	22	97
28	78	28	100

Remarks - Results	The total CO_2 evolution in control test on Day 28 was 27.82 mg/L, within the limitation of 40 mg/L; the IC/TC ratio of the test material suspension in the mineral medium at the start of the test was 0, within the limitation of 5%; the difference between the values for CO_2 production at the end of the test for the replicate test vessels was < 20%. All validation criteria given in OECD Test Guideline were satisfied and the study is considered valid. Sodium benzoate attained 100% degradation after 28 days thereby confirming the suitability of the inoculum and test conditions. The notified chemical attained 78% degradation after 28 days and failed to satisfy the 10-Day window validation criterion, whereby 60% degradation must be attained within 10 days of the degradation exceeding 10%. The test material cannot therefore be considered to be readily biodegradable under the strict terms and conditions of the Test Guideline. However, the notified chemical has exhibited the potential for rapid biodegradation.
CONCLUSION	The notified chemical cannot be considered to be readily biodegradable; however, it exhibits the potential for rapid biodegradation.
TEST FACILITY	Safepharm (2007g)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Acceptable analogue of notified chemical

METHOD	OECD TG 203 Fish, Acute Toxicity Test -in juvenile rainbow trout (*Onchorhynchus mykiss*) with exposure period of 96 hours. EC Directive 92/69/EEC C.1 Acute Toxicity for Fish - in juvenile rainbow trout (*Onchorhynchus mykiss*) with exposure period of 96 hours.
Species	juvenile rainbow trout (*Onchorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	140 mg $CaCO_3$/L (pH 8)
Analytical Monitoring	GC/MS was used for determination of the concentration of the notified chemical.
Remarks – Method	Two separate pilot tests were realized with rainbow trout (10 for each test) at the saturated concentration 1.5 mg/L of the notified chemical. A semi-static test regime was employed in the test involving a daily renewal of the test medium. A marked decline in concentration of the notified chemical was noted during the toxicity test, which was considered predominantly the result of bioaccumulation due to the test material's high log Pow (6.58), or the result of adherence to vessel walls. Slight hydrolysis is unlikely, as the notified chemical is considered stable at pH 8.

Results

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
1.5	0.78*	10	0	0	0	0	0

* Time-weighted mean test concentration calculated considering the decline of concentration during the test.

LC50	> 0.78 mg/L at 96 hours.
NOEC	0.78 mg/L at 96 hours.
Remarks – Results	The decline in concentration may indicate potential for bioaccumulation of the test material. No sub-lethal effects were observed at 1.5 mg/L, the solubility of the notified chemical in water. The test result from the analogue is considered applicable to the notified chemical.
Conclusion	The analogue is not considered to be toxic to *Onchorhynchus mykiss* up to the level of its water solubility. Therefore, the notified chemical, based on its similarity to the analogue, is not expected to be toxic to fish.
Test Facility	Safepharm (2007h)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test. EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – 48h static
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC/MS using an external standard was used to monitor concentration in test samples.
Remarks - Method	Tests were conducted at a range of nominal loading rates of 10, 18, 32, 56

and 100 mg/L of the notified chemical at 21-22˚C under static test conditions. Due to the low water solubility and complex nature of the test material, test medium was prepared as a Water Accommodated Fraction (WAF). To prepare the WAFs of different loading rates, amounts of notified chemical (25, 45, 140 and 250 mg) were each separately added to the surface of 2.5 L of reconstituted water to give the 10, 18, 32, 56 and 100 mg/L loading rates respectively. After the addition of the notified chemical, the reconstituted water was stirred by magnetic stirrer using a stirring rate such that a vortex was formed to give a dimple at the water surface (slow-stir method). After 47 hours of stirring the mixtures were allowed to stand for 1 hour. A wide bore glass tube, covered at one end with Nescofilm was submerged into the vessel, sealed end down, to a depth of approximately 5 cm from the bottom of the vessel. A length of Tygon tubing was inserted into the glass tube and pushed through the Nescofilm seal. The aqueous phase or WAFs were removed be mid-depth siphoning (the first 75-100 mL discarded) to give the 10, 18, 32, 56 and 100 mg/L loading rate WAFs. Microscopic inspection of the WAF showed no micro-dispersions or undissolved test material to be present. Analysis of the test preparations at 0 hours gave results of < LOQ.

A positive control was conducted using potassium dichromate as the reference material at concentrations of 0.32, 0.56, 1.0, 1.8 and 3.2 mg/L under static test conditions. The mean 48-Hour EC50 calculated from all positive controls was 0.81 mg/L (sd = 0.21).

RESULTS

Nominal Concentration mg/L (WAF)		*Number of D. magna*	*Number Immobilised*	
			24 h	*48 h*
10	-	20*	0	0
18	-	20	0	0
32	-	20	0	0
56	-	20	0	5
100	-	20	0	13

*Replicate tests were carried out with 10 daphnids in each.

LC50 82 mg/L (WAF) at 48 hours *[acute]*
NOEC (or LOEC) 32 mg/L (WAF) at 48 hours *[acute]*

Remarks - Results No immobilization observed up to loading rate of 32 mg/L WAF.

