File No: LTD/2056

February 2019

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Genadvance Hydra

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment and Energy.

This Public Report is available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2056	Clariant (Australia) Pty Ltd	Genadvance Hydra	ND*	≤ 5 tonnes per annum	Component of hair care products

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

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 assessed use pattern and low hazard, the notified 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 notified polymer during reformulation:
  - Enclosed and automated systems where possible

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified polymer:
  - Avoid eye and skin contact

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified polymer:
  - Eye protection
  - Chemical resistant gloves
  - 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 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 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 polymer has a number-average molecular weight of less than 1,000 g/mol;
- the final use concentration of the polymer in hair care products is intended to exceed 2%;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the polymer has changed from component of hair 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 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)
Clariant (Australia) Pty Ltd (ABN: 30 069 435 552)
Level 3 Olympus Building
3 Acacia Place
296 – 324 Ferntree Gully Rd
NOTTING HILL VIC 3168

NOTIFICATION CATEGORY
Limited: Synthetic polymer with Mn ≥ 1,000 g/mol

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is being claimed for all physical chemical properties except for water solubility.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME
Genadvance Hydra (containing the notified polymer at concentrations of ≥ 95%)

OTHER NAME(S)
Lauryl/Myristyl Polyrinicinoleate and Glycerin (INCI name)
Lauryl (poly)ricinoleate

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

ANALYTICAL DATA
Reference NMR, IR, GPC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 90%

ADDITIVES/ADJUVANTS

Chemical Name	Water		
CAS No.	7732-18-5	*Weight %*	0.4
Chemical Name	1,2,3-Propanetriol		
CAS No.	56-81-5	*Weight %*	1.5

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Yellowish to clear liquid

Property	*Value*	*Data Source/Justification*
Freezing Point	-32 °C at 101.3 kPa	SDS, Analogue 1
Boiling Point	> 345 °C	SDS, Analogue 1
Density	919 kg/m^3 at 20 °C	Measured*
Vapour Pressure	Not determined	Expected to be low based on the high molecular weight
Water Solubility	0.01 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionally but not expected to hydrolyse significantly under environmental conditions (pH 4 – 9)
Partition Coefficient (n-octanol/water)	Not determined	Expected to partition to the n-octanol phase based on its low water solubility
Adsorption/Desorption	Not determined	Expected to sorb to soil, sediment and sludge due to its low water solubility
Dissociation Constant	Not determined	No dissociable functionality
Flash Point	345 °C (closed cup)	SDS, Analogue 1
Flammability	Not determined	Not a flammable liquid based on flash point
Autoignition Temperature	Not determined	Not expected to undergo autoignition
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

* No detailed test report

DISCUSSION OF PROPERTIES
For full details of the water solubility test, refer to Appendix A.

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 into Australia in neat form (at concentrations of > 90%) for reformulation by cosmetic companies into hair care products. The notified polymer will also be imported in finished hair care products at concentrations of ≤ 2%.

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

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

PORT OF ENTRY
Major ports of Australia

IDENTITY OF RECIPIENTS
Clariant (Australia) Pty Ltd

TRANSPORTATION AND PACKAGING
The notified polymer (neat) will be imported in 180 kg drums. Finished hair care products containing the notified polymer may commonly be imported in small consumer containers (≤ 200 mL) inside shipping

containers. The imported neat notified polymer and finished products containing the notified polymer will be transported by road or rail to retailer warehouses for further distribution nationwide.

USE
The notified polymer is a hair conditioning agent. It can be used in a range of hair care products including rinse-off and leave-on conditioners, shampoos, hair oils and other similar end use products. In finished consumer products the maximum proposed use concentration of the notified polymer is ≤ 2%.

OPERATION DESCRIPTION
The notified polymer will not be manufactured in Australia. Reformulation of the notified polymer into end use hair care products will occur locally at the customer facilities.

Reformulation
At the customer reformulation sites, procedures for incorporating the notified polymer into end use products will likely vary depending on the nature of the formulated products and may involve both automated and manual transfer steps. In general, it is expected that the notified polymer will be weighed and added to the mixing tank where mixing with additional additives will occur to form finished hair care products. Subsequently, automated filling of the reformulated products into containers of various sizes (≤ 200 mL to 2 L) will occur. The blending and filling operations are expected to be typically automated with enclosed systems and adequate ventilation. During the reformation process, samples of products containing the notified polymer will be taken for quality assurance (QA) purposes.

