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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Polyglyceryl-4 Laurate/Sebacate

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
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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/1975	Croda Singapore (trading as Croda Australia)	Polyglyceryl-4 Laurate/Sebacate	ND*	≤ 1 tonne/s per annum	Cosmetic ingredient

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified polymer is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

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 3	H402 - Harmful to aquatic life

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

When used in the proposed manner, the notified polymer 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 polymer is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- No specific engineering controls, work practices or personal protective equipment are required for the safe use of the notified polymer itself. However, these should be selected on the basis of all ingredients in the formulation.

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

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

- If products and mixtures containing the notified polymer 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 polymer in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Emergency procedures

- Spills or accidental release of the notified polymer should be handled by containment, physical 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 polymer 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;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the polymer has changed from cosmetic ingredient or is likely to change significantly;
  - the amount of polymer being introduced has increased, or is likely to increase, significantly;
  - the polymer has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the polymer 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.

Safety Data Sheet
The SDS of the notified polymer provided by the notifier was reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Croda Singapore Pte Ltd (trading as Croda Australia) (ABN: 34 088 345 457)
Suite 102
Level 1, 447 Victoria Street
WETHERILL PARK NSW 2164

NOTIFICATION CATEGORY
Limited-small volume: Synthetic polymer with Mn < 1,000 Da (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, polymer constituents, residual monomers, impurities, additives/adjuvants and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: all physico-chemical endpoints.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
None.

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Polyglyceryl-4 Laurate/Sebacate (INCI name)
Polymer in NatraGem S140 (containing the notified polymer at < 35% concentration)

MOLECULAR WEIGHT
> 500 Da

ANALYTICAL DATA
Reference GPC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 75%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Viscous yellow liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Not determined	Imported in aqueous solution
Boiling Point	> 100 °C at 101.3 kPa	Estimated using EPISuite v4.11, MPBVP v1.43 (adapted Stein and Brown Method).
Density	1,200 kg/m^3	SDS
Vapour Pressure	< 0.1 kPa at 20 °C	Estimated using EPISuite v4.11, MPBVP v1.43
Water Solubility	0.26 mg/L at 25 °C	Calculated using WSKOW v1.42 (US EPA, 2009)
Hydrolysis as a Function of pH	Not determined	The notified polymer contains hydrolysable functionalities. It is expected to hydrolyse under environmental

		conditions (pH 4–9)
Partition Coefficient (n-octanol/water)	log Pow = 2.07	Calculated using KOWWIN v1.67 (US EPA, 2009)
Adsorption/Desorption	log K_{oc} = 0.84	Calculated using KOCWIN v2.00 (US EPA, 2009)
Dissociation Constant	Not determined	Expected to be ionised under environmental conditions (pH 4-9)
Flash Point	288 °C	SDS
Autoignition Temperature	Not determined	Not expected to autoignite under normal conditions of use.
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

DISCUSSION OF PROPERTIES

Reactivity
The notified polymer 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 polymer is not recommended for hazard classification according to the *Globally Harmonised System of 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 polymer will not be manufactured in Australia. It will be imported as a component of the product NatraGem S140 (at a concentration of < 35%) for formulation of cosmetic products.

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
Melbourne, Sydney, Perth

IDENTITY OF RECIPIENTS
Croda Australia.

TRANSPORTATION AND PACKAGING
The notified polymer will be transported as a component of the product NatraGem S140 (at < 35% concentration) in 25 kg plastic containers or 200 kg steel drums. The notified polymer will be transported by road or rail. Finished products containing the notified polymer will be packaged in plastic bottles or tubes for retail sale.

USE
The notified polymer will be used as an ingredient in cosmetic products at < 5% concentration.

OPERATION DESCRIPTION
The notified polymer will be imported as a component of the product NatraGem S140 (at < 35% concentration) for formulation of cosmetic products (containing the notified polymer at < 5% concentration).

Reformulation
The procedures for incorporating the notified polymer (at < 35% concentration) into end-use products will vary depending on the nature of the product being formulated and both manual and automated steps will likely be involved. However, in general, it is expected that for the reformulation process, the notified polymer will be weighed and added to the mixing tank where it will be blended with additional additives to form the finished

cosmetic products. This will be followed by automated filling of the reformulated products into containers of various sizes. The blending operations are expected to be highly automated and use closed systems and/or adequate ventilation. During the formulation process, samples of the notified polymer and the finished products will be taken for quality control testing.

