File No: LTD/1921

November 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in Z-173

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 and Energy.

This Public Report is 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:

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Director
NICNAS

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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
LTD/1921	Lubrizol International Inc.	Chemical in Z-173	Yes	< 1 tonne per annum	Additive for oil and gas well operations

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	*Hazard statement*
Flammable liquids (Category 4)	H227 – Combustible liquid
Skin corrosion/irritation (Category 2)	H315 – Causes skin irritation
Serious eye damage/eye irritation (Category 1)	H318 – Causes serious eye damage

The environmental hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute Category 2	H401 - Toxic to aquatic life
Chronic Category 2	H411 - Toxic to aquatic life with long term effects

Human health risk assessment
Provided that the recommended controls are being adhered to, under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

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

Environmental risk assessment
On the basis of the assessed use pattern, the notified chemical is not considered to pose an unacceptable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Flammable liquids (Category 4): H227 - Combustible liquid
  - Skin corrosion/irritation (Category 2): H315 – Causes skin irritation
  - Serious eye dame/eye irritation (Category 1): H318 – Causes serious eye damage

The above should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present and the intended use/exposure scenario.

- Due to the hazardous properties of the notified chemical, the notifier should consider their obligations under the Australian Dangerous Goods Code.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during use:
  - Enclosed, automated processes
  - Use in a well ventilated area

- 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
  - Avoid breathing in vapours, aerosols or mists

- 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:
  - Protective clothing
  - Impervious gloves
  - Eye protection
  - Safety boots

  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 of 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 chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

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 importation volume exceeds one tonne per annum notified chemical;
- the end-use concentration of the notified chemical exceeds, or is intended to exceed, 8%;
- the notified chemical is intended to be used in processes which are not automated/semi-automated or enclosed;
- the notified chemical is intended to be used in operations involving hydraulic fracturing;
- additional information has become available to the person as to the mutagenicity of the chemical on germ cells.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from an additive for oil and gas well operations, or is likely to change significantly;
- the amount of chemical 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.

(Material) Safety Data Sheet
The (M)SDS of the product containing 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(S)
Lubrizol International, Inc. (ABN: 52 073 495 603)
28 River Street,
SILVERWATER NSW 2128

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less 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, analytical data, degree of purity, constituents, impurities, additives/adjuvants, and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
US EPA (TSCA 2015);
Canada (NDSL 2015)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Z-173 (product containing the notified chemical at ~ 50% concentration)

MOLECULAR WEIGHT
< 1,000 Da

ANALYTICAL DATA
Reference NMR, IR, GC-MS, LC-MS, UV-Vis spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 93%

HAZARDOUS IMPURITIES AND ADDITIVES/ADJUVANTS
The notified chemical contains quinoline (CAS RN 91-22-5) as an impurity above the cut off concentration for classification as a Category 1 carcinogen (H350 – May cause cancer).

The notified chemical also contains methanol (CAS RN 67-56-1) as an additive/adjuvant above the cut off concentrations for classification as Category 3 acute toxicity and Category 1 specific target organ toxicity (single exposure) (H331 – Toxic if inhaled, H311 – Toxic in contact with skin, H301 – toxic if swallowed and H370 – Causes damage to organs).

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Red/brown liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point*	< -20 °C	Measured