End use
Consumers and professionals such as beauticians and hairdressers will use the finished hair care products containing the notified polymer at concentrations of ≤ 2%. Depending on the nature of the products, applications may be by hand or through the use of applicators.

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	4	12
Reformulation		
Formulators	8	12
Quality assurance	3	12
Packaging	8	12
Retail	4	12
Professional end users	8	365

EXPOSURE DETAILS

Transport and storage
Transport and storage workers are not expected to be exposed to the notified polymer except in the unlikely event of an accident, as the notified polymer and the products containing the notified polymer will be sealed in containers during transport and storage.

Reformulation and packaging
During reformulation operations, dermal and ocular exposure of workers to the notified polymer in neat form is possible when weighing and transferring of the notified polymer from imported containers into blending tanks. Inhalation of the notified polymer is not expected unless the polymer becomes airborne. The notifier stated that PPE, such as coveralls, gloves and eye protection will be used when handling the notified polymer. During filling operations, potential exposure of workers to the notified polymer in finished cosmetic formulations (at concentrations of ≤ 2%) will likely be through dermal or ocular routes. The exposure is expected to be minimised by the use of automated/enclosed systems and appropriate PPE.

QA staff will wear laboratory coats, gloves and safety glasses to minimise exposure to the notified polymer in samples during quality control processes.

End use
Exposure to the notified polymer in end use products (at concentrations of ≤ 2%) may occur in professions where the services provided involve the application of finished hair cosmetic products to clients (e.g. hair dressers or workers in beauty salons). The principal route of exposure will be dermal with the potential for ocular exposure to occur from splashes or wiping of eyes/face. After application residuals of the hair care products may remain on the skin if not washed off. Oral ingestion of the residuals may occur if good hygiene practices are not in place. Professional users (for instance hair dressers) may use some PPE (such as gloves) to minimise repeated exposure but this may not occur in all workplaces. Exposure of such workers is expected to be of a similar or lesser extent when compared with the exposure experienced by consumers using various hair care 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 of ≤ 2%) through the use of a range of hair care products. The main route of exposure will be dermal, while ocular and oral exposures are also possible.

6.2. Human Health Effects Assessment
The results from toxicological investigations conducted on the notified polymer or analogues are summarised in the following table. For full details of the studies on the notified polymer, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*	*Substance*
Rat, acute oral toxicity	LD50 > 5,000 mg/kg bw; low toxicity	Analogue 2 [a]
Skin irritation (*in vitro*)	non-irritating	Notified polymer
Rabbit, skin irritation	non-irritating	Analogue 2 [a]
Eye irritation (*in vitro*)	no prediction can be made (but not corrosive)	Notified polymer
Rabbit, eye irritation	non-irritating	Analogue 2 [a]
Rat, repeat dose dermal toxicity – 90 days	DNEL* 100 mg/kg bw/day	Analogue 3 [b]
Rat, repeat dose oral toxicity – 90 days	DNEL* 75 mg/kg bw/day	Analogue 3 [b]
Mutagenicity – bacterial reverse mutation	non mutagenic	Notified polymer
Mutagenicity – mammalian cell gene mutation test	non mutagenic	Notified polymer
Genotoxicity – *in vitro* chromosomal aberration	non genotoxic	Notified polymer

[a] Analogue 2 is structurally similar to the notified polymer.
[b] Analogue 3 is one of the constituents of the notified polymer.
* Derived no effect level (DNEL)

Toxicokinetics, metabolism and distribution
No information on the toxicokinetics, metabolism and distribution of the notified polymer were provided. Based on the high molecular weight of the notified polymer (Mn > 1,000 g/mol) and low water solubility, it is not expected to be readily absorbed across biological membranes.

Acute toxicity
No acute oral toxicity data on the notified polymer are currently available. An acute oral toxicity study summary on analogue 2 was submitted. Analogue 2 was found to have low acute oral toxicity in rats with an LD50 > 5,000 mg/kg bw.

