File No: STD/1537

December 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Methyl Glucose Caprate/Caprylate/Oleate

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:

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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
STD/1537	Lubrizol International Inc.	Methyl Glucose Caprate/Caprylate/Oleate	Yes	< 30 tonnes per annum	Component of rinse-off cosmetic products

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 for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the table below.

Hazard classification	*Hazard statement*
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:

R43: May cause sensitisation by skin contact

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.

When used at < 5% in rinse-off cosmetic products, the notified chemical is not considered to pose an unreasonable 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 an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Skin sensitisation (Category 1): H317 – May cause an allergic skin reaction

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.

- The Delegate (and/or the Advisory Committee on Chemicals Scheduling) should consider the notified chemical for listing on the SUSMP.

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 reformulation processes:
  - Enclosed, automated processes, where possible

- 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 during reformulation processes:
  - Avoid contact with skin

- 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 during reformulation processes:
  - Impervious gloves and coveralls

  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.

Public Health

- The following measures should be taken formulators to minimise public exposure to the notified chemical:
  - The notified chemical should only be used at < 5% in rinse-off cosmetic products.

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

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 intended to be used in leave-on cosmetic products;

- the concentration of the notified chemical exceeds or is intended to exceed 5% in rinse-off cosmetic products;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of rinse-off cosmetic products, 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 a 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
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, CAS number, other names, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, additives/adjuvants, import volume and use details.

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, acute inhalation toxicity, repeated dose toxicity, in vivo genotoxicity, bioaccumulation.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
Canada (2014), Japan (2013).

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Methyl Glucose Caprate/Caprylate/Oleate (INCI name)
Glucamate™ CCO Thickener (product containing the notified chemical at ≤ 80% concentration).

OTHER NAME(S)
GMT1009
Z-150

MOLECULAR WEIGHT
UVCB

ANALYTICAL DATA
Reference NMR, IR, HPLC, GC, HR-GPC, TGA and UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
UVCB

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Yellow liquid.

Property	Value	Data Source/Justification
Melting Point/Freezing Point	30 ± 3 °C	Measured
Boiling Point	Decomposed from ~ 293 °C at 100.9 kPa	Measured
Density	1.11 x 10^3 kg/m^3 at 20.0 ± 0.5 °C	Measured
Vapour Pressure	2.8 x 10^{-8} kPa at 25 °C	Measured
Water Solubility	6.33 x 10^{-2} g/L at 20 °C (0.1 g/L loading rate)	Measured

	0.49 g/L at 20 °C (1.0 g/L loading rate)	
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities. However, the notified chemical is not expected to be significantly hydrolysed under normal environmental conditions (pH 4-9).
Partition Coefficient (n-octanol/water)	log Pow < 0.3 to 6.84 (for 77% of the test item)	Measured. Expected to partition to the interface between octanol and water, based on its surfactant properties.
	log Pow > 10.0 (for 22.4% of the test item)	
Surface Tension	36.0 mN/m at 22.0 ± 0.5 °C	Measured
Adsorption/Desorption	log K_{oc} < 1.25 to 2.97 (for 30.7% of the test item)	Measured. Expected to partition to phase boundaries based on its surfactant properties.
	log K_{oc} > 5.63 (for 69.3% of the test item)	
Dissociation Constant	Not determined	Does not contain ionisable functionalities
Flash Point	227 ± 2 °C at 101.3 kPa	Measured
Autoignition Temperature	352 ± 5 °C	Measured
Explosive Properties	Predicted negative	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Predicted negative	Contains no functional groups that would imply oxidising properties.

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. Direct sources of heat (elevated temperatures), freezing and contact with oxidising agents should be avoided.

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.

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. The notified chemical will be imported into Australia (as manufactured) at ≤ 80% concentration, as well as a component of various formulated end-use rinse-off cosmetic products (at concentrations < 5%).

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	1 - 10	1 - 10	10 - 20	10 - 20	20 - 30

PORT OF ENTRY
Ports in Western Australia, Queensland and Victoria.

IDENTITY OF MANUFACTURER/RECIPIENTS
Lubrizol International Inc.

