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AUSTRALIAN INDUSTRIAL CHEMICALS INTRODUCTION SCHEME (AICIS)

PUBLIC REPORT

Polymer in Coltide Radiance-LQ-(WD)

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals Act 2019* (the IC Act) and *Industrial Chemicals (General) Rules 2019* (the IC Rules) by following the *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Act 2019* (the Transitional Act) and *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Rules 2019* (the Transitional Rules). The legislations are Acts of the Commonwealth of Australia. The Australian Industrial Chemicals Introduction Scheme (AICIS) is administered by the Department of Health, and conducts the risk assessment for human health. The assessment of environmental risk is conducted by the Department of Agriculture, Water and the Environment.

This Public Report is available for viewing and downloading from the AICIS website. For enquiries please contact AICIS at:

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Executive Director
AICIS

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SUMMARY

The following details will be published on our website:

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1726	Croda Singapore Pte Ltd trading as Croda Australia	Polymer in Coltide Radiance-LQ-(WD)	ND*	≤ 10 tonnes per annum	Component of laundry care products

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
As only limited toxicity data were provided for the assessed polymer, the assessed polymer cannot be classified 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*
Chronic Category 2	H411 – Toxic to aquatic life with long lasting effects

Human Health Risk Assessment
Under the conditions of the occupational settings described, the assessed polymer is not considered to pose an unreasonable risk to the health of workers.

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

Environmental Risk Assessment
On the basis of the PEC/PNEC ratio, the assessed polymer is not considered to pose an unreasonable risk to the environment.

Recommendations

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 assessed polymer during reformulation:
  - 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 assessed polymer during reformulation:
  - Avoid contact with skin and eyes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the assessed polymer during reformulation:
  - Impervious gloves

  - Safety glasses or goggles
  - Protective clothing

  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 assessed 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.

Emergency procedures

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

Disposal

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

Regulatory Obligations

Specific Requirements to Provide Information
This risk assessment is based on the information available at the time of the application. The Executive Director may initiate an evaluation of the chemical based on changes in certain circumstances. Under section 101 of the IC Act the introducer of the assessed chemical has post-assessment regulatory obligations to provide information to AICIS when any of these circumstances change. These obligations apply even when the assessed polymer is listed on the Australian Inventory of Industrial Chemicals (the Inventory).

Therefore, the Executive Director of AICIS must be notified in writing within 20 working days by the applicant or other introducers if:

  - the final use concentration of the assessed polymer exceeds 1% in laundry care products;
  - the assessed polymer is proposed to be used in spray products;
  - information on sensitisation of the assessed polymer becomes available;
  - the function or use of the polymer has changed from a component of laundry care products, 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 human health, or the environment.

The Executive Director will then decide whether an evaluation of the introduction is required.

Safety Data Sheet
The SDS of a product containing the assessed polymer provided by the applicant was reviewed by AICIS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND APPLICATION DETAILS

APPLICANT(S)
Croda Singapore Pte Ltd trading as Croda Australia (ABN: 34 088 345 457)
Suite 2, Level 6, 111 Phillip Street
PARRAMATTA NSW 2150

APPLICATION CATEGORY
Standard: Synthetic polymer with Mn < 1,000 g/mol (more than 1 tonne per year)

PROTECTED INFORMATION (SECTION 38 OF THE TRANSITIONAL ACT)
Data items and details taken to be protected information include: chemical name, CAS number, other name(s), molecular and structural formulae, molecular weight, analytical data, polymer constituents, residual monomers/impurities, introduction concentration and analogue identities.

VARIATION OF DATA REQUIREMENTS (SECTION 6 OF THE TRANSITIONAL RULES)
Schedule data requirements are varied for all physical and chemical properties, all toxicological endpoints, bioaccumulation, fish toxicity and inhibition of bacteria respiration.

PREVIOUS APPLICATION IN AUSTRALIA BY APPLICANT(S)
None

APPLICATION IN OTHER COUNTRIES
Canada (2019)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Coltide Radiance-LQ-(WD) (product containing < 35% assessed polymer)

MOLECULAR WEIGHT
Number average molecular weight (Mn) is < 500 g/mol.

ANALYTICAL DATA
Reference GPC data were provided.

