File No: STD1523

October 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

HC-3354

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (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 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.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This 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:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, 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

SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1523	Lubrizol International Inc.	HC-3354	No	≤ 100 tonnes per annum	Component of refrigeration lubricants

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

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

Environmental risk assessment
On the basis of its limited aquatic exposure and assessed use pattern, the notified chemical is not expected to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid contact with skin and eyes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - coverall, goggles, impervious gloves

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

- A copy of the (M)SDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified polymer in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

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(2) of the Act; if
- the function or use of the chemical has changed from component of refrigeration lubricants, or is likely to change significantly;
- the amount of chemical/polymer being introduced has increased, or is likely to increase, significantly;
- 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 (M)SDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT
Lubrizol International Inc. (ABN: 52 073 495 603)
28 River Street, P.O. Box 6445
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, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, polymer constituents, residual monomers, impurities, additives/adjuvants, import volume, site of reformulation, identity of manufacturer/recipients and analogue identity.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: hydrolysis as a function of pH, dissociation constant, acute inhalation toxicity, repeated dose toxicity, in vivo genotoxicity and bioaccumulation studies.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2009), Europe (2009), USA (2009)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
HC-3354

OTHER NAME(S)
OS291098
Z-133
Polyol Ester (Generic name listed in the (M)SDS)

MOLECULAR WEIGHT
> 500 Da

ANALYTICAL DATA
Reference NMR, IR, GC, TGA and UV spectra were provided.

3. ANALOGUE DATA

No repeated dose toxicity data on the notified chemical was provided. However, a 28-day repeat dose toxicity study on an analogue chemical was provided by the notifier as a substitute to fill the data gap for the notified chemical. Like the notified chemical, the analogue is also an ester which is expected to have a common metabolic fate, undergoing stepwise hydrolysis to fatty acids and polyols.

4. COMPOSITION

DEGREE OF PURITY
> 95%

5. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Clear colourless liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -48 °C	(M)SDS
Boiling Point	> 400 °C at 101.5 kPa	Measured
Density	940 kg/m^3 at 20 °C	Measured
Vapour Pressure	3.2 × 10^{-9} kPa at 25 °C	Measured
Water Solubility	≤ 2.04 × 10^{-3} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Not considered to be feasible due to low solubility in water.
Partition Coefficient (n-octanol/water)	log Pow > 9.4	Measured
Surface Tension	72.9 ± 0.5 mN/m at 21.8 ± 0.5 °C	Measured
Adsorption/Desorption	log K_{oc} > 5.63	Measured/
Dissociation Constant	Not determined	No dissociable functionality
Flash Point	224 ± 2 °C at 101.7 kPa	Measured
Autoignition Temperature	408 ± 5 °C	Measured
Explosive Properties	Predicted negative	Estimated
Oxidising Properties	Predicted negative	Estimated

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

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

6. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. The notified chemical will be imported into Australia in pure form at a concentration of > 95 % or in formulated products at a concentration of 20–> 95%.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	8–10	15–20	45–50	70–75	90–100

PORT OF ENTRY
Queensland, Victoria and Western Australia

TRANSPORTATION AND PACKAGING
The imported end-use lubricant oils containing the notified chemical at a concentration up to > 95 % will be imported in various sizes ranging from 1 L and 4 L containers to 205 L drums. The products will be transported by road either to the notifier's warehouse or directly to the customers.

USE
The notified chemical will be utilized as a component in refrigeration lubricants. The concentration of the notified chemical in the formulated products will range from 20 to > 95% by weight.

OPERATION DESCRIPTION
The notified chemical will be imported as a component of end-use lubricating products at various concentrations. No reformulation or repackaging will occur within Australia. At the site of use, the lubrication fluid containing the notified chemical will be transferred manually or using an automated system to the fluid reservoir of the industrial equipment or refrigeration system. Empty containers after use are expected to be steam cleaned with residual waste sent to on-site wastewater treatment facilities.

7. HUMAN HEALTH IMPLICATIONS

7.1. Exposure Assessment

7.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage workers	0–2	100–225
Industrial equipment service workers	6–8	100–225

EXPOSURE DETAILS

The primary work undertaken by transport and warehouse workers will include the handling, loading and off-loading of containers. The workers may come into contact with the notified chemical at a concentration of up to > 95% only in the event of accident when there is container breach and/or chemical spill. The potential routes of occupational exposure under such circumstances are dermal and ocular.

