File No: LTD/2005

January 2018

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Poly[oxy(methyl-1,2-ethanediyl)], α,α'-[(dimethyliminio)di-2,1-ethanediyl]bis[ω-[[3-(4-methoxyphenyl)-1-oxo-2-propen-1-yl]oxy]-, methyl sulfate (1:1) (INCI name: Quaternium-95)

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:

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX:	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

TABLE OF CONTENTS

SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2005	Croda Singapore Pte Ltd	Poly[oxy(methyl-1,2-ethanediyl)], α,α'-[(dimethyliminio)di-2,1-ethanediyl]bis[ω-[[3-(4-methoxyphenyl)-1-oxo-2-propen-1-yl]oxy]-, methyl sulfate (1:1) (INCI name: Quaternium-95)	Yes	1 tonne per annum	Component of shampoos and conditioners

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

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

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	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

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified polymer should be classified as follows:
  - Skin corrosion/irritation (Category 2): H315 – Causes skin irritation
  - Serious eye damage/eye irritation (Category 1): H318 – Causes serious eye damage

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

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

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 as introduced in shampoos and conditioners at < 1% concentration. 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.

Public Health

- Product formulators should take into account the potential for the notified polymer to cause skin and eye irritation when manufacturing cosmetic products containing the notified polymer.

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 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 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 polymer;
  - the concentration of the notified polymer exceeds or is intended to exceed 1% in shampoos and conditioners;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the polymer has changed from a component of shampoos and conditioners, 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 a product containing 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 (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: other name(s), molecular and structural formulae, molecular weight, analytical data, 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 for all physico-chemical endpoints.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
European Union and United States

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Chromaveil-LQ-(MH) (product contains 60-100% notified polymer)

CAS NUMBER
1030827-59-8

CHEMICAL NAME
Poly[oxy(methyl-1,2-ethanediyl)], α,α'-[(dimethyliminio)di-2,1-ethanediyl]bis[ω-[[3-(4-methoxyphenyl)-1-oxo-2-propen-1-yl]oxy]-, methyl sulfate (1:1)

OTHER NAME
Quaternium-95 (INCI name)

MOLECULAR WEIGHT
Number Average Molecular Weight (Mn) is < 1,000 g/mol.

ANALYTICAL DATA
Reference GPC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
99.9%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Amber liquid*

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Not determined	Imported and used in aqueous solution
Boiling Point	Not determined	Imported and used in aqueous solution

Density	Not determined	Imported and used in aqueous solution
Vapour Pressure	Not determined	Imported and used in aqueous solution
Water Solubility	Not determined	There is no solubility report. The polymer is known to be partly soluble through design and experience in use.
Hydrolysis as a Function of pH	Not determined	The notified polymer contains esters, but is not expected to hydrolyse under normal environmental conditions (pH 4-9).
Partition Coefficient (n-octanol/water)	Not determined	The notified polymer is expected to be surface active. It would be difficult to determine partitioning to water or n-octanol without large uncertainty.
Surface Tension	42.9 mN/m*	Measured; report not provided
Adsorption/Desorption	Not determined	The notified polymer is intended to modify protein surfaces. Thus, it is likely to adsorb to organic material, from which it will not readily desorb.
Dissociation Constant	Not determined	The notified polymer is cationic, and is expected to be present in aqueous solution as a dissociated salt that will not dissociate further.
Flash Point	130 °C*	SDS
Flammability	Not determined	Imported and used in aqueous solution
Autoignition Temperature	Not determined	Imported and used in aqueous solution
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties.
Oxidising Properties	Not determined	Contains no functional groups that imply oxidising properties.

* Properties of Chromaveil-LQ-(MH) (product contains 60-100% notified polymer)

DISCUSSION OF PROPERTIES

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

Physical hazard classification
Based on the 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. The recommended hazard classification is presented in the following table.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified polymer will not be manufactured or reformulated within Australia. The notified polymer will be imported into Australia as a component of shampoos and conditioners at < 1% concentration.

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, Brisbane and Perth

TRANSPORTATION AND PACKAGING
The notified polymer will be imported as a component of shampoos and conditioners in ready-for-use commercial packaging.