Property	Value	Data Source/Justification
Boiling Point*	Not determined	Measured. The test substance decomposed from 135 °C at 98.3 to 100.5 kPa.
Density†	> 1,050 kg/m^3 at 20 ± 0.5 °C	Measured
Vapour Pressure†	< 1.1 × 10^{-3} Pa at 25 °C	Measured
Water Solubility†	0.0402 - 0.0516 g/L at 20 °C	Measured
Water Solubility‡	0.0808 g/L at 20 °C	Measured
Hydrolysis as a Function of pH†	Not determined	The notified chemical contains functional groups that are expected to hydrolyse. However, the notified chemical has low water solubility and significant hydrolysis is not expected under environmental conditions.
Partition Coefficient (n-octanol/water)*	log Pow = -0.21 to 3.57 at 20 °C	Measured
Adsorption/Desorption*	log K_{oc} = 1.25 - 4.65 at 30 °C	Measured
Dissociation Constant	Not determined	The notified chemical is a salt that is expected to be ionised under environmental conditions.
Surface Tension†	64.5 mN/m at 19.5 °C	Measured
Flash Point†	74.7 ± 2 °C at 98.1 kPa	Measured
Flammability limits	Not determined	Expected to be a combustible liquid based on the flash point
Autoignition Temperature†	448 ± 5 °C	Measured
Explosive Properties	Non explosive	Predicted negative based on the chemical structure
Oxidising Properties	Not determined	Not expected to have oxidising properties based on the chemical structure

** Notified chemical at 80% concentration in methanol*
† Notified chemical at > 93% concentration. The test substance had a solid/liquid transition state and the tests were performed on the liquid upper layer.
‡ Notified chemical at 80% concentration in propylene glycol

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, refer to Appendix A. The notified chemical is a UVCB substance. Some of the analytical tests were performed in solvents at different concentrations.

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 recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	*Hazard statement*
Flammable liquid (Category 4)	H227 – Combustible liquid

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported into Australia at concentrations 40-50%.

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

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

PORT OF ENTRY
Western Australia, Queensland, and Victoria

IDENTITY OF MANUFACTURER/RECIPIENTS
Lubrizol International Inc.

TRANSPORTATION AND PACKAGING
The notified chemical will be transported via isotainer or 330 gallon IBC containers or in 55 gallon drums within Australia by road.

USE
The notified chemical will not be used in coal seam gas operations (hydraulic fracturing). The notified chemical will be used as a solid conglomeration additive for down-hole treatment of oil and gas wells to prevent undesirable production of solids (sand, proppant) following formation of the wellbore.

OPERATION DESCRIPTION
The notified chemical will not be manufactured in Australia. However, at on-shore or off shore customer sites, the imported product containing the notified chemical at up to 50% will be blended with other substances/additives to produce a mixture containing the notified chemical at concentrations 4-8%. The notified chemical will be used as a sand control additive in down-hole for oil and gas drillings. It will not be part of the drilling fluids, but used to close the wellbore.

At the drilling sites, the notified chemical will be mixed with a hydrocarbon drilling fluid at the drilling rig site and pumped into the wellbore. The notified chemical will be absorbed onto the subterranean rock and permanently bonded to the rock surfaces to close the wellbore. A small amount of the notified chemical (at 4-8% concentration) will return to the surface through capture of crude oil collection. The operations are expected to be automatic or semi-automatic in closed systems.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport/Storage	1-3	4-6
Plant Operator	<1	50
Maintain/Clean	2-4	10-20
Plant Operator - Sampling	<1	100

EXPOSURE DETAILS
It is anticipated that transport and storage workers would only be exposed to the notified chemical (at a concentration of up to 50%) in the event of an accident.

At end-use sites, dermal, ocular and/or inhalation exposure to the notified chemical at up to 50% concentration may occur during transfer, mixing, pumping and cleaning processes. The potential for exposure is expected to be minimised through the use of PPE (such as protective aprons, nitrile or neoprene gloves, goggles and boots as appropriate) in the presence of engineering controls including good condition of ventilation and enclosed automatic or semi-automatic processes.

6.1.2. Public Exposure
The notified chemical is intended for industrial use only and will not be available to the public. Therefore, direct exposure to the notified chemical for the public is not expected.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified 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 > 2000 mg/kg bw; low toxicity
Skin irritation (*in vitro*)	irritating
Eye irritation (*in vitro*)	corrosive
Mutagenicity – bacterial reverse mutation	mutagenic

Toxicokinetics, metabolism and distribution
No toxicokinetic data on the notified chemical were submitted. Absorption of the notified chemical through the skin and gastrointestinal tract may occur based on the water solubility (0.0402 – 0.0808 g/L), partition co-efficient (Log Pow = -0.21 to 3.57) and the presence of low molecular weight species.