At the site of end-use, industrial equipment service workers may experience dermal and ocular exposure to the notified chemical in the lubricating products from drips, spills and splashes during the transfer of the lubricant as well as from handling equipment contaminated with the lubricating products.

The notifier anticipates that the use of appropriate personal protective equipment (PPE) including impervious gloves, coveralls, safety glasses and suitable respiratory protection when the ventilation is inadequate along with proper training should reduce the exposure.

7.1.2. Public Exposure

The notified chemical will be used as a lubricant for industrial purposes only and under normal circumstances the general public would not come in to contact with the notified chemical.

7.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical and / or analogue chemical are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	slightly-irritating
Rabbit, eye irritation	slightly-irritating
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days*	NOAEL ≥ 1,450 mg/kg bw/day (males) ≥ 1,613 mg/kg bw/day (female)
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro Mouse lymphoma assay	non genotoxic
Genotoxicity – in vitro Chromosome aberration test	non genotoxic

***** *test conducted on an analogue chemical*

Toxicokinetics, metabolism and distribution.

No information on the toxicokinetics of the notified chemical was provided. Based on the water solubility (≤ 0.204×10^{-3} g/L at 20 °C), partition coefficient (log Pow > 9.4) and the high molecular weight (> 500 Da) of the notified chemical, passive diffusion of the notified chemical across the skin and the gastrointestinal tract is not likely to occur.

Acute toxicity.

The notified chemical was found to be of low toxicity via the oral and dermal routes.

Irritation and sensitisation.

A dermal irritation study carried out on rabbits indicated that the notified chemical was slightly irritating to the skin with two of the three treated animals showing very slight erythema which lasted for < 48 hours. An eye

irritation study on rabbits indicated that the notified chemical is slightly irritating to the eye With conjunctival redness, chemosis and discharge observed in all treated eyes and lasting for < 48 hours.

A skin sensitization study carried out on mice (Local Lymph Node Assay) using the notified chemical at up to > 95% concentration showed no evidence of skin sensitization.

Repeated dose toxicity.
Repeated dose toxicity information on the notified chemical was not provided. In a 28 day oral toxicity study conducted with the analogue, rats were fed with diet containing the analogue chemical (Zeneca 1993). The doses selected were 1,000, 5,000 and 12,500 ppm, which equated to 112 mg, 562 mg and 1,450 mg/kg body weight/day for male rats and 119 mg, 586 mg and 1,613 mg/kg body weight/day for female rats.

No toxicologically significant changes in body weight, food consumption and clinical conditions were noted up to the highest dose tested. Hepatocyte hypertrophy was observed in male rats exposed to 1,450 mg/kg bw/day. Microscopic examinations showed the presence of hyaline droplets and tubular basophilia in the kidneys of all male rats exposed to the analogue chemical at all concentrations. These effects were considered to be adaptive and not relevant to the human by the study author and thus a NOA(E)L of 1,450 mg/kg bw/day and 1,613 mg/kg bw/day was established for male and female rats, respectively.

Mutagenicity/Genotoxicity.
The notified chemical was not mutagenic in a bacterial reverse mutation study and was not clastogenic in *in vitro* mammalian chromosome aberration and mouse lymphoma tests.

Health hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

7.3. Human Health Risk Characterisation

7.3.1. Occupational Health and Safety
Based on toxicological studies on the notified chemical and an analogue it is expected that it will be of low toxicity, presenting only as slight skin and eye irritant.

Workers may come into contact with the notified chemical during the loading / off-loading of the containers and transfer of lubricant fluid containing the notified chemical to the fluid reservoir of the industrial equipment or refrigeration system. The potential routes of exposure are dermal and ocular.

The use of appropriate PPE including impervious gloves, coveralls, safety glasses and suitable respiratory protection when the ventilation is inadequate along with proper training should reduce the exposure to the notified chemical.

Overall, given the expected low toxicity of the notified chemical and the control measures in place to minimise exposure it is not considered to pose an unreasonable risk to the health of workers.

7.3.2. Public Health
The notified chemical will be used as a component of lubricant for industrial purposes only and under normal circumstances the general public would not come in to contact with the notified chemical. Therefore, the notified chemical is not considered to pose an unreasonable risk to public health.