3. COMPOSITION

DEGREE OF PURITY
> 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: yellow, amber liquid*

Property	*Value*	*Data Source/Justification*
Melting Point	Not determined	Will be introduced and used in liquid form
Boiling Point	Not determined	Will be introduced and used in liquid form
Density	Not determined	Will be introduced and used in liquid form
Vapour Pressure	Not determined	Expected to be low
Water Solubility	Not determined	Expected to be miscible based on the structure of the assessed polymer
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionality, but significant hydrolysis not expected in the environmental pH range (4-9)
Partition Coefficient (n-octanol/water)	Not determined	Expected to be miscible with n-octanol and water based on the assessed polymer having both hydrophobic and hydrophilic functionality

Property	*Value*	*Data Source/Justification*
Adsorption/Desorption	Not determined	Expected to adsorb to soil, sediment and sludge based on the presence of cationic functionality
Dissociation Constant	Not determined	Contains cationic functionality
Flash Point*[#]	68 °C	Measured[^]
Flammability	Not determined	Not expected to be highly flammable
Autoignition Temperature	Not determined	Not expected to auto-ignite
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

* Property of the imported product containing < 35% assessed polymer
[#] The low flash point was considered to be attributed to the solvents in the product.
^ Study summary was provided.

DISCUSSION OF PROPERTIES

Reactivity
The assessed polymer is expected to be stable under normal conditions of use.

Physical Hazard Classification
Based on the limited physico-chemical data depicted in the above table, the assessed polymer cannot be 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 ASSESSED CHEMICAL (100%) OVER NEXT 5 YEARS
The assessed polymer will not be manufactured in Australia. It will be imported into Australia at < 35% concentration for reformulation into end-use products or as a component of end-use products at ≤ 1% concentration.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	10	10	10	10	10

PORT OF ENTRY
Brisbane, Melbourne, Perth, and Sydney

IDENTITY OF RECIPIENT
Croda Singapore Pte Ltd trading as Croda Australia

TRANSPORTATION AND PACKAGING
The assessed polymer will be imported into Australia by sea and transported by road in containers ranging from 500 mL to 200 L. Imported or locally reformulated end-use products containing the assessed polymer will be distributed by road to various warehouses and retailers.

USE
The assessed polymer will be used in liquid laundry care products at ≤ 1% concentration. The assessed polymer may also be packaged in dissolvable laundry capsules at ≤ 1% concentration.

OPERATION DESCRIPTION
Reformulation of the imported formulations containing the assessed polymer (at < 35% concentration) into finished laundry care products may vary depending on the type of product and may involve both automated and manual transfer steps. Typically, reformulation processes may incorporate blending operations that are highly automated and occur in a fully enclosed/contained environment, followed by automated filling of the reformulated end-use products into containers of various sizes.

End-use products containing the assessed polymer at ≤ 1% concentration will be used by consumers and professionals such as laundry workers. Consumers and laundry workers will open the product container and manually measure out the required volume (typically 50 mL) using the cap of the container or a dispensing cup before adding the product to the washing machine or hand-washing container. The assessed polymer may also be packaged in dissolvable laundry capsules which will be added to the washing machine.

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 Warehouse	2 – 3	25
Reformulation	2 – 3	25
Quality control	1 – 2	4 – 5
Packaging	2 – 3	25
Waste management	1	40
Laundry worker (details not provided)	8	252

EXPOSURE DETAILS

Transport and Storage
Transport, warehouse and retail workers may come into contact with the assessed polymer only in the unlikely event of accidental rupture of containers.

Reformulation
Dermal and ocular exposure of workers to the assessed polymer at < 35% concentration may occur during connection and disconnection of transfer lines, quality control and cleaning and maintenance of equipment. Exposure is expected to be limited through the use of enclosed systems and personal protective equipment (PPE) such as protective clothing, safety glasses and impervious gloves, as stated by the applicant. Inhalation exposure is not expected given the estimated low vapour pressure of the assessed polymer and formulation into an aqueous mixture.

End-use
Exposure of professional laundry workers to the assessed polymer is expected to be of a similar extent to that experienced by consumers using laundry care products containing the assessed polymer in washing machines (see section 6.1.2).

6.1.2. Public Exposure
Dermal and ocular exposure of the public to laundry care products containing the assessed polymer at ≤ 1% concentration may occur through spills and splashes during handling. Exposure from hand-washing processes is expected to be low as the assessed polymer will be further diluted in the wash water.