TRANSPORTATION AND PACKAGING

The notified chemical (at ≤ 80% concentration) will be imported into Australia in 55 gallon steel drums or 5 gallon white plastic pails. The end-use products (< 5% notified chemical) will be packaged in typical consumer-sized containers suitable for retail sale.

The notified chemical will be transported from the port of entry by road to the notifier's warehouse facilities for storage in its original packaging until transportation to the customer site. Alternatively, the notified chemical and products containing it will be shipped directly from the port of entry to the customer site.

USE
The notified chemical will be used as a thickener component for surfactant systems in a variety of rinse-off cosmetic and personal care formulations (at < 5% concentration). Example products that will contain the notified chemical include shampoo, facial cleansers, liquid hand soaps and shower gels.

OPERATION DESCRIPTION
No manufacturing, processing, reformulating or repackaging of the notified chemical (≤ 80% concentration) will occur at the notifier's facility. The imported products containing the notified chemical will be stored at this facility until they are transported to customer facilities (in original importation packaging).

At the customer facilities, the procedures for incorporating the imported product (containing ≤ 80% notified chemical) into end-use products will likely vary depending on the nature of the products formulated, and may involve both automated and manual transfer steps. In general it is expected that the reformulation processes will involve blending operations that will be highly automated and occur in a fully enclosed environment, followed by automated filling of the reformulated products into containers of various sizes.

End use products
The finished rinse-off cosmetic products containing the notified chemical at < 5% concentration will be used by consumers and professionals (such as beauticians and hairdressers). Depending on the nature of the product, application of products could be by hand or through the use of an applicator. In some cases the products will be diluted with water prior to application. All products containing the notified chemical are intended to be rinsed off after application.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

EXPOSURE DETAILS
Transport and storage
Transport and storage workers may come into contact with the notified chemical, at ≤ 80% concentration or as a component of the end-use products (< 5% concentration), only in the event of accidental rupture of containers.

At the notifier facility, the primary work activity undertaken by transport and warehouse workers will include the handling, loading and off-loading of drums containing the notified chemical at ≤ 80% concentration. Exposure of these workers will be limited to situations of an accidental discharge, spill or leaking drum, requiring clean up. If such an event occurs, a worker may be exposed through dermal or ocular contact.

Formulation of end use products
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical (at ≤ 80% concentration) may occur during weighing and transfer stages, blending, and cleaning and maintenance of equipment. The notifier states that exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems, and through the use of appropriate PPE.

Professionals using the end products
Exposure to the notified chemical in end-use products may occur in professions where the services provided involve the application of rinse-off cosmetic products (at < 5% concentration) to clients (e.g. hair dressers, workers in beauty salons). The principal route of exposure will be dermal, while ocular exposure is also possible. In some cases the products will be diluted with water prior to use and the products are intended to be rinsed off after use. Such professionals may use some PPE to minimise repeated exposure and good hygiene practices are

expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical through the use of the rinse-off cosmetic products (< 5% concentration in individual products). The principal route of exposure will be dermal, while ocular exposure is also possible. Systemic exposure to the notified chemical is expected to be limited by the rinse-off nature of the cosmetic products.

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 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration	non genotoxic
Genotoxicity – in vitro mammalian cell gene mutation	non mutagenic

Toxicokinetics, metabolism and distribution.
Based on the UVCB nature of the notified chemical (components with molecular weight < 500 Da) and the physico-chemical properties (including water solubility, partition coefficient and surface active nature) of the notified chemical, passive diffusion across the gastrointestinal (GI) tract and dermal absorption is possible.

Acute toxicity.
The notified chemical was found to have low acute toxicity via the oral and dermal routes in studies in rats.

No acute inhalation toxicity data were provided for the notified chemical.

Irritation.
In an acute dermal irritation study in rabbits, a single 4-hour, semi-occluded application of the notified chemical did not result in any signs of irritation.

In a rabbit eye irritation study, mild reddening of the conjunctivae and sclerae, ocular discharge and slight iris light reflex was noted in some of the treated eyes 1 hour after treatment. These effects were no longer evident 24 hours after treatment.