Acute toxicity
The notified chemical (at a concentration of 80%) is expected to have a low acute oral toxicity based on a study conducted in rats.

Irritation
The notified chemical (at a concentration of 80%) was irritating under the conditions of an *in vitro* skin irritation study (EpiSkin™ Reconstructed Human Epidermis Model). It was considered corrosive or severely irritating to the eyes under the conditions of an *in vitro* eye irritation study (Bovine Corneal Opacity and Permeability Test Assay).

Based on the available information, the notified chemical is expected to be irritating to the skin and corrosive or severely irritating to the eyes.

Mutagenicity/Genotoxicity
The notified chemical (at 80% concentration) was found to be mutagenic in a bacterial reverse mutation test. As there was no *in vivo* germ cell mutagenicity information on the notified chemical available, the potential for the chemical to induce heritable germ cell mutation remains uncertain. Germ cell mutagenicity for the notified chemical cannot be ruled out. However, it is also possible that the mutagenicity observed may be due to the presence of quinolone in the notified chemical as an impurity.

Health hazard classification
Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	***Hazard statement***
Skin corrosion/irritation (Category 2)	H315 – Causes skin irritation
Serious eye damage/eye irritation (Category 1)	H318 – Causes serious eye damage

Although not considered in this risk assessment, NICNAS notes that the notified chemical contains quinoline (CAS RN 91-22-5) as an impurity that is classified as hazardous according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. Quinoline is present in the notified chemical as introduced above the cut off concentration for classification as a Category 1 carcinogen (H350 – May cause cancer).

NICNAS also notes that the notified chemical contains methanol (CAS RN 67-56-1) as an additive/adjuvant that is classified as hazardous according to the GHS. Methanol is present in the notified chemical as introduced above the cut off concentrations for classification as to cause Category 3 acute toxicity and Category 1 specific target organ toxicity (single exposure) (H331 – Toxic if inhaled, H311 – Toxic in contact with skin, H301 – toxic if swallowed and H370 – Causes damage to organs).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

The notified chemical may cause skin irritation and serious eye damage. The potential for the chemical to cause heritable germ cell mutation cannot be ruled out. The notified chemical contains quinolone and methanol as impurity or additive/adjuvant that may cause cancer, acute toxicity and specific target organ toxicity.

However, exposure to workers during end-use application should be limited by the use of engineering controls such as enclosed and automated/semi-automated processes. Oil and gas well operations involving the use of the notified chemical are expected to occur in open areas with good condition of ventilation. Skin or eye contact with the notified chemical or mixture containing the notified chemical should be avoided. Inhalation of vapour, aerosol or mist should also be avoided. The risk to the health of workers is expected to be further migrated by the proposed use of PPE including protective aprons, imperious gloves, goggles and boots.

Given the relatively low end-use concentration of < 8%, and stated protective controls in place to minimise exposure to the notified chemical (as well as other hazardous ingredients in the product), during end-use activities, the risk to the health of workers is not considered unreasonable.

6.3.2. Public Health

The notified chemical is intended for industrial use only and will not be available to the public. Therefore, the risk to public health is not considered unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia and environmental release of the notified chemical from manufacturing is not expected. Accidental spills during importation, transport and distribution are expected to be contained for disposal in accordance with local regulations. Small amounts of the notified chemical may remain as residues in the transport containers, which are expected to be disposed of in accordance with local regulations.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be used as a solid conglomeration additive for down-hole treatment of oil and gas wells to prevent undesirable production of solids. It will not be part of the drilling fluids, but will be used to close the wellbore. At the drilling sites, the product containing the notified chemical will be blended with other substances/additives to produce a mixture. The mixture containing the notified chemical will be dispersed into a hydrocarbon drilling fluid and pumped into the well. The whole process is expected to be highly automated and significant release of the notified chemical from use is not expected.