Analysis of samples taken at 0-Hours showed measured concentration was below the limit of quantitation (LOQ) of the analytical method which was assessed to be 0.0047 mg/L. Those results indicate that the test medium might actually have a loading of up to the limit of the water solubility. In this scenario the toxicity result could only be referred to the solubility limit of the notified chemical.

CONCLUSION The notified chemical shows some toxicity to *Daphnia magna* up to the limit of the solubility.

TEST FACILITY Safepharm (2007i)

C.2.3. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Acceptable analogue of notified chemical
METHOD	OECD TG 211 Daphnia sp. *Daphnia Magna*, Reproduction test.
Species	*Daphnia magna*
Exposure Period	21 d
Auxiliary Solvent	None
Water Hardness	Total hardness 140 mg/L $CaCO_3$
Analytical Monitoring	GC/MS
Remarks - Method	Female young *Daphnia magna* aged less than 24 hours (10 replicates of a single daphnid per group) were exposed to test substances for 21 days at the following concentrations: 0.0032, 0.010, 0.032, 0.10 and 0.32 mg/L, with the test medium renewed daily. The test solution prepared from a saturation solution of 1.0 mg/L notified chemical. Solutions were renewed daily. As observed in the acute studies (above), a marked decline in concentration of the notified chemical was noted during the toxicity test. Thus the time-weighted mean test concentration was calculated from the initial test concentration and used in the toxicity characterization.

Nominal loading tested, cumulative mean number of offspring released, number of offspring released per female daphnid (*Daphnia magna*), survival of parental daphnids.

Test day	Control	0.0032 mg/L	0.010 mg/L	0.032 mg/L	0.10 mg/L	0.32 mg/L
Total Number of Offspring Released by Survived Daphnia						
21	834	763	630	574	687	600
Total Number of Offspring Released per Survived Daphnid						
21	83	85	79	72	69	67
Number of Adult Daphnids Immobilized						
21	0	1	2	2	0	1
Percent Survival						
21	100	90	80	80	100	90

21-Day EC50 (Immobilization)	> 0.10 mg/L based on the time-weighted mean measured test concentration (Nominal concentration > 0.32 mg/L).
21-Day EC50 (Reproduction)	> 0.10 mg/L based on the time-weighted mean measured test concentration (Nominal concentration > 0.32 mg/L).
Lowest-Observed – Effect loading Rate (LOELR) (mg/L)	0.018 mg/L based on the time-weighted mean measured test concentration (Nominal concentration 0.032 mg/L).
No-Observed – Effect loading Rate (NOELR) (mg/L)	0.007 mg/L based on the time-weighted mean measured test concentration (Nominal concentration 0.01 mg/L), determined based on the number offspring produced by surviving daphnids.

Remarks - Results	The mortalities of the adult *Daphnia* at the end of the test with the worst case was 2 out of 10 at concentrations of 0.010 and 0.032 mg/L, which did not exceed 20% and the test could be considered valid. The mean number of live offspring produced per female *Daphnia* surviving was above 60 and could be considered valid. The report indicates after 21 days there were no statistically significant difference between the control and the 0.0032, 0.010 and 0.032 mg/L test group in terms of the numbers of live young produced per adult. The 0.10 and 0.32 mg/L test groups showed a statistically significant difference from the control and the remaining test groups after 21 days in terms of producing fewer numbers of live young per adult.

The EC50 (reproduction) value based on nominal test concentration was estimated to be greater than 0.32 mg/L. The data was considered unsuitable for statistical analysis even though a 20% reduction on the number of live young was observed at the test concentrations of 0.10 and 0.32mg/L.

Corrected chi-squared statistical tests were performed to show whether the observed parental mortalities in the 0.0032, 0.010, 0.032 and 0.32 mg/L test groups were statistically different when compared to the control group. The results showed that the observed mortalities were not significant for all test groups.

After 21 days the length of each surviving adult was determined. The results showed that there were no statistically significant differences ($P \geq 0.05$) between the control and all the test groups in terms of length of the daphnids after 21 days exposure to the test material.

As the report did calculation including the number of offspring released from the dead adult and unhatched eggs, DEWHA repeated the statistical analysis using TOXCAL5.XLS, and found as shown in the table above that the LOEC and NOEC based on offspring released by survived daphnia are lower than those reported from the notifier.

CONCLUSION The notified chemical is toxic to *Daphnia magna* in water.

TEST FACILITY Safepharm (2007j)

C.2.4. Algal growth inhibition test

TEST SUBSTANCE Acceptable analogue of notified chemical

METHOD OECD TG 201 Algae, Growth Inhibition Test.
EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 0.84 mg/L Actual: 0.361-0.84 mg/L
Auxiliary Solvent	None
Water Hardness	15 mg $CaCO_3$/L
Analytical Monitoring	GC/MS for analysis of the test substance concentration.
Remarks - Method	*Desmodesmus subspicatus* with density of 4×10^3 cells per ml was exposed for 72 hours to the test material of an initial concentration of 0.84 mg/L at pH 7.2 at beginning and 7.7 at the end of the test. The test solution was a saturation solution of 0.84 mg/L notified chemical. The test was taken in six replicates.