8. ENVIRONMENTAL IMPLICATIONS

8.1. Environmental Exposure & Fate Assessment

8.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemical will be manufactured overseas and will be imported as finished products to be used as lubricant for industrial equipment and refrigeration systems. Any spill/leak is expected to be contained and be sent to an approved industrial facility for appropriate disposal.

RELEASE OF CHEMICAL FROM USE
The lubricants containing the notified chemical will be poured into industrial equipment, which are closed systems, in industrial settings. The notifier has indicated that there will be no do-it-yourself (DIY) application for the lubricant oils containing the notified chemical. Release of the notified chemical from professional activities is expected to be limited by the requirement for appropriate disposal of waste oil according to State/Territory regulations.

RELEASE OF CHEMICAL FROM DISPOSAL
Products containing the notified chemical are expected to be disposed of in accordance with State/Territory regulations. Consequently, the notified chemical is expected to be recycled, re-refined or used as low grade burner fuel. It is likely that the notified chemical will be degraded into simpler compounds during re-refining with any residue partitioning to the heavy fractions such as lubricating oils or asphalt. Similarly, during metal recycling, the notified chemical is expected to be completely combusted.

8.1.2. Environmental Fate
A study submitted by the notifier indicates the notified chemical is considered to be readily biodegradable. For the details of the environmental fate study please refer to Appendix C. The notified chemical is not expected to be bioaccumulative or bioavailable to aquatic organisms due to its low water solubility and anticipated limited release to the aquatic environment. Most of the notified chemical will be either thermally decomposed during use, recycling or refinement. The notified chemical is expected to be degraded into water and oxides of carbon by thermal decomposition in industrial facilities.

8.1.3. Predicted Environmental Concentration (PEC)
The notifier has stated that 100% of the notified chemical will be used in industrial equipment and refrigeration systems. The notifier also indicated that the lubricant will not be used by DIY users. Therefore the notified chemical is not anticipated to be released to the aquatic environment through improper disposal by DIY users. Release of the notified chemical to the aquatic environment through leakage is not expected under normal operating conditions. The predicted environmental concentration (PEC) has not been calculated since no significant release of the notified chemical to the aquatic environment is expected from the reported use pattern.

8.2. Environmental Effects Assessment
Ecotoxicological data were submitted for the notified chemical. The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of the studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity (96 h)	LL50 > 100 mg/L* (WAF)	Not harmful to fish up to its water solubility limit
Daphnia Toxicity (48 h)	EL50 > 100 mg/L* (WAF)	Not harmful to aquatic invertebrates up to its water solubility limit
Algal Toxicity (72 h)	E_rL50 > 100 mg/L* (WAF)	Not harmful to algae up to its water solubility limit
Inhibition of Bacterial Respiration (3 h)	EC50 > 1000 mg/L	Not inhibitory to microbial respiration up to its water solubility limit

* Water accommodated fraction

Based on the above reported endpoints for the notified chemical, it is not considered to be harmful to fish, daphnia and algae. Therefore, the notified chemical is not harmful to aquatic organisms. Consequently, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009), the notified chemical has not been formally classified for acute and chronic toxicities.

8.2.1. Predicted No-Effect Concentration
A predicted no-effect concentration (PNEC) for the aquatic compartment has not been calculated since the notified chemical is not considered to be harmful up to the limit of its solubility in water and no significant aquatic exposure is expected based on the reported use pattern.

8.3. Environmental Risk Assessment
The risk quotient, Q (= PEC/PNEC), of the notified chemical has not been determined due to its low potential for release to the aquatic compartment. Lubricants containing the notified chemical, after its useful life, are expected to be disposed of according to State/Territory regulations. Exposure of the notified chemical to the aquatic

compartment is unlikely based on the reported use pattern. On the basis of its limited aquatic exposure and assessed use pattern, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Boiling Point > 400 °C at 101.5 kPa

Method OECD TG 103 Boiling Point.
Remarks Differential scanning calorimetric method. The test substance did not boil up to 400 °C
Test Facility Harlan (2013a)

Density 940 kg/m^3 at 20 °C

Method OECD TG 109 Density of Liquids and Solids.
Remarks Pycnometer method. Test performed in duplicates
Test Facility Harlan (2013b)

Vapour Pressure 3.2×10^{-9} kPa at 25 °C

Method OECD TG 104 Vapour Pressure.
Remarks Vapour pressure balance method.
Test Facility Harlan (2012a)

Water Solubility $\leq 2.04 \times 10^{-3}$ g/L at 20 °C

Method OECD TG 105 Water Solubility.
Remarks Flask Method
Test Facility Harlan (2013a)

Partition Coefficient (n-octanol/water) log Pow > 9.4

Method OECD TG 117 Partition Coefficient (n-octanol/water).