No data on acute dermal and inhalation toxicity of the notified polymer are currently available.

Irritation and sensitisation
In vitro eye and skin irritation study reports were provided on the notified polymer. The results from the *in vitro* skin irritation test (EpiDerm) indicate the notified polymer as non-irritating to the skin. In an *in vitro* bovine corneal opacity and permeability (BCOP) test, the *in vitro* irritancy score (IVIS) was 21.5 indicating the polymer as not corrosive but no prediction of eye irritation could be made.

A study summary for eye and skin irritation tests conducted on analogue 2 using rabbits was provided. Results of the tests indicated that analogue 2 was non-irritating to either eyes or skin. However, it was noted in the eye

irritation test, very slight reactions of conjunctivae (score 1) and cornea (score 1) were observed in some animals 1 hour after administration of the test substance and reversed within 24 hours.

No sensitisation data were provided on the notified polymer or analogues. There are no structural alerts indicative of sensitisation potential.

Repeated dose toxicity
No repeated dose toxicity data on the notified polymer are currently available. Information on analogue 3 indicates that the analogue may be severely irritating to the skin with repeated exposure. However skin irritation effects are not expected for the notified polymer (as shown by the data mentioned above). Based on the information derived from rats, repeated dermal exposure to the analogue may result in slight changes in haematology, clinical chemistry, and organ weights at a high dose of 1,000 mg/kg bw/day.

The notifier estimated the derived no effect levels (DNELs) for repeated dose dermal and oral toxicity of analogue 3 to be 100 and 75 mg/kg bw/day respectively, using a safety factor of 10. The notified polymer is likely to be less toxic than analogue 3 as the higher molecular weight of the polymer may reduce bioavailability from dermal exposure.

Mutagenicity/Genotoxicity
The notified polymer was found to be non-mutagenic in a bacterial reverse mutation assay and in an *in vitro* mammalian cell gene mutation test (HPRT assay) using Chinese hamster ovary cells (CHO AA8). The notified polymer was also determined to be non-clastogenic in an *in vitro* mammalian chromosome aberration test using human peripheral blood lymphocytes.

Health hazard classification
Based on the limited available information, the notified 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 information available, the notified polymer may be slightly irritating to eyes. Although the repeated dose toxicity data for the notified polymer are not available, significant systemic absorption is not expected from use of the notified polymer in finished hair care products at final concentrations of ≤ 2% (see above).

Reformulation
Reformulation workers may come into contact with the notified polymer at various concentrations up to the neat form. Main route is expected to be dermal but accidental ocular exposure is also possible. Inhalation exposure is unlikely unless aerosols are formed during reformulation activities. Safe work practices, engineering controls and use of PPE, including eye protection, chemical resistant gloves, and protective clothing would reduce the risk of any adverse health effects.

End use
Cleaners and beauty care professionals will handle end use products containing the notified polymer at concentrations of ≤ 2%. As certain protective measures including PPE may be used by these professionals, the risk to the workers 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 (see section below).

Provided control measures are in place to limit exposure, the risk to the health of reformulation workers is not considered to be unreasonable.

6.3.2. Public Health
Members of the public may experience repeated exposure to the notified polymer through the use of finished hair care products (containing the notified polymer at concentrations of ≤ 2). The main route of exposure is expected to be dermal with some potential for accidental ocular or oral exposure.

The notified polymer may have potential to cause slight irritation to the eyes. Given the relatively low proposed final use concentrations (≤ 2%) and the high molecular weight of the notified polymer limiting dermal

absorption, adverse effects are not expected from the use of finished hair care products containing the notified polymer.

Therefore, based on the information available, the risk to the public associated with use of the notified polymer at the proposed concentrations of ≤ 2% in finished hair care 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 neat into Australia for reformulation into finished hair care products, or as a component of finished hair care products. There is unlikely to be any significant release to the environment from transport and storage. In the event of spills, the notified polymer and products containing the notified polymer are 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 is expected to occur within a fully enclosed environment. Therefore, significant release of the notified polymer from this process to the environment is not expected. The process will be followed by automated filling of the formulated products into containers of various sizes suitable for retail. Wastes containing the notified polymer generated during reformulation include equipment wash water, empty import containers, and spilt materials. Wastes may be collected and released to sewers in a worst case scenario, or disposed of to landfill in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The notified polymer is a component of hair care products. The formulated products will be applied to the hair, and will be washed off the hair with ultimate release to the sewer.