End-use
Finished products containing the notified polymer at < 5% concentration will be used by the public and may also be used by professionals such as hairdressers and workers in beauty salons. Depending on the nature of the product, these could be applied by hand, sprayed or by using an applicator.

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 and Storage	2 - 3	25
Process Operator (formulator)	2 - 3	25
Quality Control	1 - 2	4 – 5
Packers (dispensing and capping)	2 - 3	25
Waste Management	1	40
Professional users – (e.g. hair and beauty salon workers)	Not specified	Not specified

EXPOSURE DETAILS
Transport, storage and retail workers may come into contact with the notified polymer at < 35% concentration, as a component of the product NatraGem S140 or at < 5% concentration in cosmetic products only in the event of accidental rupture of packages.

Reformulation
During reformulation into cosmetic products, dermal, ocular and inhalation exposure of workers to the notified polymer at < 35% concentration may occur. Exposure is expected to be minimised through the use of exhaust ventilation and/or automated/enclosed systems as well as through the use of personal protective equipment (PPE) such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate).

End-use
Exposure to the notified polymer in end-use products at < 5% concentration may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. workers in beauty salons). The principal route of exposure will be dermal, while ocular exposure is also possible. Such professionals may use some PPE to minimise repeated exposure, but this is not expected to occur in all workplaces. However, 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 polymer.

6.1.2. Public Exposure
There will be widespread and repeated exposure of the public to the notified polymer (at concentrations < 5%) through the use of cosmetic products. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible particularly if products are applied by spray.

6.2. Human Health Effects Assessment

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

Endpoint	*Result and Assessment Conclusion*
Skin irritation (in vitro) – Reconstituted Human Epidermis Model	non-corrosive (at 75% concentration)
Eye irritation (in vitro) - Reconstituted Human Corneal Epithelium Model	non-irritating (at 75% concentration)
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution
No toxicokinetic data on the notified polymer were submitted. For dermal absorption, uptake is likely to be low if the water solubility is < 1 mg/L. Moderate dermal uptake through the epidermis is favoured if the partition coefficient (log P) values are between -1 and 4. However, dermal absorption is not favourable for molecular weights > 500 Da (ECHA, 2014). Dermal absorption of the notified polymer is expected to be low based on the molecular weight (> 500 Da) and water solubility (0.26 mg/L at 25 °C) of the notified polymer. Polyglyceryl esters have been shown to increase dermal penetration of other chemicals. Where present in micro-emulsions, Polyglyceryl-4 Laurate (a component of the notified polymer) has been shown to increase the skin permeation of ceramide (CIR, 2016).

Polyglyceryl fatty acid esters such as the notified polymer are expected to be hydrolyzed in the gastrointestinal tract and the fatty acid moiety metabolized in a normal manner. Accumulation of the polyglycerol component in body tissues has not been indicated (CIR, 2016).

Acute toxicity
Polyglyceryl fatty acid esters are of low acute oral and dermal toxicity (> 2,000 mg/kg bw in all 19 studies reported) and subsequently the notified polymer is not expected to be acutely toxic via the oral or dermal route (CIR, 2016).

Irritation and sensitisation
Studies examining the skin irritation effects of polyglyceryl fatty acid esters have shown that some may have mild to moderate skin and eye irritation effects on rabbits although most studies showed no signs of irritation (CIR, 2016). The notified polymer was found to be non-corrosive at 75% concentration in an *in vitro* skin (RHE) irritation study and non-irritating at 75% concentration in an *in vitro* eye (RHCE) irritation study.

The notified polymer does not contain any structural alerts for sensitisation, and studies on polyglyceryl fatty acid esters (analogues to the notified polymer) indicate that this class of polymers are not expected to be skin sensitisers (CIR, 2016).

Based on the available information, the notified polymer is not expected to be irritating to the eye or skin, and is not expected to show skin sensitisation effects.

Repeated dose toxicity
The notified polymer is not expected to show any significant adverse effects following repeated dose exposure in single and multi-generational studies based on dietary studies using polyglyceryl analogues to the notified polymer (CIR, 2016).

Mutagenicity/Genotoxicity
No mutagenic effects were seen in a bacterial reverse mutation assay conducted on a close analogue of the notified polymer. Additional *in vivo* and *in vitro* studies on other polyglyceryl fatty acid esters (CIR, 2016) did not indicate genotoxic properties. There are no structural alerts associated with impurities of polyglyceryl fatty acids (free fatty acids and their esters). The notified polymer is not expected to be genotoxic based on the results of these studies.