USE
The notified polymer will be used as a colour stabiliser in shampoos and conditioners, at < 1% concentration, to reduce photolytic colour degradation of dyes. The hair care products containing the notified polymer will be supplied to professional hairdressing salons and may be sold to consumers through salons.

OPERATION DESCRIPTION
The notified polymer and products containing it will not be reformulated or repackaged within Australia. The shampoos and conditioners containing the notified polymer may be used by consumers and professional hairdressers and are expected to be applied by hand.

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)*
Dockside workers	< 1	1-5
Transport workers	1-8	5-10
Salon workers	≤ 8	235

EXPOSURE DETAILS

Transport and storage
Transport and storage workers may come in contact with the notified polymer at < 1% concentration in consumer products only in the event of an unlikely accidental rupture of containers.

End-use
Dermal and ocular exposure of professional hairdressers to the notified polymer in end-use products at < 1% concentration may occur during applying shampoos and conditioners containing the notified polymer to customers. Such professionals may use personal protective equipment (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 polymer.

6.1.2. Public Exposure
There will be widespread and repeated exposure of the public to the notified polymer at < 1% concentration through the use of shampoos and conditioners containing the notified polymer.

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*)*	irritating
Eye irritation (*in vitro*)*	severely irritating
Human, skin sensitisation – RIPT*	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation*	non mutagenic
Human, dermal phototoxicity*	non phototoxic

* Tested on a product containing the notified polymer at a concentration of 60-100%

Toxicokinetics
Toxicokinetic data on the notified polymer was not provided. For dermal and gastrointestinal absorption, molecular weights below 100 g/mol are favourable for absorption and molecular weights above 500 g/mol do not favour dermal absorption (ECHA, 2017). Additionally absorption of quaternary ammonium ions is expected to be reduced due to binding to the skin (ECHA, 2017). Although the number average molecular weight is < 1,000 g/mol, the weight % of Low MW Species < 500 g/mol is < 50% and therefore, the potential for the notified polymer to be absorbed across biological membranes is reduced. Additionally, absorption is expected to be limited by the ionic character of the notified polymer.

Irritation
The notified polymer was predicted to be slightly/moderately irritating to the skin in an *in vitro* study using a reconstructed human epidermis model (EpiDerm).

Solutions at up to 5% concentration of a product containing 60-100% notified polymer (equivalent to 3-5% notified polymer) were classified as severely irritating to eyes in a hen's egg test – chorioallantoic membrane (HET-CAM).

Sensitisation
A product containing the notified polymer at 60-100% concentration did not show any evidence of sensitisation in a human repeat insult patch test (HRIPT). However, the limited study size of the study (55 subjects) decreases the probability of detecting a sensitising effect, with at least 100 subjects recommended (IPCS, 2008; McNamee *et al*., 2008; Politano *et al*., 2008). No other dermal sensitisation studies were provided for the notified polymer.

Mutagenicity/Genotoxicity
The notified polymer was not mutagenic in a bacterial reverse mutation study.

Phototoxicity
In a phototoxicity study conducted in human volunteers (12 subjects), the notified polymer was considered to be not phototoxic. No other phototoxicity studies were provided for the notified polymer.

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

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

6.3. Human Health Risk Characterisation
Based on the available information the notified polymer is expected to be a mild to moderate skin irritant and a severe eye irritant. The systemic toxicity of the notified chemical is unknown; however, absorption of the notified polymer through the skin is expected to be low.

6.3.1. Occupational Health and Safety
Dermal and ocular exposure to the notified polymer (at < 1% concentration) may occur for hairdressers during use of end-products. The risk to these workers is expected to be of similar or lesser extent than that experienced by consumers using hair care products containing the notified polymer. Such professionals may use PPE (i.e., gloves and glasses) to minimise repeated exposure, and good general hygiene measures are expected to be in place to minimise exposure. Based on the low use concentration and assessed use patterns, the risk to workers associated with use of the notified polymer is not considered to be unreasonable.

