File No: LTD/1842

July 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Hexanedioic acid, polymer with 2,2-dimethyl-1,3-propanediol, 2-octyldodecyl ester, 2-cyano-3,3-diphenyl-2-propenoate (INCI name: Polyester-8)

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

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1842	Estee Lauder Pty Ltd	Hexanedioic acid, polymer with 2,2-dimethyl-1,3-propanediol, 2-octyldodecyl ester, 2-cyano-3,3-diphenyl-2-propenoate (INCI name: Polyester-8)	ND*	≤ 1 tonne per annum	Cosmetic ingredient

*ND = Not determined.

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified polymer is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

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 assessed use pattern and expected low exposure to aquatic environment, the notified polymer is not expected to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A copy of the (M)SDS should be easily accessible to employees.
- If products and mixtures containing the notified polymer are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

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

Emergency procedures

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

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the concentration of the notified polymer exceeds or is intended to exceed 5%;
- additional information becomes available on the skin sensitisation potential of the notified polymer;
- information becomes available on the repeated dose toxicity potential of the notified polymer;

or

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

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

(Material) Safety Data Sheet
The (M)SDS of the notified polymer and a product containing the notified polymer provided by the notifier were reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Estee Lauder Pty Ltd (ABN: 63 008 444 719)
165–175 Mitchell Road
ERSKINEVILLE NSW 2043

NOTIFICATION CATEGORY
Limited-small volume: Synthetic polymer with Mn ≥ 1,000 Da.

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: polymer constituents, molecular and structural formula, molecular weight, hazardous impurities, references (selected testing laboratories) and spectral data.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for melting/freezing point, boiling point, density, vapour pressure, hydrolysis as a function of pH, absorption/desorption, dissociation constant, flash point, flammability, autoignition temperature, explosive and oxidising properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
TGA (2008)

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Polyester-8 (INCI name)
Polycrylene

CAS NUMBER
862993-96-2

CHEMICAL NAME
Hexanedioic acid, polymer with 2,2-dimethyl-1,3-propanediol, 2-octyldodecyl ester, 2-cyano-3,3-diphenyl-2-propenoate

OTHER NAME(S)
RX 13938
M06-0877.0

MOLECULAR WEIGHT
Number Average Molecular Weight (Mn) > 1,000 Da

ANALYTICAL DATA
Reference GPC spectrum was provided.

3. COMPOSITION

DEGREE OF PURITY
> 98%

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)
None specified.

ADDITIVES/ADJUVANTS
None specified.

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: light yellow, viscous liquid.

Property	Value	Data Source/Justification
Boiling Point	Not determined	Imported in formulated products only
Density	1,070 kg/m^3	(M)SDS
Vapour Pressure	< 1.3 × 10^{-9} kPa	Estimated, based on the NAMW > 1,000 Da (US EPA, 2013)
Water Solubility	3.42 × 10^{-3} g/L at 20 °C	Measured.
Water Extractability	0.33%	Measured. Loading rate was 1 g/L.
Hydrolysis as a Function of pH	Not determined.	Contains hydrolysable functionalities, but hydrolysis is not expected to occur in the environmental range of pH 4–9 due to low solubility.
Partition Coefficient (n-octanol/water)	log Pow between < 3.0 and 6.8 (50% of test substance) at 35 °C log Pow > 7.2 (50% of test substance) at 35 °C	Measured
Adsorption/Desorption	Not determined.	Given its hydrophobic nature, the notified polymer is likely to partition to organic carbon and sludge.
Dissociation Constant	Not determined.	No dissociable functionality.
Flash Point	> 204 °C	(M)SDS
Autoignition Temperature	Not determined.	Imported in formulated products only. Not expected to autoignite under normal conditions of use.
Explosive Properties	Not determined.	Not expected to be explosive based on chemical structure.
Oxidising Properties	Not determined.	Not expected to be oxidising based on chemical structure.

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, refer to Appendix A.