Sensitisation.
The notified chemical was found to be a skin sensitiser in mice (Local Lymph Node Assay; stimulation indices of 2.6, 7.2 and 6.6 at 25, 50 and 75% concentrations, respectively). The EC_3 value was calculated to be 27.2%.

Repeated dose toxicity.
No repeated dose toxicity data were provided for the notified chemical.

Mutagenicity/Genotoxicity.
The notified chemical was not mutagenic in bacterial reverse mutation and mammalian cell gene mutation studies and non-clastogenic in an in vitro mammalian chromosome aberration test.

Health hazard classification
Based on the available information, the notified chemical is 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. The recommended hazard classification is presented in the following table.

Hazard classification	***Hazard statement***

Skin Sensitisation (Category 1)	H317 – May cause an allergic skin reaction

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase(s):

R43: May cause sensitisation by skin contact

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Reformulation

Exposure of workers to the notified chemical (at ≤ 80% concentration) may occur during blending operations. The notified chemical is considered to be a skin sensitiser and the repeated dose toxicity effects of the notified chemical have not been determined. Therefore, caution should be exercised when handling the notified chemical during reformulation processes.

Therefore, provided that control measures are in place to minimise worker exposure, including the use of automated processes and PPE, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

End-use

Beauty care professionals will handle the notified chemical at < 5% concentration, similar to public use. Therefore, the risk to workers who regularly use products containing the notified chemical is expected to be of a similar or lesser extent than that experienced by members of the public who use such products on a regular basis. For details of the public health risk assessment see Section 6.3.2.

6.3.2. Public Health

Skin sensitisation

The main risk associated with use of the notified chemical at the proposed concentrations of < 5% in rinse-off cosmetics, is its potential to cause sensitisation by skin contact.

Methods for the quantitative risk assessment of dermal sensitisation have been proposed and been the subject of significant discussion (see for example, Api *et al.*, 2008 and RIVM, 2010). Using hand wash soap (containing 5% notified chemical) as an example product that may contain the notified chemical, as a worst case scenario, the Consumer Exposure Level (CEL) is estimated to be 11.63 μg/cm^2 (SCCS, 2012). Following consideration of the available data on skin sensitisation and application of appropriate safety factors, an Acceptable Exposure Level (AEL) of 25.16 μg/cm^2 was derived (using the EC3 value of 27.2%, which was obtained in the LLNA study on the notified chemical). In this instance, the factors employed included an interspecies factor (3), intraspecies factor (10), a matrix factor (3.16) and a use and time factor (3.16), giving an overall safety factor of ~300.

As the AEL > CEL, the risk to the public of the induction of sensitisation that is associated with the use of the notified chemical in rinse-off cosmetic products (using hand wash soap as a worst case example) at < 5% concentration is not considered to be unreasonable. Based on the lower expected exposure level from use of other rinse-off cosmetic products (< 5% notified chemical), by inference, the risk of induction of sensitisation associated with the use of these products is also not considered to be unreasonable. It is acknowledged that consumers may be exposed to multiple products containing the notified chemical, and a quantitative assessment based on the aggregate exposure has not been conducted.

Repeated-dose toxicity

The repeated dose toxicity effects of the notified chemical have not been determined. However, systemic exposure to the notified chemical is expected to be limited by the rinse-off nature of the cosmetic products.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at < 5% concentration in rinse-off cosmetic products, is not considered to be unreasonable. In the absence of data on the repeated dose toxicity potential of the notified chemical, use of the notified chemical is supported only under limited exposure conditions, which are reflected in the rinse-off nature of the cosmetic products.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured in Australia; therefore there will be no release of the notified chemical to the environment from this activity. Environmental release during importation, transport and distribution may occur as a result of accidental spills. In the event of a spill, the notified chemical is expected to be contained and collected with an inert absorbent material and disposed of in accordance with local regulations.

During reformulation processes, limited release of the notified chemical is expected from cleaning of equipment as washings will be reused. A small percentage of the import volume is estimated to be generated as waste from residues in empty containers and spills during reformulation. Empty containers containing the notified chemical will either be recycled or disposed of through an approved waste management facility.