Developmental and reproductive toxicity
In two separate studies in rats, one a three generation study and the other a repeated dose study with a reproductive/developmental screening test, there were no adverse developmental or reproductive effects attributed to the polyglyceryl fatty acid esters tested (CIR, 2016).

Health hazard classification
Based on the available information, the notified polymer is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified polymer is expected to be of low systemic toxicity and is not expected to have the potential to cause skin or eye irritation effects.

Transport and Storage
Workers may experience dermal and accidental ocular exposure to the notified polymer (at < 35% concentration) in the event of a discharge via spill or drum leakage. The use of PPE (e.g. impervious gloves, goggles, coveralls, hard hats and respiratory protection, if necessary) should minimise the potential for exposure. Provided adequate control measures and safe work practices are in place to minimise worker exposure, including PPE, the risk to workers from the notified polymer is not considered to be unreasonable.

Reformulation
Exposure of workers to the notified polymer (at < 35% concentration) may occur during blending operations. Provided that adequate control measures are in place to minimise worker exposure, including the use of automated processes and PPE, the risk to workers from use of the notified polymer is not considered to be unreasonable.

End-use
Beauty care professionals will handle the notified polymer at < 5% concentration, similar to public use. Therefore the risk to workers who regularly use products containing the notified polymer 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
The public will be exposed to the notified polymer at < 5% concentration in cosmetic products. The main route of exposure is expected to be dermal with some potential for oral and inhalation exposure.

The notified polymer is of low systemic toxicity, with minimal dermal absorption expected. In addition the notified polymer is not expected to be irritating to the skin or eyes, sensitising, genotoxic or a reproductive or developmental toxicant.

Therefore, based on the expected low hazard, the risk to the public associated with the use of the notified polymer in cosmetic products is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified polymer will be imported as a component of a formulation for reformulation into cosmetic products. There is unlikely to be any significant release to the environment from transport and storage, except in the case of accidental spills and leaks. In the event of spills, the product containing the notified polymer is expected to be collected with adsorbents, and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve blending operations that will be highly automated, and are expected to occur within an enclosed environment. Therefore, significant release of the notified polymer from this process to the environment is not expected. Wastes containing the notified polymer generated during reformulation include equipment wash water, residues in empty import containers and spilt materials. This will be collected and released to sewers in a worst case scenario, or disposed of to landfill in accordance with local government regulations. Empty import containers are expected to be recycled or disposed of to landfill.

RELEASE OF CHEMICAL FROM USE
The notified polymer is expected to be released to the aquatic compartment through sewers during its use in cosmetic products.

RELEASE OF CHEMICAL FROM DISPOSAL
The notified polymer contained in product residues remaining in empty containers is expected to be disposed of to landfill, or be released to the sewer system when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate
Following its use in cosmetic products in Australia, the majority of the notified polymer is expected to enter the sewer system, before potential release to surface waters nationwide. Based on the result of the biodegradability study, the notified polymer is considered readily biodegradable (69% in 28 days). For details of the environmental fate studies, please refer to Appendix B. Based on its low calculated water solubility, the notified polymer is expected to partition to sludge and sediment under environmental pH. The notified polymer is not expected to bioaccumulate due to its low calculated partition coefficient (log KOW = 2) and ready biodegradability. Therefore, in surface waters the notified polymer is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of carbon.

The majority of the notified polymer will be released to sewer after use. A small proportion of the notified polymer may be applied to land when effluent is used for irrigation, or when sewage sludge is used for soil remediation. The notified polymer may also be applied to land when disposed of to landfill as collected spills and empty container residue. The notified polymer in landfill, soil and sludge is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)
The predicted environmental concentration (PEC) has been calculated to assume a worst case scenario, with 100% release of the notified polymer into sewer systems nationwide and no removal within sewage treatment plants (STPs).

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	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:	0.61	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 L/m2/year (10 ML/ha/year). The notified polymer 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 0.61 µg/L may potentially result in a soil concentration of approximately 4.04 µg/kg. Assuming accumulation of the notified polymer in soil for 5 and 10 years under repeated irrigation, the concentration of notified polymer in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.38 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 = 15.6 mg/L	Harmful to aquatic invertebrates

Based on the above ecotoxicological endpoints for the notified polymer, it is expected to be harmful to aquatic invertebrates. Therefore, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009), the notified polymer is formally classified as "Acute Category 3; Harmful to aquatic life". Based on the above acute toxicity and ready biodegradability of the notified polymer, it is not formally classified under the GHS for chronic toxicity.