Remarks HPLC Method
Test Facility Harlan (2013a)

Surface Tension 72.9 ± 0.5 mN/m at 21.8 ± 0.5 °C

Method OECD TG 115 Surface Tension of Aqueous Solutions.
Remarks Concentration: 90% saturated solution. Determination carried out using ring method. The test substance was considered to be not surface-active. The platinum ring used had a circumference of 4 cm instead of the recommended 6 cm by OECD.
Test Facility Harlan (2013b)

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

Method OECD TG 106 Adsorption - Desorption Using a Batch Equilibrium Method.
Remarks HPLC method
Test Facility Harlan (2013c)

Flash Point 224 ± 2 °C at 101.7 kPa

Method EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks Closed cup method.
Test Facility Harlan (2013d)

Autoignition Temperature 408 ± 5 °C

Method EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks The atmospheric pressure was between 101.5 to 103.5 kPa.
Test Facility Harlan (2013d)

Explosive Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.14 Explosive Properties.
Remarks	The structure was analysed for chemical groups that could imply explosive properties.
Test Facility	Harlan (2013d)

Oxidizing Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.21 Oxidizing Properties (Liquids).
Remarks	The structure was analysed for chemical groups that could imply oxidising properties.
Test Facility	Harlan (2013d)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity - Fixed Dose Method.
Species/Strain	Rat/Wistar (RccHan™ : WIST)
Vehicle	None
Remarks - Method	No significant deviations from the OECD protocol. The undiluted test substance was administered by oral gavage.

RESULTS

Sighting Study

Dose mg/kg bw	*Administered*	*Evident Toxicity*	*Mortality*
2000	1	None	0/1

Signs of Toxicity	None
Effects in Organs	None

Main Study

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	4 F	2,000	0/4

LD50	> 2,000 mg/kg bw
Signs of Toxicity	No signs of systemic toxicity observed during the 14-day course of the study.
Effects in Organs	No abnormalities were noted at necropsy
Remarks - Results	All animals survived the study and showed expected weight gains during the observation period.

CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Harlan (2013e)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rat/Wistar (RccHan™ : WIST)
Vehicle	Test substance administered as supplied
Type of dressing	Semi-occlusive.
Remarks - Method	No significant deviations from the OECD protocol.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 F & 5 M	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	No signs of dermal irritation
Signs of Toxicity - Systemic	No signs of systemic toxicity
Effects in Organs	No abnormalities were noted at necropsy
Remarks - Results	All animals survived the study and showed expected weight gains during the observation period.

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

TEST FACILITY Harlan (2013f)

B.3. Irritation – skin

TEST SUBSTANCE Notified chemical

METHOD
Species/Strain Rabbit/New Zealand White (Hsdlf:NZW)
Number of Animals 3
Vehicle Test substance administered as supplied.
Observation Period 72 hours
Type of Dressing Occlusive/Semi-occlusive.
Remarks - Method No significant deviations from the OECD protocol.

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	0.33	0.33	1	< 48 h	0
Oedema	0	0	0	0	–	0

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

Remarks - Results Two of the three treated sites showed very slight erythema at 1 h and 24 h observations after patch removal.

CONCLUSION The notified chemical is slightly irritating to the skin.