6.3.2. Public Health
The notified polymer is proposed to be used at < 1% concentration in shampoos as conditioners as an ultraviolet radiation absorber.

Irritation and sensitisation
The notified polymer showed the potential to cause slight/moderate irritation to the skin and severe irritation to eyes in *in vitro* studies, however, no signs of irritation were seen in a phototoxicity study at a concentration of 60-100% with 12 volunteers. However, skin and eye irritation effects are not expected from use of the notified polymer at the proposed use concentrations (< 1%) and under the assessed use patterns.

There are only HRIPT test data available for the skin sensitisation potential of the notified polymer. The HRIPT test cannot rule out the potential for skin sensitisation in the general human population effects, but rather, it is best used as a test used to confirm the lack of dermal sensitisation at an exposure level that was identified as a NOEL in an animal model or derived from quantitative structure–activity relationships (QSARs) (Basketter, 2009). Large cohorts of individuals (typically 100) are needed to give a reliable result as testing is made in

supernormal individuals (a selected group of subjects without pre-existing conditions influencing immune response), who (perhaps) are less sensitive to skin sensitisation than a normal ('unselected') population (IPCS, 2008). However, the potential for skin sensitisation effects is expected to be reduced by the use of the notified polymer at low concentrations (< 1%) and under the assessed use patterns (rinse-off hair care products).

Systemic toxicity
The acute and repeated dose toxicity effects of the notified polymer have not been determined. However, systemic exposure is expected to be very low due to the low predicted dermal absorption of the notified polymer, the low use concentrations, and the rinse off nature of the hair care products it will be used in. Therefore, based on the information available, the risk to the public associated with use of the notified polymer at < 1% concentration in shampoos and conditioners 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 not be reformulated or repackaged in Australia. The pre-formulated notified polymer is not expected to be released during storage except in the event of an accidental spill or leak. Leaks and spills are expected to be unlikely and the notified polymer will be contained, absorbed onto inert material and disposed of to landfill according to local State or Territory regulation.

RELEASE OF CHEMICAL FROM USE
The notified polymer is intended for use in hair-care products (shampoo and conditioner), and will be rinsed off the hair of consumers. Therefore, the majority of the notified polymer is expected to be released to sewers across Australia as a result of its use in cosmetic products in domestic and commercial (hair salon) settings. A negligible amount of the notified polymer is expected to directly enter local waterways and coastal areas due to recreational bathing or rinsing effects of rain on the consumer.

RELEASE OF CHEMICAL FROM DISPOSAL
It is estimated that up to 1% of the imported volume (10 kg) of the notified polymer may remain as residues in commercial packaging. Residues of the notified polymer in empty import end-use containers are likely to either share the fate of the containers and 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, the majority of the notified polymer will enter sewers and be treated at sewage treatment plants (STPs) before potential release to surface waters nationwide.

A ready biodegradation test conducted on the notified polymer indicates that it is not readily biodegradable, but inherently biodegradable (48% degradation over 28 days in OECD 301 B test). For details of the biodegradation study, please refer to Appendix C. The notified polymer is expected to be efficiently removed through adsorption of the cationic polymer to sludge or by flocculation at STPs (Boethling and Nabholz, 2013). Therefore, only a small portion of the notified polymer may be released to surface waters.

A 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, or disposed of to landfill. The notified polymer residues in landfill and soils are expected to have low mobility based on its surface activity and its high potential to adsorb to proteins in plants and soil organic matter.

The notified polymer is not expected to bioaccumulate based on its surface activity. In the aquatic and soil compartments, the notified polymer is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)
As the notified polymer will be used as a component of wash off hair-care products, the total import volume of the notified polymer is expected to be released to sewers during its use. It is also anticipated that such releases will occur over 365 days per annum into the Australian effluent volume. The notified polymer is a cationic

polymer. It is also expected to adsorb to protein, i.e., to be removed by partitioning to sludge and by flocculation at STPs (Boethling and Nabholz, 1997). However, for this assessment we assumed a worst case scenario where 100% of the notified polymer is released from the STP (0% is removed by the STP). The resultant Predicted Environmental Concentration (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	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:	2.7	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	24.4	million
Removal within STP	0%	
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10	
PEC - River:	0.56	µg/L
PEC - Ocean:	0.056	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 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 0.56 µg/L may potentially result in a soil concentration of approximately 3.7 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 19 µg/kg and 37 µg/kg, respectively.