Dermal exposure to the assessed polymer from washed clothing/linen is expected to be low as the amount of residual polymer left on clothing is expected to be very low after the washing processes are complete.

6.2. Human Health Effects Assessment
No toxicity data were submitted for the assessed polymer. The results from toxicological investigations conducted on analogue chemicals (identities are protected information) are summarised in the following table. For full details of the studies, refer to Appendix A.

Endpoint	***Result and Assessment Conclusion***
Skin irritation – *in vitro* EpiDerm™ reconstructed human epidermis model*	non-irritating
Skin irritation – *in vitro* EpiSkin™ reconstructed human epidermis model^	non-irritating
Skin irritation – human occlusive patch test (20%)*	non-irritating

Endpoint	*Result and Assessment Conclusion*
Eye irritation – *in vitro* SkinEthic reconstituted human corneal epithelium model^	non-irritating
Eye irritation – *in vitro* rabbit corneal fibroblasts cytotoxicity assay (20%)*	slightly irritating
Eye irritation – *in vitro* hen's egg test - chorioallantoic membrane*	slightly irritating
Skin sensitisation – HRIPT (5%)*	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation (26.5%)*	non mutagenic

* The test substance was Analogue A (identity is protected information).
^ The test substance was Analogue B (identity is protected information).

Toxicokinetics
No toxicokinetic data were provided for the assessed polymer. The majority of the species of the assessed polymer are greater than 500 g/mol and limited absorption across biological membranes is expected.

Systemic Toxicity
No information on the acute or repeated dose toxicity of the assessed polymer was provided.

An analogue, protein hydrolyzates, wheat, [2-hydroxy-3-(trimethylammonio)propyl], chlorides (CAS No. 156798-11-7) was reported to have low acute oral toxicity based on read-across data (NICNAS, 2015).

The main component of the assessed polymer is a hydrolysed wheat protein (HWP). HWPs are common food additives and the potential for systemic effects, other than sensitisation, from the possible dermal absorption of HWPs is much less than the potential from absorption through oral exposure (Burnett et al., 2018).

Irritation
No irritation data were provided for the assessed polymer. Analogue A and Analogue B were considered to be non-irritating in two *in vitro* assays using reconstructed human epidermis.

A human occlusive patch test for skin irritation was conducted in 11 subjects, using Analogue A at 20% concentration. All subjects completed the test. Based on a very slight skin reaction in 1 subject, the study authors concluded that the chemical was unlikely to be an irritant. However, the irritation potential of the assessed polymer at higher concentrations cannot be ruled out.

Three *in vitro* studies to assess eye irritation were conducted on analogue polymers. Analogue B was considered to be non-irritating to eyes in an *in vitro* reconstituted human corneal epithelium model test. However, Analogue A (at 20% concentration) was considered to be slightly irritating to eyes in an *in vitro* rabbit corneal fibroblast cytotoxicity assay (non-guideline study, 1992) and an *in vitro* hen's egg test-chorioallantoic membrane (HET-CAM) study (non-guideline study, 1992).

Based on the information on the analogues and that the assessed polymer has a functional group associated with irritation, the potential for irritation effects of the assessed polymer cannot be ruled out.

Sensitisation
No sensitisation data were provided for the assessed polymer. Analogue A at 5% concentration was found to be non-sensitising in a human repeat insult patch test (HRIPT) completed in 52/57 subjects. Based on the analogue data, the assessed polymer is not expected to be a skin sensitiser at up to 5% concentration. It was noted that the assessed polymer contains a functional group which is a structural alert for sensitisation. Therefore, the sensitisation potential of the assessed polymer at higher concentrations cannot be ruled out.

Mutagenicity/Genotoxicity
No mutagenicity or genotoxicity data were submitted for the assessed polymer. Analogue A (at 26.5% concentration) was negative in a bacterial reverse mutation assay.

Health Hazard Classification
As only limited toxicity data were provided for the assessed polymer, the assessed polymer cannot be classified 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

Based on the available toxicological information on analogues and that the assessed polymer has a functional group associated with irritation and sensitisation, potential for irritation and sensitisation effects of the assessed polymer at higher concentrations (> 20% for irritation and > 5% for skin sensitisation) cannot be ruled out. However, systemic exposure to the assessed polymer is expected to be limited as the majority of the species of the assessed polymer are greater than 500 g/mol.