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated based on the acute endpoint for Daphnia. A safety factor of 1000 was used given acute endpoints for only one trophic level is available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (*Daphnia*, 48 h)	15.60	mg/L
Assessment Factor	1,000	
Mitigation Factor	1.00	
PNEC:	15.60	µg/L

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated based on the predicted PEC and PNEC.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.61	15.6	0.039
Q - Ocean	0.06	15.6	0.004

The risk quotient for discharge of treated effluents containing the notified polymer to the aquatic environment indicates that the notified polymer is unlikely to reach ecotoxicologically significant concentrations in surface waters, based on its maximum annual importation quantity. The notified polymer is considered readily biodegradable, and is expected to have a low potential for bioaccumulation. On the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic products, the notified polymer is not expected to pose an unreasonable risk to the environment.

APPENDIX A: TOXICOLOGICAL INVESTIGATIONS

A.1. Irritation – skin (in vitro)

TEST SUBSTANCE	Notified chemical (at > 75% concentration)
METHOD	Similar to OECD TG 431 In vitro Skin Corrosion - Human Skin Model Test; and EC Council Regulation No 440/2008 B.40 BIS. In vitro Skin Corrosion - Human Skin Model Test EpiSkin™ Reconstituted Human Epidermis Model
Vehicle	
Remarks - Method	GLP compliant. No deviations from the protocol. No correction for purity was made. Positive (Sodium Dodecyl Sulphate) and negative (Dulbecco's Phosphate Buffered Saline with Ca^{++} and Mg^{++}) controls were conducted in parallel with the test substance and shared with other projects. A preliminary test was conducted indicating that the test substance does not directly reduce MTT.

RESULTS

Test material	*Mean OD_{540} of triplicate tissues*	*Relative mean viability (%)*
Negative control	0.761	100
Test substance	0.802	105.4
Positive control	0.029	3.8

OD = optical density

Remarks - Results	The positive and negative controls gave satisfactory results, confirming the validity of the test system.
CONCLUSION	The notified polymer was non-corrosive to the skin under the conditions of the test.
TEST FACILITY	Harlan (2010a)

A.2. Irritation – eye (in vitro)

TEST SUBSTANCE	Notified chemical (at > 75% concentration)
METHOD	Determination of Ocular Irritation Potential Using the SkinEthic Reconstituted Human Corneal Epithelium Model
Vehicle	
Remarks - Method	GLP compliant. No deviations from the protocol. No correction for purity was made. The test substance (30 µL) was applied to the tissues in triplicate. Following a 10 minute exposure period at ~37 °C, the tissues were rinsed and treated with MTT and incubated at ~37 °C for 3 hours. Following overnight extraction, the optical densities were determined (540 nm) for two of the tissues, while the remaining tissue was stored for possible tissue histopathology. The test substance was considered by the study authors to be an irritant if the relative mean tissue viability was ≤ 60%.

Controls were conducted in parallel with the test substance and shared with other projects:
- Positive control - Sodium Dodecyl Sulphate
- Negative control - Solution A (composed of sodium phosphate dibasic, glucose, HEPES, potassium chloride and sodium chloride).

A preliminary test was conducted indicating that the test substance does not directly reduce MTT.

RESULTS

Test material	*Mean OD_{540} of duplicate tissues*	*Relative mean viability (%)*
Negative control	0.989	100
Test substance	0.850	85.9
Positive control	0.389	39.3

OD = optical density

Remarks - Results: The positive and negative controls gave satisfactory results, confirming the validity of the test system.

CONCLUSION: The notified polymer was considered to be non-irritating to the eye under the conditions of the test.