7.2. Environmental Effects Assessment

The results from the ecotoxicological investigation conducted on the notified polymer are summarised in the table below. Details of the study can be found in Appendix C. No other ecotoxicological data were submitted by the notifier. Therefore, aquatic toxicity of the notified polymer has been estimated using structure activity relationship (SAR) equations (Boethling and Nabholz, 1997) for algae and fish. All measured and estimated results from the ecotoxicological investigation are summarised in the table below:

Endpoint	*Result*	*Assessment Conclusion*
Acute		
Daphnia Toxicity	EC50 = 16 mg test substance/L (≡ 9.6 mg notified polymer/L)	Harmful to aquatic invertebrates

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated based on the acute endpoint for *Daphnia*, because this was a measured toxicity endpoint. A safety factor of 1000 was used given only one measured acute endpoint for one trophic level was available. Describe how the PNEC was calculated, if possible.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
	9.6	mg/L
Assessment Factor	1,000	
Mitigation Factor	1	
PNEC:	9.6	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	0.56	9.6	**0.058**
Q - Ocean	0.056	9.6	**0.0058**

The risk quotient for discharge of effluents containing the notified polymer to the aquatic environment indicates that the notified polymer is unlikely to reach ecotoxicologically significant concentrations based on its maximum annual importation quantity. Although the notified polymer is likely to be persistent in the environmental it is not expected to be bioaccumulative due to its cationic nature. Therefore, on the basis of the PEC/PNEC ratio, the maximum annual importation volume and assessed use pattern, the notified polymer is not expected to pose an unreasonable risk to the environment.

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – skin (*in vitro*)

TEST SUBSTANCE: Chromaveil-LQ-(MH) (product containing 60-100% notified polymer)

METHOD: Similar to OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method
MatTek Corporation EpiDerm *in vitro* Toxicity Testing System

Vehicle: None

Remarks - Method: The test substance (100 µL) was applied to the tissues in triplicate. Following exposure periods of 1 hour, 4.5 hours and 20 hours (37 °C), the tissues were rinsed, treated with MTT and then incubated at 37 °C for 3 hours. The negative control was distilled water. No positive control was used. The mean OD at 570 nm was not recorded in the study reports, only the relative mean viability was provided.

RESULTS

Test material	*Relative mean Viability (%)*
Negative control	100
Test substance 1 hour	103
Test substance 4.5 hours	107
Test substance 20 hours	10

OD = optical density; SD = standard deviation

Remarks - Results: The test substance elicited an ET-50 (the time at which the percent viability would be 50%) of 10.7 hours. The result was interpreted to be mild to moderate irritancy according to MatTek Corporation guidelines (expected *in vivo* irritancy was mild to moderate in the ET-50 range between 4 hours to12 hours).

CONCLUSION: The test substance was irritating to the skin under the conditions of the test.

TEST FACILITY: CPT (2009a)

B.2. Irritation – eye (*in vitro*)

TEST SUBSTANCE: Chromaveil-LQ-(MH) (product containing 60-100% notified polymer)

METHOD: The potential of the notified polymer to cause serious damage to the eye/mucous membranes was assessed by a single topic application of 0.3 mL of the test substance at three concentrations (5%, 2.5% and 1%) to the chorionallantoic membrane (CAM) of fertilised and incubated hen eggs.

Four eggs per test substance concentration were observed immediately prior to test substance administration and at 30 seconds, 2 minutes and 5 minutes after exposure. The occurrence of vascular injury or intravascular coagulation in response to the test substance was recorded.