RELEASE OF CHEMICAL FROM USE

The majority of the notified chemical is expected to be released to sewers across Australia as a result of its use in cosmetic products, which will be washed off the hair and skin of consumers and disposed of to the sewer. A small percentage of up to 3% of the total import volume of the notified chemical, as residues in empty end use containers, is expected to be disposed of to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

It is expected that some of the product containing the notified chemical will remain in end-use containers. The containers are expected be disposed of through domestic garbage disposal and will enter landfill, or be subjected to recycling processes.

7.1.2. Environmental Fate

The notified chemical is readily biodegradable based on the provided study report. For the details of the environmental fate study please refer to Appendix C.

The majority of the notified chemical is expected to be released to Sewage Treatment Plants (STPs) via domestic wastewater. Based on its ready biodegradability, the notified chemical is expected to be largely degraded by sewage treatment processes. The notified chemical is expected to partition to phase boundaries as it is surface active. Therefore, the notified chemical released to STPs has potential to partition to sludge. Any notified chemical remaining in treated sewage effluents is likely to be released to surface waters or applied to land when used for irrigation. Notified chemical in sewage sludge is anticipated to be disposed of to landfill or applied to land when sludge is used for soil remediation. Based on its surface active property, the notified chemical is likely to partition to phase boundaries, and is therefore not expected to bioaccumulate. The notified chemical is expected to degrade in STPs, surface waters, soils and landfill due to its ready biodegradability to form water, and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The calculation for the Predicted Environmental Concentration (PEC) is summarised in the table below. Based on the reported use in cosmetic products, it is assumed that 100% of the total import volume of the chemical will be released to sewer on a nationwide basis over 365 days per year. It was assumed conservatively that none of the notified chemical will be removed during STP processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	30,000	kg/year
Proportion expected to be released to sewer	100.000%	
Annual quantity of chemical released to sewer	30,000.000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	82.19	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	22.613	million

Removal within STP	0%	
Daily effluent production:	4,523	mL
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	18.17	µg/L
PEC - Ocean:	1.82	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 L/m^2/year (10 mL/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 18.2 µg/L may potentially result in a soil concentration of approximately 121.2 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 605.8 µg/kg and 1.2 mg/kg, respectively.

7.2. Environmental Effects Assessment

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	LC50 (96 h) > 100 mg/L	Not harmful to fish
Daphnia Toxicity	EC50 (48 h) > 100 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity	E_rC50 (72 h) > 100 mg/L	Not harmful to algae
Inhibition of bacteria respiration	EC50 (3 h) > 1000 mg/L	Not inhibitory to microbial activity

On the basis of the acute toxicity data, the notified chemical is not harmful to fish, aquatic invertebrates and algae. Therefore, the notified chemical is not formally classified for either acute or chronic toxicity under the Globally Harmonised System of Classification of Chemicals (GHS; United Nations, 2009) due to a lack of aquatic toxicity.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) was calculated based on the endpoints for test species and an assessment factor of 100. The assessment factor of 100 was used since measured ecotoxicological data for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Alga)	> 100	mg/L
Assessment Factor	100	
PNEC:	> 1,000	µg/L

7.3. Environmental Risk Assessment

Based on the above PEC and PNEC values, the following Risk Quotient (Q) has been calculated:

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	18.17	> 1,000	< 0.018
Q - Ocean:	1.82	> 1,000	< 0.002

The Risk Quotients (Q = PEC/PNEC) for the notified chemical have been calculated to be < 1 for the river and ocean compartments. Therefore, the notified chemical is unlikely to result in ecotoxicologically significant concentrations in the aquatic environment from the assessed use pattern. The notified chemical is readily biodegradable, thus it is unlikely to persist in surface waters or soils. The notified chemical is considered to have low potential for bioaccumulation. Therefore, the notified chemical is not expected to pose an unreasonable risk to the aquatic environment from the assessed use pattern.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point 30 ± 3 °C

Method	OECD TG 102 Melting Point/Melting Range.
Remarks	Determined by the pour point method.
Test Facility	Harlan (2014a)