RELEASE OF CHEMICAL FROM DISPOSAL

Wastes and residue of the notified polymer in empty end use containers are likely either to share the fate of the container and to be disposed of to landfill, or to be released to sewer when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified polymer is expected to enter the sewer system through its use in hair care products, before potential release to surface waters nationwide. Based on the results of a ready biodegradability study, the notified polymer is considered to be readily biodegradable (83% in 28 days). For details of the environmental fate study, please refer to Appendix C. Based on its low water solubility, release to surface waters is unlikely as partitioning to sludge and sediment is expected. The notified polymer is not expected to bioaccumulate due to its high molecular weight. 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. A proportion of the notified polymer may also be applied to land through disposal to landfill as collected spills and empty container residue. Residues of the notified polymer in landfill, soil and sludge are expected to 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 the scenario with 100% release of the notified polymer into sewer systems nationwide over 365 days per annum. Based on the ready biodegradability and low water solubility, 90% of the notified polymer is expected to be removed during sewage treatment processes. The resultant PEC in sewage effluent on a nationwide basis is estimated as follows:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import Volume	5,000	kg/year
Proportion expected to be released to sewer	100	%
Annual quantity of chemical released to sewer	5,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	13.70	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	90%	Mitigation
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.28	µg/L
PEC - Ocean:	0.03	µg/L

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 25 mg/kg (dry wt). Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1,500 kg/m^3 and a soil-mixing zone of 10 cm, the concentration of the notified polymer may approximate 0.17 mg/kg in applied soil.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	NOEL* at 100 mg/L	The analogue of the notified polymer and by inference the notified polymer is not harmful to fish
Daphnia Toxicity	NOEL at limit of solubility	The analogue of the notified polymer and by inference the notified polymer is not harmful to invertebrates to the limit of its solubility
Algal Toxicity	NOEL at limit of solubility	The analogue of the notified polymer and by inference the notified polymer is not harmful to algae to the limit of its solubility

* No observed effect level (NOEL)

Based on the analogue studies the notified polymer is not expected to be harmful to aquatic life.

7.2.1. Predicted No-Effect Concentration

No-effect is predicted at the limit of water solubility for the notified polymer based on information derived from the analogue chemicals.

7.3. Environmental Risk Assessment

Based on the low aquatic hazard, it is unlikely that the notified polymer will reach ecotoxicologically significant concentrations in surface waters. In the aquatic environment it is unlikely to bioaccumulate based on its ready biodegradability, high molecular weight and low water solubility. Therefore, the notified polymer is not expected to pose an unreasonable risk to the environment on the basis of the assessed use pattern.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility < 0.01 g/L at 20 °C

Method	OECD TG 105 Water Solubility EC Council Regulation No 440/2008 A.6 Water Solubility
Remarks	Flask Method. Three flasks containing approx. 10 g/L test substance in water were stirred for 5 h at 30 °C. Subsequently the flasks were stirred at 20 °C for 1 day, 2 days and 3 days, respectively. After each day the content of one flask was filtered through a membrane filter (0.45 µm). The content of the test substance in the filtrate was determined by GPC. The flask method is more appropriate for substances with a water solubility of > 0.01 g/L.
Test Facility	Clariant (1995)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – skin [*in vitro* Reconstructed Human *Epidermis* Test]

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human Epidermis Test Method
Vehicle	None, test substance was used as supplied.
Remarks - Method	The EpiDerm™ Reconstructed Human Epidermis Model (EPI-200-SIT) test system was used. The positive control was aqueous solution of sodium dodecyl sulfate (SDS) at a concentration of 5% and the negative control was sterile Dulbecco's phosphate buffered saline (DPBS). The test substance was not found to be able to directly reduce 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl-tetrazolium bromide (MTT). No major deviations from the test guideline were reported.