RESULTS

Concentration	Egg No.	Scores at			
		0.5 min	2 min	5 min	Total
0% (distilled water as control)	1	0	0	0	0
	2	0	0	1	1
	3	0	3	0	3
	4	0	3	0	3
Mean					1.75

Concentration	Egg No.	Scores at						
		0.5 min		2 min		5 min		Total
5%	1	5	7	0		5		17
	2	5	7	0		0		12
	3		0	3	5	7	0	15
	4	5	7	7		0		19
Mean								15.75

Concentration	Egg No.	Scores at						
		0.5 min		2 min		5 min		Total
2.5%	1	5	7	0		5		17
	2	5	7	0		5		17
	3	5	7	7		0		19
	4	5	7	0		0		12
Mean								16.25

Concentration	Egg No.	Scores at						
		0.5 min		2 min		5 min		Total
1%	1		5	5		0		17
	2	5	7	0		5		17
	3	5	7	9	0	0		19
	4	5	7	0		5		12
Mean								16.25

Remarks - Results

All test substance solutions (5%, 2.5% and 1% concentrations) were classified as severely irritating (mean scores within range of 15.0 – 32.0).

The study authors stated that the CAM of the hen's egg was more sensitive to liquid irritants than rabbit eyes and therefore the CAM results for the test substance at 5%, 2.5% and 1% concentrations were equivalent to Draize results for the test substance at 10%, 5% and 2% concentrations respectively.

CONCLUSION

The test substance was severely irritating to the eye under the test conditions.

TEST FACILITY

CPT (2009b)

B.3. Skin sensitisation – human volunteers

TEST SUBSTANCE

Chromaveil-LQ-(MH) (product containing 60-100% notified polymer)

METHOD

Repeated insult patch test with challenge

Study Design

Induction Procedure: Patches containing approximately 0.2 mL test substance were applied 3 times per week (Monday, Wednesday and Friday) for a total of 9 applications. Following supervised removal and scoring of the first induction patch, subsequent patches were removed by applicants 24 hours after application. The evaluation of the sites was made again just prior to re-application.
Rest Period: approximately 14 days
Challenge Procedure: Patches containing 0.2 mL test substance was applied a naïve site adjacent to the original induction patch site, following the same procedure for the induction. Patches were removed and sites were graded 24 hours and 72 hours post-application.

Study Group

44 F, 12 M; age range 27-78 years

Vehicle

None

Remarks - Method

Occluded. The test substance was spread on a 1.9 cm × 1.9 cm patch.

RESULTS

Remarks - Results

55/56 subjects completed the study. One subject withdrew due to personal

reasons, none of which were related to the application of the test substance.

No irritation reactions were noted during the induction or at the 24 hours and 72 hours readings after the challenge.

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

TEST FACILITY CPT (2009c)

B.4. Genotoxicity – bacteria

TEST SUBSTANCE Chromaveil-LQ-(MH) (product containing 60-100% notified polymer)

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 mix from Aroclor 1254 induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 1.5 – 5000 µg/plate b) Without metabolic activation: 1.5 – 5000 µg/plate
Vehicle	Dimethyl sulphoxide
Remarks - Method	A dose-range test was carried out at 1.5-5000 µg/plate. The dose selection for the confirmatory test was based on the toxicity observed in the dose-range test. No significant protocol deviations.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 1500	> 5000	negative
Test 2	≥ 1500	≥ 5000	negative
Present			
Test 1	≥ 5000	> 5000	negative
Test 2	≥ 5000	> 5000	negative

Remarks - Results No significant increases in the frequency of revertant colonies were observed for any of the bacterial strains, with any dose of the test substance, either with or without metabolic activation.

The positive and negative controls gave a satisfactory response confirming the validity of the test system.

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

TEST FACILITY BioReliance (2009)

B.5. Phototoxicity – human volunteers

TEST SUBSTANCE Chromaveil-LQ-(MH) (product containing 60-100% notified polymer)

METHOD Phototoxicity evaluation in human subjects.

Study Design The minimum erythema dose (MED) was determined for each subject by exposing naïve skin to a series of UVB/UVA exposures (each 25% greater than the previous dose). The sites were then evaluated 24 hours and 48 hours following irradiation.