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

Physical hazard classification
Based on the limited 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 be imported into Australia as an ingredient in finished cosmetic products.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	0.5	0.6	0.7	0.8	0.995

PORT OF ENTRY
Sydney by sea

IDENTITY OF MANUFACTURER/RECIPIENTS
Estee Lauder Pty Ltd

TRANSPORTATION AND PACKAGING
The notified polymer will be transported as an ingredient in finished cosmetic products at a concentration of ≤ 5%. Products containing the notified polymer will be packaged in suitable containers (e.g. 50 g size) for retail sale.

USE
The notified polymer will be used as an ingredient (≤ 5%) in finished cosmetic products.

OPERATION DESCRIPTION
The products will be sold to the public in the same form in which they are imported, with no reformulation or repackaging conducted in Australia.

Transportation and storage
Dockside and warehouse workers will transport the imported products from the wharf to the central distribution centres and place the pallets of products into the warehouse before distribution to retail stores.

End-use
Products containing the notified polymer (≤ 5% concentration) may be used by consumers and professionals such as hairdressers and workers in beauty salons. Depending on the nature of the product, the application could be varied – by hand, using an applicator or sprayed.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure
Transport, storage and retail workers may come into contact with the notified polymer only in the event of accidental rupture of packages.

Exposure to the notified polymer in end-use products (at ≤ 5% concentration) may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. hair dressers, workers in beauty salons). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such professionals may use some 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 (≤ 5% concentration) through the use of cosmetic products. The principal route of exposure will be dermal, while oral, ocular and inhalation exposures are also possible, particularly if products are applied by spray, or if products are applied to the lips.

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*
Eye irritation – *in vivo* – HETCAM	slightly irritating
Human, skin sensitisation – RIPT (notified polymer)	no evidence of sensitisation at 10%
Human, skin sensitisation – RIPT (semi-occluded patch)*	no evidence of sensitisation at 3%
Human, skin sensitisation – RIPT (occluded patch)**	no evidence of sensitisation at 3%
Mutagenicity – bacterial reverse mutation	non-mutagenic
Phototoxicity – *in vitro* – 3T3 NRU phototoxicity test	no evidence of phototoxicity

* Study conducted on end product 1: Facial Cream SPF 15
** Study conducted on end product 2: Face Cream SPF 20

Toxicokinetics
No toxicokinetic data on the notified polymer were submitted.

Absorption of the notified polymer through the skin and gastrointestinal tract is expected to be limited based on the partition coefficient (Log P_{OW} > 7.2 for 50% of the notified polymer), low water solubility (3.42×10^{-3} g/L) and high molecular weight (NAMW > 1,000 Da).

The notified polymer is a copolymer of hexanedioic (adipic) acid and neopentyl glycol that is terminated with either an octyldodecanyl or a cyanodiphenylpropenoyl group. The metabolism of the notified polymer has the potential to produce metabolites of adipic acid and neopentyl glycol. Two Cosmetic Ingredient Review (CIR) reports concluded that hexanedioic (adipic) acid (CIR 2012) and neopentyl glycol (CIR 2015), respectively, were safe in current practices of cosmetic use.

Acute toxicity
No data were available on the acute toxicity of the notified polymer via the oral, dermal and inhalation routes. Due to the expected limited absorption, the notified polymer is expected to be of low acute toxicity by these routes.

In acute oral toxicity studies in rats, hexanedioic (adipic) acid was of low toxicity, with reported LD_{50} values ranging from ≥ 940 to 11,000 mg/kg bw/day (CIR 2012). In acute oral and dermal toxicity studies in rats, neopentyl glycol was of low acute toxicity, with reported oral LD_{50} values ranging from ≥ 3,200 to 6,920 mg/kg bw/day and dermal LD_{50} values ≥ 4,000 mg/kg bw/day (CIR 2015).

Irritation
In an eye irritation study, conducted in accordance with the HET-CAM assay, a non-OECD-validated test guideline, administration of the notified polymer on the chorio-allantic membrane of hen's eggs was examined. Two tissues showed hyperaemia (with one tissue showing enhanced effect of minimal haemorrhage) at the initial (0.5 minute) observation only. The other two tissues scored hyperaemia at the 2 minute and 5 minute observation, respectively. Based on the effects observed in this study, the notified polymer does not warrant classification as an eye irritant.