TEST FACILITY Harlan (2013g)

B.4. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD
Species/Strain Rabbit/New Zealand White (Hsdlf:NZW)
Number of Animals 3
Observation Period 72 hours
Remarks - Method No significant deviations from the OECD protocol.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.33	0.33	0.33	2	< 48h	0
Conjunctiva: chemosis	0.33	0.33	0.33	2	< 48h	0
Conjunctiva: discharge	0.00	0.33	0.33	2	< 48h	0
Corneal opacity	0.00	0.00	0.00	0	–	0
Iridial inflammation	0.00	0.00	0.00	0	–	0

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

Remarks - Results No corneal or iridial effects were noted during the study. All treated eyes appeared normal at the 48h observation.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Harlan (2013h)

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

TEST SUBSTANCE Notified chemical

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain Mouse/CBA/Ca strain
Vehicle Acetone/Olive oil (4:1 ratio)
Remarks - Method No significant deviations from the OECD protocol. Positive controls were not done in parallel.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	1120.94	–
25	1411.12	1.26
50	1430.56	1.28
100	1664.36	1.48

Remarks - Results The notified chemical elicited no lymphocyte proliferative response at any concentration tested.

No animals showed any abnormalities with regard to general condition or body weight change.

CONCLUSION There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY Harlan (2013i)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
Plate incorporation procedure
Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100
E. coli: WP2uvrA
Metabolic Activation System S9 fraction from phenobarbitone/β-naphtoflavone induced rat liver
Concentration Range in Main Test a) With metabolic activation: 1.5 – 5,000 µg/plate
b) Without metabolic activation: 1.5 – 5,000 µg/plate
Vehicle Acetone
Remarks - Method No significant deviations from OECD protocol. N-ethyl-N'-nitro-nitrosoguanideine, 9-Aminacridine and 4-Nitroquinoline-1-oxide were used as positive controls in test without metabolic activation and 2-Aminoanthracen and Benzo(a)pyrene were used as positive controls for test with metabolic activation. A vehicle treated group was used as negative control.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	≥ 1,500	Negative
Test 2	> 5,000	≥ 1,500	Negative

Present			
Test 1	> 5,000	≥ 1,500	Negative
Test 2	> 5,000	≥ 1,500	Negative

Remarks - Results: No significant increase in the frequency of revertant colonies was recorded for any of the bacterial strains, with any dose, either with or without metabolic activation.
The positive controls produced satisfactory responses, thus confirming the activity of S9-mix and the sensitivity of bacterial strain.

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

TEST FACILITY: Harlan (2013j)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain: Human
Cell Type/Cell Line: Lymphocytes
Metabolic Activation System: S9 fraction from phenobarbitone/β-naphtoflavone induced rat liver
Vehicle: Acetone
Remarks - Method: No significant deviations from OECD protocol. Vehicle was used as negative control and mitomycin C and cyclophosphamide were used as positive controls in absence and presence of metabolic activation respectively.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 25, 50*, 100*, 200*, 300, 400	4h	24h
Test 2	0*, 25*, 50, 100*, 200*, 300, 400	24h	24h
Present			
Test 1 (2%)	0*, 25, 50*, 100*, 200*, 300, 400	4h	24h
Test 2 (1%)	0*, 25*, 50*, 100*, 200, 300, 400	4h	24h

*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	> 2,500	> 200*	≥ 39.06	Negative
Test 2	> 2,500	> 200*		Negative
Present				
Test 1	> 2,500	> 200*	≥ 78.13	Negative
Test 2		> 100*		Negative

** Precipitation observed beyond this concentration in test.*

Remarks - Results: The maximum dose level used for assessment of cells in metaphase was limited by the onset of precipitate and not cytotoxicity.
All vehicle controls had frequencies of cells with aberrations within the range expected for normal human lymphocytes.
All positive control items induced statistically significant increases in the frequency of cells with aberrations indicating that the sensitivity of the assay and the efficacy of the S9-mix were validated.
The test item was non-toxic and did not induce any statistically significant

increases in the frequency of cells with aberrations up to the highest test concentration.

CONCLUSION The notified chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.

TEST FACILITY Harlan (2013k)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 476 In vitro Mammalian Cell Gene Mutation Test.
Species/Strain Mouse
Cell Type/Cell Line Lymphoma /L5178Y TK+/- 3.7.2c
Metabolic Activation System S9 fraction from phenobarbitone/β-naphtoflavone induced rat liver
Vehicle Acetone
Remarks - Method No significant deviations from OECD protocol. Vehicle was used as negative control and ethylmethanesulphonate and cyclophosphamide were used as positive controls in absence and presence of metabolic activation respectively.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*
Absent		
Test 1	9.75, 19.5, 39, 78, 156, 312	4 h
Test 2	9.75, 19.5, 39, 78, 156, 312	24 h
Present		
Test 1	9.75, 19.5, 39, 78, 156, 312	4 h
Test 2	9.75, 19.5, 39, 78, 156, 312	4 h