Boiling Point Decomposed from ~ 293 °C at 100.9 kPa

Method	OECD TG 103 Boiling Point.
Remarks	Determined using differential scanning calorimetry (DSC).
Test Facility	Harlan (2014a)

Density 1.11×10^3 kg/m^3 at 20.0 ± 0.5 °C

Method	OECD TG 109 Density of Liquids and Solids.
Remarks	Determined using a gas comparison pycnometer.
Test Facility	Harlan (2014a)

Vapour Pressure 2.8×10^{-8} kPa at 25 °C

Method	OECD TG 104 Vapour Pressure.
Remarks	Determined by the vapour pressure balance method.
Test Facility	Harlan (2013a)

Water Solubility 6.33×10^{-2} g/L at 20 °C (0.1 g/L loading rate)
0.49 g/L at 20 °C (1.0 g/L loading rate)

Method	OECD TG 105 Water Solubility. EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Flask Method. The results indicated that the water solubility of the test item was loading rate dependent.
Test Facility	Harlan (2014a)

Partition Coefficient (n-octanol/water) log Pow < 0.3 to 6.84 (for 77% of the test item)
log Pow > 10.0 (for 22.4% of the test item)

Method	OECD TG 117 Partition Coefficient (n-octanol/water). EC Council Regulation No 440/2008 A.8 Partition Coefficient.
Remarks	HPLC Method
Test Facility	Harlan (2014a)

Surface Tension 36.0 mN/m at 22.0 ± 0.5 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions.
Remarks	Concentration: 90% saturated solution. Determined by a ring method (4 cm ring). The test item was considered to be surface active.
Test Facility	Harlan (2014a)

Adsorption/Desorption log K_{oc} < 1.25 to 2.97 (for 30.7% of the test item)
log K_{oc} > 5.63 (for 69.3% of the test item)

Method	OECD TG 121 : HPLC Method
Remarks	The main components of the test item contained no dissociable functionalities, and therefore, the test substance was tested with an approximately neutral mobile phase.
Test Facility	Harlan (2013c)

Flash Point 227 ± 2 °C at 101.3 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks	Determined using a closed cup equilibrium method.
Test Facility	Harlan (2013b)

Autoignition Temperature 352 ± 5 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	Determined by heating aliquots of the test material in a flask and observing any ignition.
Test Facility	Harlan (2013b)

Explosive Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.14 Explosive Properties.
Remarks	Observation of functional groups that would imply explosive properties.
Test Facility	Harlan (2013b)

Oxidizing Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.21 Oxidizing Properties (Liquids).
Remarks	Observation of functional groups that would imply oxidising properties.
Test Facility	Harlan (2013b)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity – Fixed Dose Procedure.
Species/Strain	Rat/ Wistar (RccHan™:WIST)
Vehicle	Polyethylene glycol 300 (PEG 300)
Remarks - Method	No significant protocol deviations. GLP Compliance. A sighting study was conducted with 1 female animal (2000 mg/kg bw) to determine the dose level for the main study.

RESULTS

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	On day 1 after treatment, 2 animals showed ruffled fur at all observation time points (within 0.5, 1, 2, 3 and 5 hours after treatment). From day 2 onwards, no clinical signs were observed in any animal.
Effects in Organs	No macroscopic findings were recorded at necropsy.
Remarks - Results	All animals recorded body weights gains over the study period.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Harlan (2014b)

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	PEG 300
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations. GLP Compliance.

RESULTS

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

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	No local dermal signs were observed.
Signs of Toxicity - Systemic	Scratching was observed on the anterior dorsum of 1 female animal on day 1 and 2 after removal of the dressing. No further clinical signs were noted.
Effects in Organs	No macroscopic findings were recorded at necropsy.
Remarks - Results	The study authors indicated that all animals recorded body weights typical to the strain and age. However, it is noted that 3 female animals showed slight body weight decreases (< 5 g) between days 8 and 15.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Harlan (2014c)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 F
Vehicle	None specified.
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations. The study authors noted that the body weights recorded for the 3 animals at treatment (1791 – 1967 g) were slightly below the given range in the study plan (2.5 kg ± 20%). However, this was not considered to have impacted on the validity of the study. GLP Compliance.