TEST FACILITY: Harlan (2010b)

A.3. Genotoxicity – bacteria

TEST SUBSTANCE: Analogue 1 (at > 75% concentration)

METHOD: OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure (test 1) and Pre incubation procedure (test 2)

Species/Strain: *S. typhimurium*: TA1535, TA1537, TA98, TA100
E. coli: WP2*uvrA*

Metabolic Activation System: S9 fraction from phenobarbitone/β-Naphthoflavone induced rat liver

Concentration Range in Test 1: a) With metabolic activation: 15, 50, 150, 500, 1500, 5,000 µg/plate
b) Without metabolic activation: 15, 50, 150, 500, 1500, 5,000 µg/plate

Concentration Range in Test 2: a) With metabolic activation: 5, 15, 50, 150, 500, 1500, 5,000 µg/plate
b) Without metabolic activation:
(i) *S. typhimurium*: TA100: 0.15, 0.5, 1.5, 5, 15, 50, 150 µg/plate.
(ii) *S. typhimurium*: TA1535, TA1537: 0.5, 1.5, 5, 15, 50, 150, 500 µg/plate
(iii) *S. typhimurium* TA98 and *E. coli* WP2*uvrA:* 5, 15, 50, 150, 500, 1,500, 5,000 µg/plate.

Vehicle: Water

Remarks - Method: GLP Compliant.
Concentration Range in Preliminary Test: 0, 0.15, 0.5, 1.5, 5, 15, 50, 150, 500, 1,500 and 5,000 µg/plate. Test was performed on TA100 and WP2*uvrA*
Positive controls: with metabolic activation – 2-Aminoanthracene (TA100, TA1535, TA1537, WP2*uvrA*), Benzo(a)pyrene (TA98); without metabolic activation – N-ethyl-N'-nitro-N-nitrosoguanidine (WP2*uvrA*, TA100, TA1535), 9-Aminoacridine (TA1537), 4-Nitroquinoline-1-oxide (TA98).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1		≥ 1,500	≥ 1,500	non-mutagenic
Test 2 (i)	> 5,000	> 150	> 150	non-mutagenic
Test 2 (ii)		> 500	> 500	non-mutagenic
Test 2 (iii)		≥ 5000	≥ 1,500	non-mutagenic
Present				
Test 1	> 5,000	> 5,000	≥ 1,500	non-mutagenic
Test 2		≥ 1,500	≥ 1,500	non-mutagenic

Remarks - Results

Precipitation was observed at ≥ 1,500 µg/plate in the presence and absence of metabolic activation.

No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains in the presence or absence of metabolic activation, under any of the test conditions.

Positive and negative controls confirmed the validity of the test results.

CONCLUSION

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

TEST FACILITY

Harlan (2010c)

APPENDIX B: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

B.1. Environmental Fate

B.1.1. Ready biodegradability

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 301 B Ready Biodegradability: CO2 Evolution Test.
Inoculum	Activated sewage sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Carbon Dioxide ($ThCO_2$)
Remarks - Method	Conducted in accordance with the test guidelines above, and in compliance with GLP standards and principles.

RESULTS

Test substance		*Toxicity control*		*Sodium acetate*	
Day	*% Degradation*	*Day*	*% Degradation*	*Day*	*% Degradation*
2	14	2	14	2	33
9	58	9	48	9	70
14	64	14	65	14	76
23	69	23	77	23	83
28	69	28	81	28	84

Remarks - Results	All validity criteria for the test were satisfied. The percentage degradation of the reference compound (sodium acetate) surpassed the threshold level of 60% at 14 days (76%), and attained 84% degradation at 28 days. Therefore, the test indicates the suitability of the inoculums. The percentage degradation of the toxicity control surpassed the threshold level of 25% at 14 days (65%; 81% at 28 days), showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance after 28 days was 69%. Therefore, the test substance is considered to be readily biodegradable according to the OECD (301 B) guideline.
CONCLUSION	The notified polymer is considered to be readily biodegradable.
TEST FACILITY	Chemex (2010a)

B.2. Ecotoxicological Investigations

B.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – Static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	156 mg $CaCO_3$/L
Analytical Monitoring	Not reported
Remarks - Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Concentration mg/L		*Number of D. magna*	*Immobilised (%)*	
Nominal	*Actual*		*24 h [acute]*	*48 h [acute]*
0		20	0	0
6.5		20	5	10
13		20	15	40
25.0		20	50	75
50.0		20	85	95
100.0		20	100	100

EC50	15.6 mg/L (95% CI 12.1-19.7 mg/L) at 48 h
NOEC	13 mg/L at 48 h
Remarks - Results	All validity criteria of the test guideline were satisfied. The 48 h EC50 and NOEC for Daphnia were determined to be 15.6 mg/L (95% CI 12.1-19.7 mg/L) and 13 mg/L, respectively. Analytical monitoring of the test substance concentration was not reported.
CONCLUSION	The notified polymer is considered to be harmful to aquatic invertebrates.
TEST FACILITY	Chemex (2010a)

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