RESULTS

Biomass		*Growth*	
E_bC_{50} *mg/L at 72 h*	NOE_bC *mg/L*	E_rC_{50} *mg/L at 72 h*	NOE_rC *mg/L*
> 0.55	0.55	> 0.55	0.55

Remarks - Results The cell concentration of the control cultures increased by a factor of 45 after 72 hours, which was in line with the OECD Guideline that states the enhancement must be at least by a factor of 16 after 72 hours.

The mean variation coefficient for the control section-section daily growth rates was 61% and hence exceeded the recommended maximum

	of 35% given in the OECD Guideline. This was considered as the result of the abnormally high concentration of the algal suspension added to the test medium. Given that the validation criteria relating to increase in control cell density and coefficient of variation of the control average growth rates for the test period were satisfied the study is considered valid. A marked decline in the concentration of the notified chemical in the test period was detected and was considered the result of hydrolysis and absorption of the notified chemical to the organism during the test. Geometric mean measured concentrations of the samples were thus calculated and used for toxicity characterization of the notified chemical to algae in water. No statistically significant inhibition to alga in terms of growth rate, yield or biomass integral was observed up to the limit of its water solubility.
CONCLUSION	The notified chemical, based on its similarity to the analogue, is not expected to be toxic to algae.
TEST FACILITY	Safepharm (2007k)

C.2.5. Inhibition of microbial activity

TEST SUBSTANCE	Acceptable analogue of notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test. EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Activated Sewage Sludge
Exposure Period	3 hours
Concentration Range	Nominal: 1000 mg/L Actual: 1000 mg/L
Remarks – Method	Three replicate tests were conducted by exposing activated sewage sludge to 1000 mg/L dispersion of the notified chemical. The test water had a total hardness of 100 mg/L as $CaCO_3$. Variation in respiration rates of control tests was 3% after both 30 minutes and 3 hours contact. EC_{50} (3- hour contact time) for reference substance 3,5-dichlorophenol was 5.4-9.0 mg/L. The study is thus considered valid according to Test Guideline.
RESULTS	No significant effect was observed at the dispersion of notified chemical at concentration of 1000 mg/L highly in excess of the solubility of the chemical.
IC50	> 1000 mg/L
NOEC	1000 mg/L
Remarks – Results	
CONCLUSION	The notified chemical, based on its similarity to the analogue, is not expected to be harmful to microbial respiration.
TEST FACILITY	Safepharm (2007m)

BIBLIOGRAPHY

NOHSC (1994) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2003) National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd edition [NOHSC:2011(2003)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

Safepharm (2006a), [Analogue]: Acute Dermal Toxicity (Limit test) in Rat (SPL Project Number: 0525/0727), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2006b), [Analogue]: Acute Dermal Irritation in the Rabbit (Project Number: 0525/0728), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2006c), [Analogue]: Evaluation of Ocular Irritancy Potential (SPL Project Number: 0525/0729), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2006d), [Analogue]: Local Lymph Node Assay in the Mouse (SPL Project Number: 0525/0730), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007a), [Notified chemical]: Determination of General Physico-Chemical Properties (SPL Project Number: 525/0780), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007b), [Notified chemical]: Determination of Hazardous Physico-Chemical Properties (SPL Project Number: 525/0781), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007c), [Notified chemical]: Acute Oral Toxicity in the Rat – Fixed Dose Method (SPL Project Number: 0525/0782), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007d), [Analogue]: 28 Day Repeated Dose Oral (Gavage) Toxicity in Rats (SPL Project Number: 0525/0731), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007e), [Notified chemical]: Reverse Mutation Assay "Ames test" using *Salmonella typhimurium* and *Escherichia coli* (SPL Project Number: 0525/0783), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007f), [Analogue]: Chromosome Aberration Test in Human Lymphocytes In Vitro (SPL Project Number: 0525/0738), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007g), [Notified chemical]: Assessment of Ready Biodegradability: CO2 Evolution Test (SPL Project Number: 0525/0785), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007h), Acute Toxicity to Rainbow Trout (SPL Project Number: 0525/0734), , Shardlow, UK ().

Safepharm (2007i), [Analogue]: Acute Toxicity to *Daphnia Magna* (SPL Project Number: 0525/0784), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007j), [Analogue]: *Daphnia Magna* Reproduction Test (SPL Project Number: 0525/0735), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007k), [Analogue]: Algal Inhibition Test (SPL Project Number: 0525/0736), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

Safepharm (2007m), [Analogue]: Assessment of Inhibitory Effect on the Respiration of Activated Sewage Sludge (SPL Project Number: 0525/0739), Safepharm Laboratories Ltd, Shardlow, UK (unpublished report provided by notifier).

United Nations (2003) Globally Harmonised System of Classification and Labelling of Chemicals (GHS). United Nations Economic Commission for Europe (UN/ECE), New York and Geneva.