No *in vitro* or *in vivo* skin irritation studies were provided on the notified polymer. However, in three human repeat insult patch tests (HRIPT) (discussed below), the notified polymer did not produce dermal irritant effects.

Sensitisation
The notified polymer has a structural alert for sensitisation, and is also structurally similar to octocrylene (CAS No. 6197-30-4), a recognised sensitiser (Esdaile & Cooper, 2012). However, the available data presents conflicting information for the potential of the notified polymer to act as a skin sensitiser.

The notified polymer (at 10% concentration in vehicle) was not a skin sensitiser in a HRIPT study. The limited study size (49 subjects, where at least 100 subjects preferred) increases the uncertainty in considering the results from the study. Skin sensitisation responses were not observed in another two HRIPT studies using two different end-use face cream products (featuring SPF 15 and SPF 20, applied with a semi-occluded and an occluded patch, respectively), both containing the notified polymer at 3% concentration. The study sizes were larger at 106 and 636 subjects, respectively. However, the sample volumes applied to the patches were not recorded.
In a clinical report conducted on the notified polymer at 3% in a sunscreen moisturiser (SPF 25), positive reactions were recorded in the patient on days 2 and 4 (Esdaile & Cooper, 2012). In addition, the patient was tested with all 50 ingredients of the product and compared with octocrylene. A positive reaction was observed in the patient for the notified polymer but not octocrylene. The study concluded that, while copolymers are thought to be unlikely to sensitise owing to their large molecular size, there are case reports of sensitisation effects (Quartier et al 2006) and it is becoming clear that their sensitising capacity has been underestimated and that the notified polymer may be an emerging allergen. The nature of the hapten is still unknown and sensitisation could be due to an additive, impurity, polymerisation product, residual monomer or a degradation product.

Repeated dose toxicity
No data was available on the repeated dose toxicity of the notified polymer.

Information on the repeated dose toxicity of hexanedioic (adipic) acid and neopentyl glycol has been reported by the Cosmetic Ingredient Review (CIR 2012, 2015). These reports generally indicate the absence of effects deemed toxicologically adverse at doses ≤ 100 mg/kg bw/day. However, these chemicals are not likely to have identical patterns of physiological action to the notified polymer, due to individual dermal penetration ability, differing log K_{ow} and the varied presence of specific functional groups, which together limit the usefulness of such chemicals for read-across of toxicological data to the notified polymer.

Mutagenicity/Genotoxicity
The notified polymer was not mutagenic in a bacterial reverse mutation study. No further *in vitro* or *in vivo* genotoxicity data were provided for the notified polymer.

Phototoxicity
In an *in vitro* phototoxicity study (BALB/c 3T3 cells), the notified polymer was predicted to not be phototoxic.

It is noted that the notified polymer carries structural capabilities of a photostabiliser. The cyanodiphenyl propenoate moiety has the ability to absorb in the UVB range, with an absorption maximum at 303 nm (Esdaile & Cooper, 2012).

Health hazard classification
Based on the available information, the notified polymer is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Limited toxicological data are available on the notified polymer; however, based on the information available the notified polymer has potential to be a slight eye irritant.

Dermal, ocular and inhalation exposure to the notified polymer (≤ 5% concentration) may occur for hairdressers and beauty salon workers 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 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 the potential for exposure. Based on the information available, 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 ≤ 5% concentration in leave-on and rinse-off cosmetic products.

Irritation and sensitisation
There are only HRIPT test data available for the skin sensitisation potential of the notified polymer. The HRIPT test is not a predictor of general human population effects, but rather, it is 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).

While the risk of skin sensitisation from use of the notified polymer has not been quantitatively determined, based on the large cohort in one of the studies (> 600 participants), it is likely to be low at the concentration proposed to be used. However, based on the available information, the potential for skin sensitisation cannot be ruled out.

The notified polymer has the potential to cause slight irritation to eyes. However, eye irritation effects are not expected from use of the notified polymer at the proposed use concentrations and assessed use pattern.

Repeat dose toxicity
The repeated dose toxicity effects of the notified polymer have not been determined. However, exposure is expected to be limited by the low predicted dermal absorption of the notified polymer.