RELEASE OF CHEMICAL FROM DISPOSAL

After being injected into the wells, the majority of notified chemical is expected to remain inside the wells and will be permanently bonded to the rock surfaces. Disposal of large amount of the notified chemical after use is not expected.

A small amount of the notified chemical may be returned to the surface through capture of crude oil collection. Residual notified chemical contained in crude oil is expected to share the fate of crude oil. The notified chemical is expected to be removed from oil as waste during oil refinery and be disposed of safely or be thermally decomposed during the use of oil.

7.1.2. Environmental Fate

The notified chemical is expected to be persistent based on 0% biodegradation over 28 days. However, the notified chemical is not expected to have high potential for bioaccumulation based on the measured n-octanol/water partition coefficient (log Pow = -0.21 to 3.57). For the details of the environmental fate studies please refer to Appendix C.

The notified chemical is designed to bind permanently to the rock surface in the down-hole treatment of oil and gas wells to prevent undesirable production of solids. Therefore, the notified chemical is expected to remain

immobile in the environment. Any spills or accidental release of the product containing the notified chemical at the well site are expected to be handled by physical containment, collection and subsequent safe disposal consistent with local requirements. In the unlikely case if the notified chemical is released in the water system, the majority of the notified chemical is expected to partition to sludge based on ionic characteristic, low water solubility and relatively high log K_{oc} (1.25-4.65).

In water and landfill, the notified chemical is expected to degrade by biotic and abiotic processes to form water, oxides of carbon, nitrogen and phosphorus. For the details of the environmental fate studies please refer to Appendix C.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) for the notified chemical has not been calculated since no significant release of the notified chemical to the aquatic environment is expected based on its use pattern and physico-chemical properties.

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	Result	Assessment Conclusion
Fish Toxicity	96 hours LL > 6.0 mg *WAF/L	May be toxic to fish
Daphnia Toxicity	48 hours EL50 = 48 mg WAF/L	Harmful to aquatic invertebrates
Algal Toxicity	72 hours E_rL50 = 5.1 mg WAF/L	Toxic to algae
Inhibition of Bacterial Respiration	3 hours IC50 = 100 mg/L	No inhibitory effects on bacterial activity

WAF: Water accommodation fraction.

Based on the acute endpoint determined on algae, the notified chemical is formally classified as 'Acute category 2; toxic to aquatic life" under the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* (United Nations, 2009). The notified chemical was determined to be acutely toxic to algae and was not readily biodegradable. On this basis, the notified chemical is formally classified as 'Chronic category 2; Toxic to aquatic life with long term effect" under GHS (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated from the most sensitive endpoint for aquatic invertebrates. A safety factor of 100 was used given acute endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EL50 (Algae, 72 h)	5.1	mg/L
Assessment Factor	100	
PNEC:	51	µg/L

7.3. Environmental Risk Assessment

A risk Quotient (Q = PEC/PNEC) value has not been calculated since no PEC were derived. The notified chemical is not expected to have high potential for bioaccumulation based on the measured n-octanol/water partition coefficient and relatively high molecular weight. The notified chemical will be used in a closed-loop drilling system and is expected to bind permanently to the rock surface in the down-hole treatment of oil and gas wells. Therefore, release of the notified chemical to the aquatic environment is expected to be minimal. Although the notified chemical is toxic to aquatic life, it is not expected to reach ecotoxicologically significant concentrations in surface waters based on the assessed use pattern. Therefore, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -20 °C

Method	OECD TG 102 Melting Point/Melting Range. EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature.
Remarks	Pour point method. The material tested was the notified chemical in 20% methanol (20.9 mg in 20 mL methanol).
Test Facility	Harlan Laboratories Ltd, (2014a)