RESULTS

Test Material	*Mean OD_{570} of Triplicate Tissues*	*Relative Mean Viability (%)*	*SD of Relative Mean Viability*
Negative control	1.816	100	0.155
Test substance	1.811	99.7	0.036
Positive control	0.058	3.2	0.004

OD = optical density; SD = standard deviation

Remarks - Results	The acceptance criteria for both the negative and positive controls were satisfied, and the variation between replicates was satisfactory. As the relative mean viability of tissues exposed to the test substance was > 50%, the test substance did not meet the criteria for classification as a skin irritant according to the test guidelines.
CONCLUSION	The notified polymer was non-irritating to the skin under the conditions of the test.
TEST FACILITY	Bioneeds (2017a)

B.2. Irritation – eye [*in vitro* Bovine Corneal Opacity and Permeability (BCOP) Test]

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 437 Bovine Corneal Opacity and Permeability Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage
Vehicle	None, test substance was used as supplied.
Remarks - Method	The positive control was ethanol (at 99% concentration) and the negative control was sodium chloride solution (at 0.9% concentration). No major deviations from the test guideline were reported.

RESULTS

Test Material	*Corrected Mean Opacities of Triplicate Tissues (SD)*	*Corrected Mean Permeabilities of Triplicate Tissues (SD)*	*IVIS*
Negative control	–	–	0
Test substance	14.8 (± 2.7)*	0.353 (± 0.07)*	21.5
Positive control	77.8 (± 7.1)*	1.885 (± 0.14)*	106.0

SD = Standard deviation; IVIS = *in vitro* irritancy score
* Corrected for background values taken from negative control

Remarks - Results

The acceptance criteria for the negative and positive controls were satisfied.

The corneas treated with the test substance did not show any abnormalities; however an appreciable increase in permeability (mean value of 0.353) was observed compared to the negative control.

The corneas treated with the positive control showed expected microscopic damages in all 3 samples.

The IVIS for the test substance was determined to be 21.5. As the IVIS for the test substance was > 3 but ≤ 55, no predication can be made regarding the potential for corrosivity or severe irritancy of the test substance.

CONCLUSION

Based on the IVIS (< 55), no prediction can be made for the notified polymer under the conditions of the test. However, it is not corrosive to eyes.

TEST FACILITY

Bioneeds (2017b)

B.3. Genotoxicity – bacteria

TEST SUBSTANCE

Notified polymer

METHOD

OECD TG 471 Bacterial Reverse Mutation Test
Plate incorporation procedure/Pre-incubation procedure

Species/Strain

Salmonella typhimurium: TA1535, TA1537, TA98, TA100,
Escherichia coli: WP2uvrA (pKM101)

Metabolic Activation System

Sodium phenobarbitone and β-naphthoflavone induced rat liver S9 homogenate

Concentration Range in Main Test

a) With metabolic activation: 0.05 – 5 µL/plate
b) Without metabolic activation: 0.05 – 5 µL/plate

Vehicle

Dimethyl sulphoxide (DMSO)

Remarks - Method

The test substance was miscible in DMSO at a concentration of 50 µL/mL and resulted in no precipitation up to 5 µL/plate.

Concentrations for main test were chosen based on the results from an initial cytotoxicity test conducted on TA100 (base-pair substitution type). The test item resulted in no precipitation up to 5 µL/plate

Test 1 was conducted on TA100, TA1535 and WP2 uvrA pKM101 (base-pair substitution type) and on TA98 and TA1537 (frameshift type) using the plate incorporation method.

As the results of plate incorporation method were negative, a second test (Test 2) using the pre-incubation method was conducted on the same tester strains and concentration range as in Test 1.

Tests with vehicle control and positive controls were run concurrently. Positive controls were:

- With metabolic activation: 2-aminoanthracene (TA98, TA100,

TA1535, TA1537and WP2uvrA) and benzo[*a*]pyrene (TA98)
- Without metabolic activation: 2-nitrofluorene (TA98); sodium azide (TA100, TA1535); 9-aminoacridine (TA1537) and 4-nitroquinoline 1-oxide (WP2uvrA).

No major deviations from the test guideline were reported.