Therefore, based on the information available, the risk to the public associated with use of the notified polymer at ≤ 5% in cosmetic and personal 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 not be manufactured or reformulated in Australia. It will be imported as a component of finished cosmetic products (e.g. lotion cream for face and body). There is unlikely to be any significant release of the notified polymer to the environment from storage and transport, except in the case of accidental spills. Accidental spills are expected to be contained and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified polymer is a component in finished cosmetic products. The formulated product will be applied to the skin and will either be ingested, wiped off by tissues and disposed of to domestic garbage, or washed off the body and ultimately released to sewer.

RELEASE OF CHEMICAL FROM DISPOSAL

Expired waste and residue of the notified polymer in the empty containers (3%) is likely either to share the fate of the container and be disposed of to landfill, or to be washed to sewer when containers are rinsed before recycling.

7.1.2. Environmental Fate

The majority of the notified polymer will be disposed of to the sewer and, as it is a high molecular weight non-ionic polymer, it is estimated to be removed by ≤ 90% in sewage treatment plants by partitioning to sediment and sludge (Boethling & Nabholz, 1997). The notified polymer that partitions to sludge will be removed with the sludge for disposal to landfill or used in soil remediation. Hence, it is not anticipated to be significantly bioavailable to aquatic organisms. In the aquatic environment it is unlikely to bioaccumulate based on its high molecular weight and low water solubility. In landfill it is expected to degrade biotically and abiotically to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

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

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	995	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	995	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.73	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.603	µg/L
PEC - Ocean:	0.060	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 0.603 µg/L may potentially result in a soil concentration of approximately 0.004 mg/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 0.02 mg/kg and 0.04 mg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. High molecular weight chemicals without significant ionic functionality are of low concern to the aquatic environment. Due to its low import volume, low solubility and likelihood for adsorption to sludge and sediment, the notified polymer is not expected to be present in water at concentrations that are hazardous to aquatic organisms.

7.2.1. Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) was not calculated since no ecotoxicity data were available for the notified polymer.

7.3. Environmental Risk Assessment

The majority of notified polymer disposed of to the sewer is expected to be removed by partitioning to sludge and sediment during sewage treatment plant processes. As a result, it is not likely to be present in ecotoxicologically significant concentrations in the aquatic environment. In the aquatic environment it is unlikely to bioaccumulate based on its 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 Extractability 0.33 % at a loading rate of 1 g/L at 20 °C

Method	OECD TG 120 Water Extractability.
Remarks	Flask Method The water solubility at a loading rate of 1 g/L was measured to be 3.42 10^{-3} g/L. The results indicate that the solution/extraction behaviour of the notified polymer is loading rate dependent.
Test Facility	Harlan (2013)

Partition Coefficient (n-octanol/water) log Pow ranged between < 0.3 and 6.8 for 50% of the test substance at 35 °C
log Pow > 7.2 for the remaining 50% of the test substance at 35 °C

Method	OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks	HPLC Method
Test Facility	WIL (2013)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – eye

TEST SUBSTANCE: Notified polymer (2.5% v/v)

METHOD: HET-CAM test (modified Kemper and Luepke method)
Similar to the ICCVAM – Recommended test method protocol (NIH, 2010)
Alternative to Draize Test (OECD TG 405 Acute Eye Irritation).

Species/Strain: Hen/White Leghorn
Number of Animals: 4 chick egg CAM's (chorioallantoic membrane) used.
Observation Period: 5 minutes.
Remarks - Method: GLP Compliance (Quality Assurance statement included).

The study authors equated the notified polymer at 2.5% in warm corn oil tested on the CAM of the hen's egg to 5% notified polymer tested via the Draize test in rabbits.

No negative control test was conducted in this study.

2 positive control tests were conducted in parallel to the test substance using Johnson's Baby Shampoo (50%) and Head & Shoulders Shampoo (50%) (both known eye irritants). The results of these parallel tests were compared to historical scores using the Draize Scale.