Boiling Point Not determined – decomposed before boiling

Method	OECD TG 103 Boiling Point. EC Council Regulation No 440/2008 A.2 Boiling Temperature.
Remarks	Differential scanning calorimetry method. The test substance (20.9 mg notified chemical in 20 mL methanol) decomposed from approximately 135 °C. No value for the boiling point could be determined.
Test Facility	Harlan Laboratories Ltd, (2014a)

Density > 1,050 kg/m^3 at 20 ± 0.5 °C

Method	OECD TG 109 Density of Liquids and Solids. EC Council Regulation No 440/2008 A.3 Relative Density.
Remarks	Pycnometer method. The test substance had a solid/liquid transition state and the test was performed on the liquid upper layer. The density of the total sample was assumed to be higher than that obtained on the upper layer.
Test Facility	Harlan Laboratories Ltd, (2014b)

Vapour Pressure < 1.1 × 10^{-6} kPa at 25 °C

Method	OECD TG 104 Vapour Pressure. EC Council Regulation No 440/2008 A.4 Vapour Pressure.
Remarks	Vapour pressure balance method, carried out on the test substance (the test substance had a solid/liquid transition state and the test was performed on the liquid upper layer).
Test Facility	Harlan Laboratories Ltd, (2014d)

Water Solubility 0.0402 - 0.0516 g/L at 20 °C

Method	OECD TG 105 Water Solubility. EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Flask Method. The test substance is complex mixture and some of the components are more soluble in water than others (the test substance had a solid/liquid transition state and the test was performed on the liquid upper layer). The measured water solubility values were from 0.0402 – 0.0516 g/L.
Test Facility	Harlan (2014b)

Water Solubility 0.0808 g/L at 20 °C

Method	OECD TG 105 Water Solubility. EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Flask Method. The test substance (containing the notified chemical at 80% concentration) is complex mixture and total organic carbon (TOC) analysis was selected as being the most appropriate technique.
Test Facility	Harlan (2014c)

Partition Coefficient (n-octanol/water) log Pow = -0.21 - 3.57 at 20 °C

Method	OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks	HPLC Method. The notified chemical is complex mixture and the HPLC chromatograms of

the test substance show seven peaks. The measured log Pow values for these seven peaks were from -0.21 to 3.57.

Test Facility Opus (2013)

Surface Tension 64.5 mN/m at 19.5 °C

Method OECD TG 115 Surface Tension of Aqueous Solutions.
EC Council Regulation No 440/2008 A.5 Surface Tension.

Remarks Ring method. The test substance had a solid/liquid transition state and the test was performed on the liquid upper layer.
Concentration: 90% saturated solution (upper liquid layer only)

Test Facility Harlan Laboratories Ltd, (2014b)

Adsorption/Desorption – screening test log K_{oc} = 1.25 - 4.65 at 30 °C

Method OECD TG 121 Adsorption - Desorption Using the HPLC screening method.

Remarks The notified chemical is complex mixture and measured log K_{oc} values were from -1.25 - 4.65 were recorded for the test substance (20.9 mg notified chemical in 20 mL methanol)

Test Facility Harlan (2014a)

Flash Point 74.7 ± 2 °C at 98.1 kPa

Method EC Council Regulation No 440/2008 A.9 Flash Point.

Remarks Closed cup method. The test substance had a solid/liquid transition state and the test was performed on the liquid upper layer.

Test Facility Harlan Laboratories Ltd, (2014e)

Autoignition Temperature 448 ± 5 °C

Method EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases).

Remarks A procedure designed to be compatible with method A15 was used on the notified chemical. The test substance had a solid/liquid transition state and the test was performed on the liquid upper layer.

Test Facility Harlan Laboratories Ltd, (2014e)

Explosive Properties Non explosive

Method EC Council Regulation No 1272/2008 of 16 December 2008. Explosive Properties.