RESULTS

Metabolic Activation	*Test Substance Concentration (µL/plate) Resulting in:* *Cytotoxicity*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative
Present			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative

Remarks - Results

The test substance, tested up to the highest concentration of 5 µL/plate in *S. typhimurium* and *E. coli*, did not result in an increase of more than twice the number of revertant colonies in comparison to the negative control. In addition, no dose-related response was observed in any strains for base-pair substitution type or frame-shift type mutations, with or without metabolic activation.

The positive and vehicle controls provided a satisfactory response confirming the validity of the test system.

CONCLUSION

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

TEST FACILITY

Bioneeds (2017c)

B.4. Genotoxicity – *in vitro* Mammalian Chromosome Aberration Test

TEST SUBSTANCE

Notified polymer

METHOD

OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test

Cell Type/Cell Line

Human peripheral blood lymphocytes

Metabolic Activation System

Sodium phenobarbitone and β-naphthoflavone induced rat liver S9 homogenate

Vehicle

Dimethyl sulphoxide (DMSO)

Remarks - Method

Lymphocytes from the blood of three healthy, non-smoking male volunteers were used for each test.

Based on the solubility and precipitation tests, 2 mg/mL was selected as the highest dose for preliminary cytotoxicity test.

Mitomycin C (MMC) and cyclophosphamide (CP) were used as positive controls.

No major deviations from the test guideline were reported.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0, 0.5, 1, 2	3 h 27 m	24 h
Test 2	0, 0.5, 1, 2	21 h 50 m	24 h
Present			
Test 1	0, 0.5, 1, 2	3 h 27 m	24 h

All cultures were selected for metaphase analysis.

RESULTS

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

Remarks - Results

The test substance did not induce any statistically significant increases in the frequency of cells with chromosome aberrations either in the absence or presence of metabolic activation when compared with the vehicle control at any of the concentrations tested.

The positive and vehicle controls provided a satisfactory response confirming the validity of the test system.

CONCLUSION

The notified polymer was not clastogenic to human peripheral blood lymphocyte cells treated *in vitro* under the conditions of the test.

TEST FACILITY

Bioneeds (2017d)

B.5. Genotoxicity – *in vitro* Mammalian Cell Gene Mutation Test

TEST SUBSTANCE

Notified polymer

METHOD

OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test

Species/Strain: Hamster

Cell Type/Cell Line: Chinese hamster ovary/CHO AA8

Metabolic Activation System: Sodium phenobarbitone and β-naphthoflavone induced rat liver S9 homogenate

Vehicle: Dimethyl sulphoxide (DMSO)

Remarks - Method

Hypoxanthine-guanine phosphoribosyl transferase (HPRT) method was used.

Tests with vehicle control and positive controls were run concurrently. Positive controls were:

- With metabolic activation: benzo[*a*]pyrene
- Without metabolic activation: 4-nitroquinoline 1-oxide.

Based on precipitation and pH test, 2 mg/mL was selected as the highest dose for preliminary cytotoxicity test. Concentrations for the main test were chosen based on the preliminary cytotoxicity test. When compared with the respective controls, the relative survival, both in the presence and absence of metabolic activation, was > 20%. Hence, the concentrations of 0.25, 0.5, 1 and 2 mg/mL were selected.

No major deviations from the test guideline were reported.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0.25, 0.5, 1, 2	3 h 15 min	9 days
Present			
Test 1	0.25, 0.5, 1, 2	3 h 15 min	9 days

All cultures selected for metaphase analysis.

RESULTS

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

Remarks - Results

The test substance did not result in a statistically significant and/or dose dependent increase in the frequency of cells with HPRT gene mutation compared to the vehicle control groups, both with or without metabolic activation.

The positive controls demonstrated the sensitivity of the assay and the metabolising activity of the rat liver S9 preparations.

CONCLUSION

The notified polymer was not mutagenic to Chinese hamster ovary (CHO) AA8 cells treated *in vitro* under the conditions of the test.

TEST FACILITY

Bioneeds (2017e)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical CO_2 production ($ThCO_2$)
Remarks - Method	The test was conducted in accordance with the test guideline above with no significant deviation from the protocol reported.