Tissues were observed and scored at time intervals of 0.5, 2 and 5 minutes. Despite two test groups (test substance and positive control group 2) continuing to show scores at the end of the study period (5 minutes), no further observations were conducted.

RESULTS

Test Material	*Mean Scores for Each Tissue*.***				*Mean Score over Observation Period*.***	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3	4				
Test substance	1.67	2	1	0.33	1.25	5–7	5 minutes	1
Positive control 1	2	2	1.33	2	1.83	5–7	< 5 minutes	0
Positive control 2	4	4	4.33	3.67	4	7	5 minutes	5–7

* Calculated on the basis of the scores at 0.5, 2, and 5 minutes for each CAM tissue.
** Scores given the range of 2 numbers were averaged for calculation of the mean scores for each tissue.

Remarks - Results: Two tissues showed hyperaemia (with 1 tissue showing enhanced effect with minimal haemorrhage) at the initial (0.5 minute) observation only. The other two tissues scored hyperaemia at the 2 minute and 5 minute observation, respectively. Excluding this remaining effect in the one tissue, signs in all other tissues had resolved by the end of the study period.

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

The test substance was deemed to cause slight ocular irritation at 2.5% v/v (equivalent to 5% concentration).

CONCLUSION	The notified polymer is slightly irritating to the eye under the conditions of the test.
TEST FACILITY	Laboratory 1 (2005)

B.2. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified polymer (10% w/w)
METHOD	Repeated insult patch test with challenge.
Study Design	Induction Procedure: Patches containing 0.2 mL test substance were applied 3 times per week (Mondays, Wednesdays and Fridays) for a total of 9 applications. Patches were removed by the subjects after 24 hours and graded after an additional 24 hours (or 48 hours for patches applied prior to weekends). Rest Period: approximately 2 weeks Challenge Procedure: A patch was applied to a naïve site. Patches were removed by technicians after 24 hours. Sites were graded 24, 48, 72 and 96 hours post-patch removal.
Study Group	42 F, 17 M; age range 18–76 years
Vehicle	Corn oil
Remarks - Method	The test substance was spread on a 1.905 cm^2 (¾" x ¾") occluded patch. A panel of 59 healthy human subjects (devoid of any physical or dermatological conditions) was amassed.
RESULTS	
Remarks - Results	49/59 subjects completed the study. The 10 subjects who discontinued were deemed by study authors to do so for reasons unrelated to the test material. Discontinuation occurred in the induction phase (0–9 induction observations recorded). No reactions were evident in any test subject during the induction and challenge phases.
CONCLUSION	The notified polymer was non-sensitising under the conditions of the test.
TEST FACILITY	Laboratory 1 (2015)

B.3. Skin sensitisation – human volunteers

TEST SUBSTANCE	End-use product (SPF 15 facial cream) containing the notified polymer at 3% w/w concentration.
METHOD	Repeated insult patch test with challenge.
Study Design	Induction Procedure: 1.905 cm^2 (¾" x ¾") patches were applied 3 times per week for a total of 9 applications. Patches were removed by the subjects after 24 hours and graded after an additional 24 hours (or 48 hours for patches applied prior to weekends). Rest Period: approximately 2 weeks Challenge Procedure: A patch was applied to a naïve site. Patches were removed by technicians after 24 hours. Sites were graded 24, 48, 72 and 96 hours post-patch removal.
Study Group	89 F, 23 M; age range 18–70 years

Vehicle	Notified polymer applied in end-use product (facial cream).
Remarks - Method	The test substance was applied to semi-occluded patch (volume of test substance and patch size were not reported). Prior to patch application, the test area was wiped with 70% isopropyl alcohol and allowed to dry. A panel of 112 healthy human subjects (devoid of any physical or dermatological conditions) was amassed.
RESULTS	
Remarks - Results	106/112 subjects completed the study. The 6 subjects who discontinued were deemed by study authors to do so for reasons unrelated to the test material. Discontinuation occurred in the induction phase (0–3 induction observations recorded). No reactions were evident in any test subject during the induction and challenge phases.
CONCLUSION	The notified polymer was non-sensitising under the conditions of the test.
TEST FACILITY	CRL (2009)