Remarks Predicted negative based on the chemical structure of the test substance.

Test Facility Harlan Laboratories Ltd, (2014e)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical (at 80% concentration in propylene glycol)
METHOD	OECD TG 420 Acute Oral Toxicity – Fixed Dose Procedure EC Council Regulation No 440/2008 B.1 bis Acute toxicity (oral) fixed dose method
Species/Strain	Rat/ Wistar (RccHan™:WIST)
Vehicle	Dimethyl sulphoxide
Remarks - Method	Purity of the chemical in the test substance was not accounted for. No deviations from protocol. GLP compliant

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	1 F	300	0/1
2	1 F	2000	0/1
3	4 F	2000	0/4

LD50	> 2000 mg/kg bw
Signs of Toxicity	None
Effects in Organs	None
Remarks - Results	Hunched posture was observed in all animals post-exposure. Ataxia was observed in all 4 animals in group 3. Red/brown staining of the eyes and hunched posture were observed in 2/4 animals in group 3 at the 24 hour observation. Recovery was indicated in all animals at the 48 hour observation with 2/4 animals in group 3 showing recovery at the 24 hour observation. All animals made the expected gains in bodyweight
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Harlan (2015a)

B.2. Irritation – skin (*in vitro*)

TEST SUBSTANCE	Notified chemical (at 80% concentration in propylene glycol)
METHOD	OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method EpiSkin™ Reconstructed Human Epidermis Model
Vehicle	None
Remarks - Method	GLP compliant No deviations from protocol Positive control – Sodium Dodecyl Sulphate at 5% w/v Negative Control – Phosphate Buffered Saline Dulbecco's (PBS) with Ca^{++} and Mg^{++}

RESULTS

Test material	*Mean OD_{562} of triplicate tissues*	*Relative mean Viability (%)*	*SD of relative mean viability*
Negative control	1.165 ± 0.078	100	6.8
Test substance	0.283 ± 0.131	24.2	11.3
Positive control	0.108 ± 0.007	9.3	0.6

OD = optical density; SD = standard deviation

Remarks - Results	Positive and negative controls performed as expected.
CONCLUSION	The notified chemical (at 80% concentration) was irritating to the skin under the conditions of the test.
TEST FACILITY	Harlan (2014f)

B.3. Irritation – eye (*in vitro*)

TEST SUBSTANCE	Notified chemical (at 80% concentration in propylene glycol)
METHOD	OECD TG 437 Bovine Corneal Opacity and Permeability Test Assay
Vehicle	None.
Remarks - Method	GLP compliant No deviations from protocol Positive control – Ethanol Negative Control – 0.9% w/v Sodium Chloride solution

RESULTS

Test material	*Mean opacities of triplicate tissues (SD)*	*Mean permeabilities of triplicate tissues (SD)*	*IVIS (SD)*
Vehicle control	-	-	2.2 (0.7)
*Test substance**	31.0 (15.5)	1.695 (0.307)	56.4 (20.0)
*Positive control**	20.7 (2.3)	1.325 (0.543)	40.5 (5.9)

SD = Standard deviation; IVIS = *in vitro* irritancy score
*Corrected for background values

Remarks - Results	Positive and negative controls performed as expected.
CONCLUSION	The notified chemical (at 80% concentration) was corrosive or a severe eye irritant under the conditions of the test.
TEST FACILITY	Harlan (2014g)