RESULTS

Remarks - Results	No clinical signs or skin reactions were noted in any animal during the study period.
CONCLUSION	The notified chemical is non-irritating to the skin.
TEST FACILITY	Harlan (2014d)

B.4. Irritation – eye

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 F
Observation Period	72 hours
Remarks - Method	No significant protocol deviations. GLP Compliance.

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	0	0	1	< 24 hours	0
Conjunctiva: chemosis	0	0	0	0	-	0
Conjunctiva: discharge	0	0	0	3	< 24 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results	Mild reddening of the conjunctivae (2/3) and sclerae (2/3), ocular discharge (2/3) and slight iris light reflex (1/3) was noted in treated eyes 1 hour after treatment. These effects were no longer evident 24 hours after treatment.
CONCLUSION	The notified chemical is slightly irritating to the eye.
TEST FACILITY	Harlan (2014e)

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/CaOlaHsd
Vehicle	Acetone:olive oil (AOO) 4:1 v/v
Remarks - Method	No significant protocol deviations. GLP Compliance. A pre-test was conducted to determine the appropriate vehicle and the highest non-irritant test concentrations for the main study. The maximum technically achievable concentration (75%) was used. A concurrent positive control test was conducted using alpha-hexacinnamaldehyde in AOO 4:1 v/v.

RESULTS

Concentration (% w/w)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	93 ± 41	-
25	241 ± 69	2.6
50	669 ± 270	7.2
75	613 ± 189	6.6
Positive Control		
25	831 ± 128	8.9

Remarks - Results	No clinical signs of irritation on the ears or systemic toxicity were observed in any of the animals during the study period. There was no ear thickness increase ≥ 25%. An EC3 value of 27.2% was determined. The control groups produced satisfactory responses, thus confirming the validity of the test system.
CONCLUSION	There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	Harlan (2014f)

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-naphthoflavone-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	Dimethyl sulphoxide (DMSO)
Remarks - Method	No significant protocol deviations. GLP Compliance. No preliminary toxicity study was conducted. Positive control tests were conducted in parallel to the main test using N-ethyl-N'-nitro-N-nitroguanidine (WP2uvrA, TA100 and TA1535), 9-aminoacridine (TA1537) and 4-nitroquinoline-1-oxide (TA98) in the

absence of S9 and 2-aminoanthracene (WP2uvrA, TA100, TA1535 and TA1537) and benzo(a)pyrene (TA98) in the presence of S9 mix.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	-	> 5,000	> 5,000	negative
Test 2	-	> 5,000	> 5,000	negative
Present				
Test 1	-	> 5,000	> 5,000	negative
Test 2	-	> 5,000	> 5,000	negative

Remarks - Results

A test item film (cream-coloured in appearance) was observed on the 5,000 µg/plates with and without metabolic activation, however, the study authors indicated that this observation did not prevent the scoring of revertant colonies.

There were no statistically significant increases in the number of revertant colonies at any dose level, with or without metabolic activation under the conditions of the test.

The positive controls produced satisfactory responses, thus confirming the validity of the test system.

CONCLUSION

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

TEST FACILITY

Harlan (2013d)

B.7. 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 phenobarbital/β-naphthoflavone-induced rat liver

Vehicle: DMSO

Remarks - Method: No significant protocol deviations.
GLP Compliance.

A preliminary toxicity study was performed (4 hour exposure, with and without activation, and a continuous 24 hour exposure without activation) at concentrations 19.53 – 5,000 µg/mL. A precipitate was seen in the cultures at ≥ 156.25 µg/mL in the absence of metabolic activation and at ≥ 312.5 µg/mL in the presence of metabolic activation. Based on this study, the maximum dose in the mutagenicity tests was limited by test item-induced toxicity (as indicated by marked reductions in relative suspension growth).

Vehicle and positive controls (ethylmethanesulphonate without metabolic activation and cyclophosphamide with metabolic activation) were used in parallel with the test material.