	Patches containing approximately 0.2 mL test substance were applied to 2 naïve sites on the back and removed after 24 hours. One treated site was then exposed to UVB irradiation (0.5 MED) and then UVA irradiation (20 joules). Test and control sites were evaluated immediately after irritation and at 24 hours and 48 hours after patch removal. Irradiation was performed with a solar simulator with filter (producing spectrum of UVB: 290 – 320 nm and UVA: 320 – 400 nm; and UVA only).
Study Group	9 F, 3 M; reported age range 26 – 62 years
Vehicle	None
Remarks - Method	Occluded. The test substance was spread on a 1.9 cm × 1.9 cm patch. Two negative control groups were run in parallel to the test substance (1 treated with test substance but not irradiated and 1 untreated but irradiated)
RESULTS	
Remarks - Results	No dermal reactions were noted at any site (irradiated untreated site, irradiated treated site and non-irradiated treated site) in any subject.
CONCLUSION	The test substance was considered by the study authors to not induce a response indicative of a phototoxic reaction, under the conditions of the test.
TEST FACILITY	CPT (2009d)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Chromaveil-LQ-(MH) (product containing 60-100% notified polymer)
METHOD	OECD TG 301 B Ready Biodegradability: CO2 Evolution Test
Inoculum	Activated sludge
Exposure Period	29 days
Auxiliary Solvent	None
Analytical Monitoring	CO_2 measured as Dissolved Inorganic Carbon (DIC) UV-Persulfate Analyser
Remarks - Method	No significant deviations from the test guidelines were reported. The test substance was weighed onto microscope cover slips and added directly to the test bioreactors. A toxicity control was included in the test design.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation*	*Day*	*% Degradation*
0	0	0	0
7	26	7	63
14	40	14	69
28	48	28	70
29	49	29	72
29	50	29	81

Remarks - Results	Validity criteria for the test were met. A maximum value of 81% degradation of the sodium acetate was achieved on day 29; and there was 69% degradation in the reference substance by day 14 (test guideline > 60%), indicating the suitability of the inoculums. The toxicity control had 86% degradation after 14 days (> 25%), showing that toxicity was not a factor inhibiting the biodegradability of the test substance. A value of 16.2 mg CO_2/L (4.4 9 mg C/L) was recorded for the inoculum blank at the end of the test (< 40 mg CO_2/L (10.9 mg C/L) for the test to be valid). The degree of degradation of the test substance, which contained 75% of the notified polymer was 48 % after 28 days. Although the test substance containing the notified polymer may be biodegradable it does not meet the criteria for being readily degradable.
CONCLUSION	The notified polymer is not readily degradable.
TEST FACILITY	Chemex Environmental International Ltd (2008a)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Chromaveil-LQ-(MH) (product containing 60-100% notified polymer)
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test and Reproduction Test – Static test conditions EC Council Regulation No 440/2008 C.2 Acute Toxicity for Daphnia
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	156 mg $CaCO_3$/L (typical hardness of ISO water used in test)
Analytical Monitoring	None

Remarks - Method	Conditions of the test were stable and suitable for the test species over the testing period: culture conditions were temperature of 21 to 22 °C (20 ± 1 °C), dissolved oxygen of 88 to 100% (> 60%) and a pH ranging between 6.8 and 8.0 (between 6 to 9). The photoperiod was 16 h of light and 8 h dark. *Daphnia* were not fed during the test. The test substance was not measured throughout the testing period so it was not possible to determine whether the level of test substance changed throughout the testing period, and the stock solution was slightly cloudy, indicating the test substance did not fully dissolve.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal (mg test substance/L)	*Calculated (mg notified polymer/L)*		*24 h*	*48 h*
0	0	20	0	0
10	7.5	20	0	0
18	13.5	20	10	70
32	24	20	18	100
56	42	20	20	100
100	75	20	20	100

EC50	19.3 mg test substance/L at 24 hours (95% confidence intervals of 16.4 and 22.5 mg/L) 16 mg test substance/L at 48 hours (95% confidence intervals of 16.4 and 22.5 mg/L). The Department calculates (using a 60% content of the notified polymer) that: 11.6 mg notified polymer/L at 24 hours 9.6 mg notified polymer/L at 48 hours
Remarks - Results	No Daphnia were immobilised in the control and the dissolved oxygen was > 60% air saturation value. Therefore, the validity criteria for the test guideline were met. A clear dose-response relationship was observed for the study. The EC50 was determined using Trimmed Spearman-Karber Method.