B.4. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical (at 80% concentration in propylene glycol)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC commission Regulation 440/2008 B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	Phenobarbitone/β-Naphthoflavone induced male rat liver homogenate (S9fraction)
Concentration Range in Main Test	a) With metabolic activation: 1,5, 5, 15, 50, 150, 500, 1500, 5000 µg/plate b) Without metabolic activation: 1,5, 5, 15, 50, 150, 500, 1500, 5000 µg/plate
Vehicle	Dimethyl sulphoxide
Remarks - Method	GLP compliant. No deviations from protocol. Positive control: without metabolic activation: N-ethyl-N'-nitro-N-nitrosoguanidine (WP2*uvrA,* TA100, TA1535), 9-Aminoacridine (TA1537), 4-Nitroquinoline-1-oxide (TA98); with metabolic activation: 1-Aminoanthracene (TA100, TA1535, TA1537), Benzo(a)pyrene (TA98)

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity in Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 500 µg/plate	> 5000 µg/plate	mutagenic
Present			
Test 1	≥ 500 µg/plate	> 5000 µg/plate	non-mutagenic

Remarks - Results

A visible reduction in the growth of the bacterial lawn was observed in the presence and absence of metabolic activation in all strains from 500 µg/plate. No precipitation was observed on any of the plates; however a brown colour was noted at and above 1500 µg/plate.

The test substance induced dose-related and statistically significant increases in the frequency of revertant colonies in strain TA98 in the presence of metabolic activation at sub-toxic dose levels. The increase of revertants between 5 and 150 µg/plate was obvious with a maximum of 5.7-fold noted at 150 µg/plate. Increase of revertants was also noted for all other *Salmonella* strains; however the responses were not clearly dose-related. In the absence of metabolic activation, increase of revertants in strain WP2uvrA was also recorded at the dose level of 500 µg/plate and above.

All positive controls induced expected increase of revertants, confirming the sensitivity of the bacterial strains.

The test substance was considered by the study authors to be mutagenic under the conditions of the test.

CONCLUSION

The notified chemical was mutagenic to bacteria under the conditions of the test.

TEST FACILITY

Harlan (2014h)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical (at 80% concentration in propylene glycol)
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Carbon dioxide production
Remarks - Method	The test substance is poorly soluble in water. Therefore, the test substance was adsorbed on to granular silica gel prior to dispersion in the test medium to increase the exposure of the test substance to micro-organisms. The test was conducted according to the test guideline above with no significant deviation from the protocol.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	6	2	30
8	2	8	63
14	0	14	79
21	0	21	81
28	0	28	87

Remarks - Results	The position control attained 79% biodegradation in 14 days, satisfying validation value of 60% in 14 day. The total CO_2 evolution in the blank control met the validation criterion of less than 40 mg/L (37.14 mg/L in 28 days). The inorganic carbon content of the test item in the control was 0% of the total carbon content, satisfying the validation criterion of less than 5% The toxicity test attained 36% biodegradation in 14 day and 38% biodegradation in 28 days(> threshold value of 25%. Therefore the chemical is not considered to have inhibitory effects on sludge micro-organisms.
CONCLUSION	The notified chemical is not considered to be readily biodegradable.
TEST FACILITY	Harlan (2014i)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical (at 80% concentration in propylene glycol)
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi-static
Species	*Oncorhynchus mykiss*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	140 mg $CaCO_3$/L
Analytical Monitoring	HPLC-MS

Remarks – Method	Water accommodation fractions (WAFs) were used in the test as the test substance is poorly soluble in water. WAFs were prepared by adding weighed amount of test substance in water with stirring for 23 hours. The mixtures were allowed to stand for 1 hour and then removed the undissolved substance by filtration. The aqueous phase of WAFs was separated by mid-depth siphoning. The test preparations were renewed daily. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Concentration WAF mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*3 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	-	7	0	0	0	0	0
6.0	NA	7	0	0	0	0	0

LL50	> 6.0 mg/L WAF at 96 hours.
NOEL	6.0 mg/L WAF at 96 hours.
Remarks – Results	All validation criteria were satisfied. The test substance is a mixture and its toxicity should be attributed to the test substance as a whole but not a single component or mixture of some components. However, the analytical method (HPLC-MS) used in this test was specific to only the detectable species present in the test substance but not the test substance as a whole. Therefore, the test results were based on nominal test concentration.