The S9 fraction was used in Test 1 at 2% final concentration and in Test 2 at 1% final concentration.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Section Time*
Absent				
Test 1	0*, 9.75*, 19.5*, 39*, 78*, 117*, 156*, 234, 312	4 h	48 h	10-14 days
Test 2	0*, 4.88, 9.77*, 19.53*, 39.06*, 78.13*, 117.19*, 156.25*, 234.38	24 h	48 h	10-14 days
Present				
Test 1	0*, 19.5*, 39*, 78*, 156*, 312*, 416*, 520, 624	4 h	48 h	10-14 days
Test 2	0*, 25*, 50*, 100*, 200*, 400, 450, 500, 550	4 h	48 h	10-14 days

*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	≥ 312.5	≥ 234	≥ 117	negative
Test 2	≥ 312.5	≥ 234.38	≥ 156.25	negative
Present				
Test 1	≥ 625	≥ 520	≥ 312	negative
Test 2		≥ 400	≥ 400	negative

Remarks - Results

The study authors noted that due to the steepness of the toxicity curve, optimum toxicity was difficult to achieve, but considered that the test item had been adequately tested.

No statistically significant or dose-related increases in the number of mutant cells were recorded at any dose level, with or without metabolic activation, in either of the two experiments.

The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.

CONCLUSION

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

TEST FACILITY

Harlan (2013e)

B.8. 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-naphthoflavone induced rat liver.

Vehicle: DMSO.

Remarks - Method: No significant protocol deviations.
GLP Compliance.

A preliminary toxicity study was performed (4 hour exposure, with and without activation followed by a 20 hour recovery period, and a continuous 24 hour exposure without activation) at concentrations 19.53 – 5,000 µg/mL. Haemolysis was noted at 5,000 µg/mL in both 4 hour exposure groups and at ≥ 1,250 µg/mL in the 24 hour exposure group. In addition, precipitate was seen in the cultures at ≥ 156.25 µg/mL.

Vehicle and positive controls (mitomycin C without metabolic activation and cyclophosphamide with metabolic activation) were used in parallel

with the test material

The S9 fraction was used in Test 1 at 2% final concentration and in Test 2 at 1% final concentration.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 45, 90*, 180*, 360*, 540, 720	4 h	24 h
Test 2	0*, 40*, 80*, 160*, 240, 320, 480, 640	24 h	24h
Present			
Test 1	0*, 90, 180*, 360*, 720*, 1080, 1440	4 h	24 h
Test 2	0*, 80*, 160, 320, 480*, 640, 720*	4 h	24 h

*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	≥ 625	≥ 540	≥ 180	negative
Test 2	≥ 312.5	≥ 240	≥ 480	negative
Present				
Test 1	≥ 1,250	≥ 720	≥ 360	negative
Test 2		≥ 720	≥ 320	negative

Remarks - Results

Precipitate was observed at lower concentrations than in the preliminary test. A steep toxicity curve was evident, as indicated by the absence of metaphase cells at doses above the analysed concentrations in Test 1 and the optimum level of toxicity being exceeded at ≥ 240 µg/mL in Test 2 in the absence of activation.

No statistically significant increases in the number of cells with aberrations or polyploidy cells were noted at any dose level, with or without metabolic activation, in either of the two experiments.

The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.

CONCLUSION

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

TEST FACILITY

Harlan (2014g)

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	Nil
Analytical Monitoring	CO_2 Evolution
Remarks - Method	No significant protocol deviations. GLP Compliance.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	16	2	46
10	68	10	76
14	82	14	86
28	86	28	86

Remarks - Results	All validity criteria for the test were satisfied. The reference compound, aniline, reached the 60% pass level by day 7 indicating the suitability of the inoculum. The toxicity control exceeded 25% biodegradation within 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance after the cultivation period was 86% within 28 days and satisfied the 10-day window validation criterion. Therefore, the test substance can be classified as readily biodegradable according to the OECD (301 B) guideline
CONCLUSION	The notified chemical is readily biodegradable
TEST FACILITY	Harlan (2013f)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi-static Test
Species	Zebra Fish (*Danio rerio*)
Exposure Period	96 hours
Auxiliary Solvent	Not reported
Water Hardness	125 mg $CaCO_3$/L
Analytical Monitoring	HPLC-MS
Remarks - Method	No significant protocol deviations. GLP Compliance.