Reformulation

Workers may experience dermal and ocular exposure to the assessed polymer at < 35% concentration during reformulation. Inhalation exposure is not expected given the estimated low vapour pressure of the assessed polymer and formulation into an aqueous mixture. Given potential for irritation and sensitisation effects of the assessed polymer cannot be ruled out, control measures to prevent worker exposure are required when handling the assessed polymer during reformulation processes.

Provided that control measures are in place to minimise worker exposure, including the use of enclosed, automated processes and PPE such as impervious gloves, safety glasses and protective clothing, the risk to the health of workers during the handling of the assessed polymer is not considered to be unreasonable.

End-use

Workers at commercial laundry operations will handle the assessed polymer at ≤ 1% concentration, similar to public use. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. Therefore, the risk to workers who use products containing the assessed polymer is expected to be of a similar or lesser extent than consumers who use such products on a regular basis. For details of the public health risk assessment see section 6.3.2 below.

6.3.2. Public Health

Members of the public may experience frequent incidental exposure to the assessed polymer at ≤ 1% concentration through use of laundry care products. The main route of exposure is expected to be dermal, with some potential for accidental ocular exposure. Dermal exposure to low levels of the assessed polymer from hand-washing processes (in which the assessed polymer will be further diluted in the wash water) and the washed fabrics may also be possible.

Although the potential for irritation and sensitisation effects of the assessed polymer at higher concentrations cannot be ruled out, risk of skin and eye irritation and skin sensitisation is not expected at the proposed low concentrations (≤ 1%) in end-use products.

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

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The assessed polymer will be imported into Australia as a component of end-use laundry products, or a component of a formulation for reformulation into end-use products. Typically, reformulation processes incorporate blending operations that are highly automated and occur in a fully enclosed environment, followed by automated filling of the reformulated products into end-use containers. The applicant estimates release of the assessed polymer from local reformulation or repackaging and accidental spills is up to 2% of the total annual import volume, which is expected to be collected and disposed of, in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The assessed polymer is a component of laundry products, which will be directly applied to the clothes during washing. The laundry products will be rinsed off the clothes and enter the drainage/sewerage system, where it will be directed to various sewage treatment facilities.

RELEASE OF CHEMICAL FROM DISPOSAL
The empty containers are expected to be sent for recycling. It is expected that there may be residual assessed polymer of up to 1% of the total annual import volume remaining within the empty containers.

7.1.2. Environmental Fate

Following its use, the majority of the assessed polymer is expected to enter the sewer system across Australia. The assessed polymer is not expected to be readily biodegradable (46% degraded in 28 days), but showed inherent biodegradability (72 % degraded in 57 days). For details of the environmental fate studies, refer to Appendix B. Based on the molecular weight distribution (protected information) of the assessed polymer, a significant portion of the assessed polymer is expected to absorb to sewage sludge (Boethling & Nabholz 1997). Therefore, the assessed polymer is expected to be removed effectively through biodegradation and adsorption to sludge at sewage treatment plants before potential release to surface waters nationwide. The sewage sludge containing the assessed polymer may be disposed of to landfill or applied to agriculture land for remediation. A minor proportion of the assessed polymer may also enter landfill as collected spills and container residues. In landfill and soil, the assessed polymer is expected to have low mobility based on its cationic characteristic. The assessed polymer is not expected to bioaccumulate due to its expected low n-octanol/water partition coefficient and inherent biodegradability. In surface waters, soil and landfill, the assessed polymer is expected to eventually degrade through abiotic and biotic processes to form water and oxides of carbon, nitrogen and silicon.