CONCLUSION The notified chemical may be toxic to fish

TEST FACILITY Harlan (2014j)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical (at 80% concentration in propylene glycol)

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test – static

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC-MS
Remarks - Method	Water accommodation fractions (WAFs) were used in the test as the test substance is poorly soluble in water. WAFs were prepared by adding different amount of test substance separately in water. The mixtures were stirred for 23 hours and allowed to stand for 1 hour. Undissolved substance was removed by filtration. The aqueous phase of WAFs was separated by mid-depth siphoning and used separately in the test. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Concentration WAF mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	-	20	0	0
Solvent control	-	20	0	0
1.0	NA	20	0	0

3.2	NA	20	0	0
10	NA	20	0	0
32	NA	20	0	3
100	NA	20	20	20

EL50 48 mg/L WAF at 48 hours (95% confidence limits: 40-57 mg/L WAF)
NOEL 10 mg/L WAF at 48 hours
Remarks - Results All validation criteria were satisfied.

The test substance is a mixture and its toxicity should be attributed to the test substance as a whole but not a single component or mixture of some components. However, the analytical method (HPLC-MS) used in this test was specific to only the detectable species present in the test substance but not the test substance as a whole. Therefore, the test results were based on nominal test concentration.

CONCLUSION The notified chemical is harmful to aquatic invertebrates.

TEST FACILITY Harlan (2014k)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical (at 80% concentration in propylene glycol)

METHOD OECD TG 201 Alga, Growth Inhibition Test.
Species *Pseudokirchneriella subcapitata*
Exposure Period 72 hours
Concentration Range Nominal: Control, 0.10, 0.32, 1.0, 3.2 and 10 WAF mg/L
Actual: Not determined
Auxiliary Solvent None
Water Hardness Not available
Analytical Monitoring HPLC-MS
Remarks - Method Water accommodation fractions (WAFs) were used in the test as the test substance is poorly soluble in water. WAFs were prepared by adding different amount of weighed test substance in the culture medium individually. The mixtures were stirred for 23 hours and allowed to stand for 1 hour. Undissolved substance was removed by filtration. The aqueous phase of WAFs was separated by mid-depth siphoning and used in the test.

The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Biomass		*Growth*	
EL50	*NOEL*	*EL*	*NOEL*
mg/L WAF at 72h	*mg/L WAF at 72 h*	*mg/L WAF at 72 h*	*mg/L WAF at 72 h*
2.9	1.0	5.1	1.0

Remarks - Results All validation criteria were satisfied.

The test substance is a mixture and its toxicity should be attributed to the test substance as a whole but not a single component or mixture of some components. However, the analytical method (HPLC-MS) used in this test was specific to only the detectable species present in the test substance but not the test substance as a whole. Therefore, the test results were based on nominal test concentration.

CONCLUSION The notified chemical is toxic to algae

TEST FACILITY	Harlan (2014l)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical (at 80% concentration in propylene glycol)
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sludge
Exposure Period	3 hours
Concentration Range	Nominal: Control, solvent control, 10, 100, 1000 mg/L Actual: Not determined
Remarks – Method	The test substance is poorly soluble in water. Therefore, the test substance was adsorbed on to granular silica gel prior to dispersion in the test medium to increase the exposure of the test substance to micro-organisms.
RESULTS	
IC50	100 mg/L
NOEC	Not available
Remarks – Results	The oxygen uptake rate in the blank controls was 27.75 and 36 mg per one gram of activated sludge, greater than the threshold value of 20 mg oxygen per one gram of activated sludge. The reference item has a determined 3 h EC50 = 8.0 mg/L, in the range of the validation value 2 mg/L – 25 mg/L. Therefore, all validation criteria were met.
CONCLUSION	The notified chemical is not considered to be inhibitory to microbial respiration.
TEST FACILITY	Harlan (2014m)

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