CONCLUSION	The notified polymer is harmful to aquatic invertebrates
TEST FACILITY	Chemex Environmental International Ltd (2008b)

BIBLIOGRAPHY

Basketter, D. A. (2009) The human repeated insult patch test in the 21st century: A commentary. Cutaneous and Ocular Toxicology, **28**(2):49–53.

BioReliance (2009) Chromaveil: Bacterial Reverse Mutation Assay (Study No. AC22JR.503.BTL, June, 2009). Rockville, Maryland, United States of America, BioReliance Co (Unpublished report submitted by the notifier).

Boethling, R. and Nabholz, J. (2013) Interpretive Assistance Document for Assessment of Polymers Sustainable Futures Summary Assessment Updated June 2010, https://www.epa.gov/sites/production/files/2015-05/documents/06-iad_polymers_june2013.pdf .

Boethling, R. and Nabholz, J. (1996) Environmental Assessment of Polymers Under the U.S. Toxic Substances Control Act (Report No. 20460-0001). Washington D. C., United States of America.

Chemex Environmental International Ltd (2008a) An Evaluation of the Ready Biodegradability of [Chromaveil] using the OECD 301B $C0_2$ evolution test (Study No. ENV8354/050830, September, 2008). Cambridge, United Kingdom, Chemex Environmental International Limited (Unpublished report submitted by the notifier).

Chemex Environmental International Ltd (2008b) The Acute Toxicity of [Chromaveil] to *Daphnia magna* Over A 48 Hour Exposure Period (Study No. ENV8460/050830, October, 2008). Cambridge, United Kingdom, Chemex Environmental International Limited (Unpublished report submitted by the notifier).

CPT (2009a) Chromaveil: The MatTek Corporation EpiDerm Skin Model In Vitro Toxicity testing System (Study No. V08-5664-1, January, 2009). Fairfield, New Jersey, United States of America, Consumer product testing Co (Unpublished report submitted by the notifier).

CPT (2009b) Chromaveil: The Hen's Egg Test – Utilising the Chorioallantoic Membrane (HET-CAM) (Study No. V08-5664-2, January, 2009). Fairfield, New Jersey, United States of America, Consumer product testing Co (Unpublished report submitted by the notifier).

CPT (2009c) Chromaveil: Repeated Insult Patch Test (Study No. C09-0852.01, April, 2009). Fairfield, New Jersey, United States of America, Consumer product testing Co (Unpublished report submitted by the notifier).

CPT (2009d) Chromaveil: Phototoxicity Test Procedure (Study No. S08-5656.01, January, 2009). Fairfield, New Jersey, United States of America, Consumer product testing Co (Unpublished report submitted by the notifier).

ECHA (2017) Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7c: Endpoint specific guidance, June 2017, version 3.0. European Chemicals Agency, http://echa.europa.eu/documents/10162/13632/information_requirements_r7c_en.pdf.

Henderson, CR and Riley, EC (1945) Certain statistical considerations in patch testing. Journal of Investigative Dermatology, **6**(3):227-230.

IPCS (2008) Harmonisation Project Document No. 5: Skin Sensitisation in Chemical Risk Assessment, International Programme on Chemical Safety (IPCS). Accessed November 2017 at http://www.who.int/ipcs/methods/harmonization/areas/sensitization/en/.

McNamee, PM, Api, AM, Basketter, DA, Gerberick, GF, Gilpin, DA, Hall, BM, Jowsey, I and Robinson, MK (2008) A review of critical factors in the conduct and interpretation of the human repeat insult patch test. Regulatory Toxicology and Pharmacology, **52**:24-34.

Politano, VT and Api, AM (2008) The Research Institute for Fragrance Materials' human repeated insult patch test protocol. Regulatory Toxicology and Pharmacology, **52**:35-38.

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