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 2,500	≥ 312	≥ 39.06	Negative
Test 2	>2,500	≥ 312	≥ 39.06	Negative
Present				
Test 1	>2,500	≥ 312	≥ 39.06	Negative
Test 2		≥ 312	≥ 39.06	Negative

Remarks - Results With no evidence of significant toxicity, the maximum dose level used in the test was limited by the onset of greasy/oily precipitate.
The test item did not induce any statistically significant or dose related increases in the mutation rate.
Acceptable levels of toxicity and mutation frequency with positive control and vehicle validating the test procedure.

CONCLUSION The notified chemical was not clastogenic to mouse L5178Y lymphoma cells treated in vitro under the conditions of the test.

TEST FACILITY Harlan (2013l)

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 sludge
- Exposure Period: 28 days
- Auxiliary Solvent: NONE
- Analytical Monitoring: Total Organic Carbon (TOC)
- Remarks - Method: The test was conducted according to the guidelines above using good laboratory practice (GLP). No significant deviations from the test guidelines were reported.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	0	2	56
8	45	8	70
14	69	14	82
28	114	28	90
29*	104	29	92

*Day 29 values corrected to include any carry-over CO_2

- Remarks - Results: All validity criteria for the test were satisfied. The reference compound, sodium benzoate, reached the 60% pass level by day 3 indicating the suitability of the inoculum. The degree of degradation of the notified chemical attained 104% after 28 days which satisfied the 10 day window validation criteria, whereby 60% degradation must be attained within 10 days of the degradation exceeding 10%. Therefore, the test substance is classified as readily biodegradable according to the OECD (301 B) guideline.

CONCLUSION: The notified chemical is readily biodegradable

TEST FACILITY: Harlan (2012b)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 203 Fish, Acute Toxicity Test –Static Test
- Species: Rainbow trout (*Oncorhynchus mykiss*)
- Exposure Period: 96 hours
- Auxiliary Solvent: Not reported
- Water Hardness: 140 mg $CaCO_3$/L
- Analytical Monitoring: Gas Chromatography (GC)
- Remarks – Method: The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.
  The fish ecotoxicity test was conducted in a water accommodated fraction (WAF) of the notified chemical as it has low water solubility. A WAF of the nominal loading rate of 100 mg/L was prepared by magnetically

stirring the test substance in dilution water for 23 hours. Following the mixing period, the WAF was allowed to settle for approximately 1 hour. The aqueous phase was removed by mid-depth siphoning to give 100 mg/L loading rate WAF.

RESULTS

Concentration mg/L Nominal (WAF)	*Number of Fish*	*Mortality*			
		24 h	*48 h*	*72 h*	*96 h*
Control	7	0	0	0	0
100	7	0	0	0	0

LL50	> 100 mg/L at 96 hours (WAF)
NOEL	100 mg/L at 96 hours (WAF)
Remarks – Results	All validity criteria for the test were satisfied. The toxicity test was conducted as a limit test. The end points were determined based on the nominal loading rates only.

CONCLUSION The notified chemical is not harmful to fish

TEST FACILITY Harlan (2013m)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test - Static test

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Not reported
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	Gas Chromatography (GC)
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported. The daphnia ecotoxicity test was conducted in a water accommodated fraction (WAF) of the notified chemical as it has low water solubility. A WAF of the nominal loading rate of 100 mg/L was prepared by magnetically stirring the test substance in dilution water for 23 hours. Following the mixing period, the WAF was allowed to settle for approximately 1 hour. The aqueous phase was removed by mid-depth siphoning to give 100 mg/L loading rate WAF.

RESULTS

Concentration mg/L Nominal (WAF)	*Number of D. magna*	*Number Immobilised*	
		24 h [acute]	*48 h [acute]*
Control	20	0	0
100	20	0	0

EL50	>100 mg/L at 24 hours (WAF)
NOEL	100 mg/L at 48 hours (WAF)
Remarks - Results	All validity criteria for the test were satisfied. The end points were determined based on the nominal loading rates only. The end points were determined based on the nominal loading rates only. The end points were determined by visual observations.