7.1.3. Predicted Environmental Concentration (PEC)

The proposed use pattern will result in most of the assessed polymer being washed into the sewer. The predicted environmental concentration (PEC) has been calculated based on the realistic scenario of 100% release of the assessed polymer into sewer systems nationwide over 365 days per annum. The extent to which the assessed polymer is removed from the effluent in STP processes is based on the information regarding its behaviour in the STP. The assessed polymer is cationic with the majority of its species greater than 500 g/mol and it is inherently biodegradable. Based on Boethling & Nabholz (1997) and Struijs (1996), it is estimated that more than 50% of the assessed polymer will be removed by partitioning to sludge and biodegradation at wastewater treatment plants. Based on this the PEC in sewage effluent on a nationwide basis is estimated as follows:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment	
Total Annual Import/Manufactured Volume	10,000
Proportion expected to be released to sewer	100%
Annual quantity of chemical released to sewer	10,000
Days per year where release occurs	365
Daily chemical release:	27.40
Water use	200.0
Population of Australia (Millions)	24.386
Removal within STP	50%
Daily effluent production:	4,877
Dilution Factor – River	1.0
Dilution Factor – Ocean	10.0
PEC - River:	2.81
PEC - Ocean:	0.28

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The assessed polymer in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 2.8 µg/L may potentially result in a soil concentration of approximately 0.0187 mg/kg. Based on the assessed polymer's biodegradability, annual accumulation is not expected.

7.2. Environmental Effects Assessment

The applicant has cited three 96 h fish toxicity study reports (EC50 = 0.28 mg/L – *Oryzis latipes*, EC50 = 0.19 mg/L - *Lepomis macrochirus* and EC50 = 1.04 mg/L – *Lepomis macrochirus)* based on an analogue chemical, having the same cationic functionality, which is expected to be the main contributor to aquatic toxicity (Boethling & Nabholz 1997, pp 214). However, no study reports were provided. Therefore the information was only used to determine whether the PNEC calculated on two aquatic toxicity endpoints with the default assessment factor is sufficiently conservative.

The results from ecotoxicological investigations conducted on the assessed 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 > 100 mg/L	Not toxic to aquatic invertebrates
Algal Toxicity	72 h ECr50 = 1.5 mg/L	Toxic to algae

Based on the ecotoxicological endpoints for the assessed polymer, it is expected to be toxic to algae on an acute basis. As no chronic endpoints were available, the aquatic chronic hazard is determined using the acute data. Therefore, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009), the assessed polymer is formally classified as "Chronic Category 2; Toxic to aquatic life with long lasting effects".

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) was calculated using the algal toxicity endpoint (EC50 = 1.5 mg/L) of the assessed polymer and a conservative assessment factor of 500 as the ecotoxicity endpoint for only two trophic level were available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
72 h EC50 for algae	1.5	mg/L
Assessment Factor	500	
PNEC:	3	µg/L

A further determination of whether the PNEC is sufficiently conservative was made based on the results of three fish ecotoxicity studies supplied by the applicant. The geometric mean of the three results is 0.38 mg/L. This value is considered within the range of fish toxicity typical of cationic polymers (Boethling & Nabholz 1997, pp 224-225). Basing the PNEC on the most sensitive species for all three trophic levels and an assessment of 100 results in the following.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
96 h LC50 for fish (geometric mean of three values)	0.38	mg/L
Assessment Factor	100	
PNEC:	3.8	µg/L

This is similar to the PNEC based on two trophic levels and an assessment factor of 500. Therefore the PNEC of 3 µg/L was considered sufficiently conservative to calculate the Risk Quotient (Q).

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated for a worst-case discharge scenario based on the predicted PEC and PNEC.

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	2.81	3	**0.936**
Q - Ocean:	0.28	3	**0.094**

The assessed polymer is not persistent and is not likely to bioaccumulate. The assessed used pattern results in Q values of less than 1 for the aquatic environment, indicating that the assessed polymer is unlikely to reach ecotoxicologically significant concentrations. Therefore, on the basis of the aquatic PEC/PNEC ratio, the assessed polymer is not considered to pose an unreasonable risk to the environment.

APPENDIX A: TOXICOLOGICAL INVESTIGATIONS

A.1. Skin Irritation – *In Vitro* Human Skin Model Test

TEST SUBSTANCE	Analogue A
METHOD	In-house method similar to OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method EpiDerm™ Reconstructed Human Epidermis Model
Vehicle	None
Remarks – Method	The test substance (100 µL) was applied to the tissues for periods of 1 h, 4.5 h and 20 h. The tissues were then rinsed and incubated with MTT [3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] at 37 °C for 3 hours. Positive (Triton X-100; 1%) control and negative control (unspecified in the report) were run in parallel with the test substance. Information on whether each substance was tested on duplicate samples was not included. The optical densities were determined at 570 nm.