The fish ecotoxicity test was conducted in a Water Accommodated Fraction (WAF) of the notified chemical as it is a complex mixture and has low water solubility. The WAF was prepared by dispersing the pre-measured quantity of the test item in test water. The stock solution was inverted several times to ensure adequate mixing and homogeneity.

RESULTS

Nominal loading rate (WAF;mg/L)	*Number of Fish*	*Mortality (%)*				
		3 h	*24 h*	*48 h*	*72 h*	*96 h*
Control	7	0	0	0	0	0
100	7	0	0	0	0	0

LL50	> 100 mg/L at 96 hours (WAF)
NOEL	100 mg/L
Remarks - Results	All validity criteria for the test were satisfied. The test was conducted as a limit test. The treatment WAF solutions were renewed every 24 hours. The concentrations of the new and old WAF solutions were measured at every renewal. However, the LL50 value was estimated based on the nominal loading rates as the toxicity cannot be attributed to a single component or mixture of components but to the test substance as a whole. The 96-hour EL_{50} was estimated by visual observations.
CONCLUSION	The notified chemical is not harmful to aquatic invertebrates
TEST FACILITY	Harlan (2014h)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – Semi-static Test
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Not reported
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC-MS
Remarks - Method	No significant protocol deviations. GLP Compliance. The daphnia ecotoxicity test was conducted in a WAF of the notified chemical as it is a complex mixture and has low water solubility.

RESULTS

Nominal loading rate (WAF;mg/L)	*Number of D. magna*	*Cumulative % Immobilised*	
		24 h	*48 h*
Control	20	0	0
100	20	0	0

EL50	> 100 mg/L at 48 hours (WAF)
NOEL	100 mg/L
Remarks - Results	All validity criteria for the test were satisfied. The treatment WAF solutions were renewed every 24 hours. The concentrations of the new and old WAF solutions were measured at every renewal. However, the EL50 value was estimated based on the nominal loading rates as the toxicity cannot be attributed to a single component or mixture of components but to the test substance as a whole. The 48-hour EL_{50} was estimated by visual observations.
CONCLUSION	The notified chemical is not harmful to aquatic invertebrates
TEST FACILITY	Harlan (2013g)

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: 1.0, 3.2, 10, 32, and 100 mg/L
Auxiliary Solvent	Not reported
Water Hardness	Not reported
Analytical Monitoring	HPLC-MS
Remarks - Method	No significant protocol deviations. GLP Compliance. The algae ecotoxicity test was conducted in a WAF of the notified chemical as it is a complex mixture and has low water solubility. The WAF was prepared by dispersing the pre-measured quantity of the test item in test water. The stock solution was inverted several times to ensure adequate mixing and homogeneity.

RESULTS

Biomass (72 h)		*Growth (72 h)*	
E_yC50 (WAF;mg/L)	*NOE_yC (WAF;mg/L)*	*E_rC50 (WAF;mg/L)*	*NOE_rC (WAF;mg/L)*
26	32	> 100	32

Remarks - Results	All validity criteria for the test were satisfied. The treatment WAF solutions were renewed every 24 hours. The concentrations of the new and old WAF solutions were measured at every renewal. However, the EL50 value was estimated based on the nominal loading rates as the toxicity cannot be attributed to a single component or mixture of components but to the test substance as a whole. The 72-hour E_rL_{50} was estimated by visual observations.
CONCLUSION	The notified chemical is not harmful to algae
TEST FACILITY	Harlan (2014i)

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 1,000 mg/L
Remarks – Method	No significant protocol deviations. GLP Compliance.
RESULTS	
EL50	> 1,000 mg/L (loading rate)
NOEL	1,000 mg/L (loading rate)
Remarks – Results	All validity criteria for the test were satisfied.
CONCLUSION	The notified chemical is not expected to inhibit microbial activity.
TEST FACILITY	Harlan (2013h)

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