RESULTS

Test Substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
6	45	6	60
14	76	14	79
21	81	21	81
28	83	28	83

Remarks - Results	The validity criteria for the test were satisfied. The total CO_2 evolution in the inoculum control at the end of the test was 42 mg/L. The degradation of the functional control reached the pass level of ≥ 60 % within 6 days. The percentage degradation of the toxicity control surpassed the threshold level of 25% in 6 days. The test substance attained 83% degradation by 28 days. Therefore, the test substance is considered to be readily biodegradable according to the OECD (301 B) guideline.
CONCLUSION	The notified polymer is readily biodegradable.
TEST FACILITY	Noack Laboratorien (2018)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Analogue 2
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static EEC Directive 92/69/ C.1, L 383A/163 Acute Toxicity for Fish - static
Species	Zebra fish (*Brachydanio rerio*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	67 mg $CaCO_3$/L
Analytical Monitoring	Dissolved and total organic carbon (DOC and TOC)
Remarks – Method	Dissolved organic content analysis was only conducted at the beginning of the experiment. A preliminary study was conducted and on this basis only a limit test of 100 mg/L was conducted.

RESULTS

Concentration			Number of Fish	Mortality				
Nominal (mg/L)	*Actual TOC (mg C/L)*	*Actual DOC (mg C/L)*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
100	39	6	7	0	0	0	0	0
Control	1	1	7	0	0	0	0	0

LL50	> 100 mg/L at 96 hours
NOEL	> 100 mg/L at 96 hours
Remarks – Results	All validity criteria were met. However, no evidence was provided that the concentration of the test substance was maintained over the test period. Dissolved oxygen content > 60%.

CONCLUSION The analogue of the notified polymer is not toxic to fish.

TEST FACILITY Dr U. Noack-Laboratorium (2000)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Analogue 1

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test - static

Species	*Daphnia magna*
Exposure Period	48 hours [acute]
Auxiliary Solvent	None
Water Hardness	180 mg $CaCO_3$/L
Analytical Monitoring	TOC
Remarks - Method	Test was conducted as per the above guidelines, no major deviations were reported. A preliminary study was conducted and on this basis a limit test was conducted on a saturated solution at 1 mL/L. A positive control study was also conducted using $K_2Cr_2O_7$, less than 3 months prior to the current study.

RESULTS

Concentration (mg/L)		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h [acute]*	*48 h [acute]*
1 (saturated)	8.08	20	0	0
control	2.16	20	0	0

LC50	> 1 mL/L of saturated solution at 48 hours
NOEC (or LOEC)	> 1 mL/L of saturated solution at 48 hours
Remarks - Results	No immobilisation was detected in any test groups. Dissolved O_2 was ≥ 8.0 mg/L. All validity criteria were met. In the positive control, an EC_{50} value of 0.6 mg/L was determined.

CONCLUSION The saturated solution of the analogue of the notified polymer with a nominal value of 1.00 mL/L is not toxic to daphnia.

TEST FACILITY Noack Laboratorien GmbH (2017)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Analogue 1

METHOD OECD TG 201 Alga, Growth Inhibition Test

	EC Council Regulation No 440/2008 C.3 Algal Inhibition Test
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominally 940 mg/L
Auxiliary Solvent	None
Water Hardness	0.24 mmol Ca + Mg/L (≡ 24 mg as $CaCO_3$)
Analytical Monitoring	TOC
Remarks - Method	No deviations from OECD TG 201. A range finding test determined the concentrations used, for the main study. A separate positive control test was also conducted using $K_2Cr_2O_7$, less than 4 months prior to the current study.

RESULTS

Remarks - Results	The analogue is not toxic to algal growth at the limit of water solubility. However, it is noted that measured TOC concentrations for the test substance in this study were indistinguishable from the control. The measured values of TOC for the test chemical were near or below the limit of quantification (2.00 mg C/L) in both the control and the test substance. The growth in the controls was 363 fold, the coefficients of variation for growth rates for section by section and between replicates were 18% and 0.59%, respectively. All validity criteria were met for this study. The positive control test showed a growth rate inhibition ErC_{50} of 0.460.
CONCLUSION	The analogue of the notified polymer is not toxic to algae to the limit of its water solubility.
TEST FACILITY	Noack Laboratorien GmbH (2016)

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