RESULTS

	Relative Mean Viability (%)		
Test material	*1 hour exposure*	*4.5 hours exposure*	*20 hours exposure*
Negative control	100*	100*	100*
Test substance	113	75	68
Positive control	90	74	7

* The mean viability of the negative control tissues was set at 100%.

Remarks – Results	For each substance, the ET-50 (time at which percent viability would be 50%) was estimated. The test substance elicited an ET-50 greater than 24 h and was considered to be non-irritating, according to the guideline provided by the test kit manufacturer (MatTek Corporation, USA).
CONCLUSION	The test substance was considered to be non-irritating to the skin under the conditions of the test.
TEST FACILITY	CPT (1998)

A.2. Skin Irritation – *In Vitro* Human Skin Model Test

TEST SUBSTANCE	Analogue B
METHOD	Similar to OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method EpiSkin™ Reconstructed Human Epidermis Model
Vehicle	None
Remarks – Method	In a pre-test, the test substance was shown not to directly reduce MTT [3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide]. The test substance (10 µL) was applied to the tissues in triplicate. Following 15 minute exposure periods, the tissues were rinsed and then incubated at 37 °C for approximately 42 hours. Following addition of MTT, the tissues were incubated at 37 °C for 3 hours. Positive (sodium dodecyl sulphate; 5%) and negative (phosphate buffered saline) controls were run in parallel with the test substance.

RESULTS

Test Material	*Mean OD_{540} of Triplicate Tissues*	*Relative Mean Viability (%)*	*SD of Relative Mean Viability*
Negative control	0.904	100*	5.9
Test substance	0.884	97.8	5.8
Positive control	0.054	6.0	1.0

OD = optical density; SD = standard deviation
* The mean viability of the negative control tissues was set at 100%.

Remarks – Results: Based on the relative mean viability of > 50%, the test substance was considered to be non-irritating, according to the guideline provided in the report.

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

CONCLUSION: The test substance was considered to be non-irritating to the skin under the conditions of the test.

TEST FACILITY: Harlan (2009a)

A.3. Skin Irritation – Human Volunteers

TEST SUBSTANCE: Analogue A (at 20% concentration)

METHOD: In-house occlusive patch test

Study Design: Patches soaked with the test substance were placed in 8 mm diameter aluminium cups and affixed to the skin with adhesive tape. The patches were removed after 24 h and each site was graded 30 min and 24 h after removal. The parameters scored were erythema, dryness, oedema, wrinkling, vesicles and glazing.

Study Group: 8 F, 3 M; age range 21-42 years

Vehicle: Unknown

Remarks – Method: Positive control - 2% sodium lauryl sulphate
Negative control - distilled water

RESULTS

Remarks – Results: 11/11 subjects completed the study. No reaction to the test substance was observed in 10 subjects. In one subject, a very slight erythema was observed 24 hours after exposure.

The positive and negative controls performed as expected.

CONCLUSION: The test substance was non-irritating under the conditions of the test.

TEST FACILITY: BIOGIR (1992a)

A.4. Eye Irritation – *In Vitro* Reconstructed Human Corneal Epithelium Model Test

TEST SUBSTANCE: Analogue B

METHOD: Similar to OECD TG 492 Reconstituted Human Corneal-like Epithelium (RhCE) Test Method for Identifying Chemicals Not Requiring Classification and Labelling for Eye Irritation or Serious Eye Damage
SkinEthic RhCE model

Vehicle: None

Remarks – Method: In a pre-test, the test substance was shown not to directly reduce MTT [3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide].

The test substance (30 µL) was applied to the tissues in triplicate for an exposure period of 10 minutes. Following addition of MTT, the tissues were incubated at 37 °C for 3 hours.

Positive (sodium dodecyl sulphate; 1%) and negative (buffer solution provided in test kit) controls were run in parallel with the test substance.

RESULTS

Test Material	*Mean OD_{540} of Triplicate Tissues*	*Relative Mean Viability (%)*
Negative control	0.941	100*
Test substance	0.812	86.3
Positive control	0.218	23.2

* The mean viability of the negative control tissues was set at 100%.

Remarks – Results: Based on the relative mean viability of ≥ 60%, the test substance was considered to be non-irritating, according to the guideline provided in the report.