CONCLUSION	The notified chemical is not harmful to aquatic invertebrates
TEST FACILITY	Harlan (2013n)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 10 and 100 mg/L
Auxiliary Solvent	Not reported
Water Hardness	Not reported
Analytical Monitoring	Gas Chromatography (GC)
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.
RESULTS	The test was conducted in a water accommodated fraction (WAF) of the notified chemical as it has low water solubility. A WAF of the nominal loading rate of 100 mg/L was prepared by magnetically stirring the test substance in dilution water for 23 hours. Following the mixing period, the WAF was allowed to settle for approximately 1 hour. The aqueous phase was removed by mid-depth siphoning to give 100 mg/L loading rate WAF.

Biomass (72 h)		*Growth (72 h)*	
E_yL50 (WAF)<	*NOEL*	*ErL50 (WAF)*	*NOEL*
mg/L	*mg/L*	*mg/L*	*mg/L*
> 100	100	> 100	100

Remarks - Results	All validity criteria for the test were satisfied. The end points were determined based on the nominal loading rate. The endpoints at 72 h were reported as standard.
CONCLUSION	The notified chemical is not harmful to algae
TEST FACILITY	Harlan (2014)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sludge
Exposure Period	3 hours
Concentration Range	Nominal: 10, 100 and 1000 mg/L
Remarks – Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.
RESULTS	
EC50	> 1000 mg/L
NOEC	1000 mg/L
Remarks – Results	All validity criteria for the test were satisfied. The EC50 was out of the tested concentration range (> 1000 mg/L).
CONCLUSION	The notified chemical is not expected to inhibit microbial respiration
TEST FACILITY	Harlan (2013o)

BIBLIOGRAPHY

Harlan (2012a) [Notified Chemical] Determination of Vapour Pressure (Study No. 41203655, December, 2012). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2012b) [Notified chemical] Assessment of Ready Biodegradability; CO_2 Evolution Test (Study No. 41203657, October, 2012). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013a) [Notified Chemical] Determination of General Physico-Chemical Properties (Study No. 41203656, January, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013b) [Notified Chemical] Determination of Density and Surface Tension (Study No. 41301547, June 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013c) [Notified Chemical] Determination of Hydrolysis as a Function of pH and Adsorption Coefficient (Study No. 41301549, June, 2013) Ohio, USA, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013d) [Notified Chemical] Determination of Hazardous Physico-Chemical Properties (Study No. 41301548, July, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013e) [Notified Chemical] Acute Oral Toxicity in the Rat – Fixed Dose Method (Study No. 41301550, July, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013f) [Notified Chemical] Acute Dermal Toxicity (Limit Test) in the Rat (Study No. 41301551, August, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013g) [Notified Chemical] Acute Dermal Irritation in the Rabbit (Study No. 41301552, July, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013h) [Notified Chemical] Acute Eye Irritation in the Rabbit (Study No. 41301553, July, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013i) [Notified Chemical] Local Lymph Node Assay in Mouse (Study No. 41301554, August, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013j) [Notified Chemical] Reverse Mutation Assay "Ames Test" using Salmonella typhimurium and Eschericia coli (Study No. 41301555, July, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013k) [Notified Chemical] Chromosome Aberration Test in Human Lymphocytes in vitro (Study No. 41301562, October, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013l) [Notified Chemical] L5178Y Mouse Lymphoma Assay (Study No. 41301563, September, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013m) [Notified Chemical] Acute Toxicity to Rainbow trout (Study No. 41301556, January, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013n) [Notified Chemical] *Daphnia sp* 48-Hour Acute Immobilization Test (Study No. 41301557, September, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2013o) [Notified Chemical] Toxicity to Activated Sludge in a Respiration Test (Study No. 41301561, August, 2013). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

Harlan (2014) [Notified Chemical] Algal Growth Inhibition Test (Study No. 41301558, January, 2014). Shardlow, UK, Harlan Laboratories Ltd (Unpublished report submitted by the notifier).

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

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/managing-risks-of-hazardous-chemicals-in-the-workplace.

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html >.

Zeneca (1993) [Analogue data] 28 Day Dietary Toxicity Study in Rats (Study No. PR0901, July 1993). Macclesfiled, UK, Zeneca Central Toxicology Laboratory (Unpublished report submitted by the notifier).