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

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

TEST FACILITY: Harlan (2009b)

A.5. Eye Irritation – *In Vitro* Rabbit Corneal Fibroblasts Cytotoxicity Assay

TEST SUBSTANCE: Analogue A (20% in culture medium deprived of fetal calf serum)

METHOD: In-house

Vehicle: Minimal Essential Medium

Remarks – Method: The test substance was applied to cultures of Statens Seruminstitut Rabbit Cornea (SIRC) fibroblasts in triplicate for exposure periods of 30 minutes, 1 hour and 4 hours. A negative control (paraffin oil) was run in parallel with the test substance for an exposure period of 30 minutes.

A cytotoxicity assay was performed using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide].

RESULTS

Test Material	*Mean OD_{570} of Triplicate Tissues*	*Relative Mean Viability (%)*
Negative Control	0.417	100*
Test Substance – 30 min exposure	0.397	95.3
Test Substance – 1 hour exposure	0.207	49.7
Test Substance – 4 hour exposure	0.139	33.3

OD = optical density; * The mean viability of the negative control tissues was set at 100%.

Remarks – Results: An exposure time-dependent cytotoxicity of 4.7% (30 min exposure) to 66.7% (4 h exposure) was observed. From these results an ocular irritation index score of 12.9 was calculated which, according to the study authors, corresponded to a rating of slightly irritating.

CONCLUSION: The test substance was considered slightly irritating to the eye under the conditions of the test.

TEST FACILITY: BIOGIR (1992b)

A.6. Eye Irritation – *In Vitro* Hen's Egg Test - Chorioallantoic Membrane

TEST SUBSTANCE	Analogue A (20% as supplied)
METHOD	*In vitro* Eye Irritation Test: Hen's Egg Test - Chorioallantoic Membrane (HET-CAM Test)
Vehicle	Not reported
Remarks – Method	The test substance was applied to the chorioallantoic membrane of 6 eggs in a volume of 0.2 ml per membrane. After 20 seconds it was removed by irrigation with 5 mL of saline. A macroscopic examination of the chorioallantoic membrane was performed 30 seconds, 2 minutes and 5 minutes after test substance application in order to score for hyperaemia, haemorrhage and coagulation. A primary irritancy index is calculated from these parameters according to a pre-determined scoring matrix.
RESULTS	
Remarks – Results	Brief results were submitted. The study authors reported some hyperaemia together with a coagulation observed on one membrane. These observations resulted in an irritancy index of 1.7, corresponding to a result for the test substance of slightly irritating.
CONCLUSION	The test substance was considered to be slightly irritating to the eye under the conditions of the test.
TEST FACILITY	BIOGIR (1992c)

A.7. Skin Sensitisation – Human Repeat Insult Patch Test

TEST SUBSTANCE	Analogue A (5%)
METHOD	Repeated insult patch test with challenge
Study Design	Induction procedure: Patches containing 0.2 mL test substance were applied 3 times per week (Monday, Wednesday and Friday) for a total of 10 applications. Patches were removed by the applicants after 24 h and graded after an additional 24 h (or 48 h for patches applied on Friday). Rest period: Approx. 14 days Challenge procedure: A patch was applied to the original site and to a naïve site. Each site was graded at 24 h and 48 h after application.
Study Group	46 F, 11 M; age range 17-75 years
Vehicle	Not reported
Remarks – Method	Semi-occluded. The test substance was spread on a 2.5 cm × 2.5 cm patch.
RESULTS	
Remarks – Results	52/57 subjects completed the study and no skin reactions were observed. Five subjects discontinued for reasons unrelated to the administration of the test substance.
CONCLUSION	The test substance was non-sensitising under the conditions of the test.
TEST FACILITY	CPT (1993)

A.8. Genotoxicity – Bacteria

TEST SUBSTANCE	Analogue A (26.5% as supplied)
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
Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100 *Escherichia coli*: WP2uvrA
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphthoflavone induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 50 - 5000 µg/plate b) Without metabolic activation: 50 - 5000 µg/plate
Vehicle	Sterile distilled water
Remarks – Method	The dose selection for the main test was based on the toxicity observed in the preliminary test carried out at 50 – 5000 µg/plate. Positive controls: Without metabolic activation: N-ethyl-N'-ntro-N-nitrosoguanidine (TA1535, TA100, WP2uvrA); 9-Aminoacridine (TA1537); 4-Nitroquinoline-1-oxide (TA98) With metabolic activation: 2-aminoanthracene (TA1535, TA1537, TA100, WP2uvrA); Benzo(a)pyrene (TA98)

RESULTS

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

* Same test

Remarks – Results	No significant increases in the frequency of revertant colonies were observed for any of the bacterial strains, at any concentration tested, either with or without metabolic activation. The concurrent positive and negative controls produced satisfactory responses, thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.
CONCLUSION	The test substance was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Harlan (2009c)

APPENDIX B: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

B.1. Environmental Fate

B.1.1. Ready Biodegradability

TEST SUBSTANCE	Assessed polymer
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test
Inoculum	Activated sludge
Exposure Period	57 days
Auxiliary Solvent	None
Analytical Monitoring	Total Organic Carbon (TOC)
Remarks – Method	No major deviations from the test guidelines were reported. The test substance was dispersed directly to the test vessels and ultra-sonicated for 15 minutes. A toxicity control was run.

RESULTS

Test Substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
6	17	6	74
14	26	14	78
21	27	21	87
28	46	28	81
57*	72	57	75

* Day 57 values corrected to include any carry-over of CO_2 detected

Remarks – Results	The toxicity control exceeded 25% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The total CO_2 evolution in the control vessels on Day 28 was 39.54 mg/L. The inorganic content of the test item suspension in the mineral medium at the start of the test was below 5% of the total inorganic content. The overall biodegradation of the assessed polymer was 46% after 28 days and 72% after 57 days.
CONCLUSION	The assessed polymer is not readily biodegradable, but inherently biodegradable.
TEST FACILITY	Covance (2019)

B.2. Ecotoxicological Investigations

B.2.1. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE	Assessed 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	Not reported
Analytical Monitoring	Total Organic Carbon (TOC)
Remarks – Method	Non-GLP screening study. A stock solution of 100 mg/L of the test substance in test medium was prepared and used as the highest test concentration. Lower test concentrations were achieved by further diluting the stock solution. The test water was sampled at the start and at the end of the experiment for TOC analysis.

RESULTS

Concentration (mg/L) Nominal	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
Control	10	0	0
0.1	10	1*	1*
1	10	0	0
10	10	0	0
100	10	1**	0

* Handling error
** The immobilisation/sublethal effect of one Daphnia at the highest test item concentration of 100 mg test item/L (at 24 h) is considered not to be substance related, since it was observed for only one animal out of ten.

EC50	> 100 mg/L at 48 hours
Remarks – Results	All validity criteria for the test were satisfied. During the test, dissolved oxygen was ≥ 8.8 mg/L. The measured concentrations of the test substance (based on TOC) were in the range of 84-101% of the nominal concentrations. Therefore, the results are based on nominal concentration.
CONCLUSION	The assessed polymer is not toxic to aquatic invertebrates.
TEST FACILITY	IBACON (2019)

B.2.2. Algal Growth Inhibition Test

TEST SUBSTANCE	Assessed polymer
METHOD	OECD TG 201 Alga, Growth Inhibition Test – Static
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 0.1, 0.32, 1.0, 3.2 and 10 mg/L
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	Total Organic Carbon (TOC)
Remarks – Method	Non-GLP screening study. A stock solution of 100 mg/L test substance was prepared and stirred for 10 minutes. Adequate volumes of this stock solution were diluted with test water to prepare the test media of the desired test concentrations. The test water was sampled at the start and at the end of the experiment for TOC analysis.

RESULTS

Biomass		*Growth*	
EyC50 (mg/L at 72 h)	*NOEC (mg/L)*	*ErC50 (mg/L at 72 h)*	*NOEC (mg/L)*
0.46 (95% CI 0.41-0.51)	0.1	1.5 (95% CI 1.35-1.66)	0.1

Remarks – Results	All validity criteria for the test were satisfied. The mean cell density in the control increased 101 times after 72 hours. The coefficient of variation of growth rate in control culture was 21.2%. The coefficient of variation of average growth between control replicates was 3.7%. The measured concentrations of the test substance (based on TOC) were in the range of 103-109% of the nominal concentrations. Therefore, the results were presented based on nominal concentration. The EC50 was calculated by Probit analysis.
CONCLUSION	The assessed polymer is toxic to algae.
TEST FACILITY	IBACON (2020)

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