B.4. Skin sensitisation – human volunteers

TEST SUBSTANCE	End-use product (SPF 20 face cream) containing the notified polymer at 3% w/w concentration.
METHOD	Repeated insult patch test with challenge.
Study Design	Induction Procedure: 1.905 cm^2 (¾" x ¾") patches were applied 3 times per week for a total of 9 applications. Patches were removed by the subjects after 24 hours and graded after an additional 24 hours (or 48 hours for patches applied prior to weekends). Rest Period: approximately 2 weeks Challenge Procedure: A patch was applied to a naïve site. Patches were removed by technicians after 24 hours. Sites were graded 24, 48, 72 and 96 hours post-patch removal.
Study Group	533 F, 139 M; age range 18–70 years
Vehicle	Notified polymer applied in end-use product (face cream).
Remarks - Method	The test substance was applied to an occluded patch (volume of test substance and patch size were not reported). Prior to patch application, the test area was wiped with 70% isopropyl alcohol and allowed to dry. A panel of 672 healthy human subjects (devoid of any physical or dermatological conditions) was amassed. The subjects were divided into 6 groups of 112 (coded A to F).
RESULTS	
Remarks - Results	636/672 subjects completed the study. The 36 subjects who discontinued were deemed by study authors to do so for reasons unrelated to the test material. Discontinuation occurred in the induction phase (0–6 induction observations recorded). No reactions were evident in any test subject during the induction and challenge phases.
CONCLUSION	The notified polymer was non-sensitising under the conditions of the test.
TEST FACILITY	CRL (2012)

B.5. Genotoxicity – bacteria

TEST SUBSTANCE	Notified polymer.
METHOD	Similar to OECD TG 471 Bacterial Reverse Mutation (AMES) Test. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA97a, TA98, TA100, TA102
Metabolic Activation System	S9 fraction from Aroclor 1254-induced rat liver
Concentration Range in Main Tests	a) With metabolic activation: 50–5,000 µg/plate b) Without metabolic activation: 50–5,000 µg/plate
Vehicle	Acetone.
Remarks - Method	GLP Compliance (Quality Assurance statement included). No preliminary toxicity test was conducted. The test articles were tested in triplicate for each tester strain. Positive control tests were conducted in parallel to the main test using sodium azide, 9-aminoacridine, daunomycin, ICR 191 acridine and mitomycin C in the absence of S9-mix, and 2-aminoanthracene with S9-mix.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	> 5,000	negative
Test 2	> 5,000	> 5,000	negative
Test 3	> 5,000	> 5,000	negative
Present			
Test 1	> 5,000	> 5,000	negative
Test 2	> 5,000	> 5,000	negative
Test 3	> 5,000	> 5,000	negative

Remarks - Results	No visible reduction in the growth of the bacterial background lawn or increases in the frequency of revertant colonies, compared to the negative control, were noted at any dose level, with or without metabolic activation. No precipitate formation was noted. The positive controls produced satisfactory responses, thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.
CONCLUSION	The notified polymer was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Laboratory 1 (2006)

B.6. Phototoxicity – skin (in vitro)

TEST SUBSTANCE	Notified polymer (10% v/v suspension).
METHOD	OECD TG 432 *in vitro* – 3T3 NRU Phototoxicity Test
Vehicle	1% v/v DMSO in HBSS.
Remarks - Method	No significant protocol deviations. GLP Compliance. Negative and positive (Chlorpromazine with the following concentration ranges: +UVA: 6.81–100 µg/mL; no UVA: 0.22–31.6 µg/mL) controls, with and without irradiation with artificial sunlight, were used in parallel

with the test substance.

A range finding experiment was conducted with the notified polymer at concentrations 0.000032–0.1%. Serial dilutions were made from the stock solution (100 µL) to prepare test concentrations with a 3.16 dilution factor. Slight phototoxicity was observed (EC_{50} value with no UV = 0.037%). The study authors noted that test article residue at the higher concentrations lead to interference during readings, masking some of the effects of the test article in both samples (+UVA and no UVA). Based on the results, the concentration range selected for the definitive test was 0.0022–0.032% (for both +UVA and no UVA).

MPE values were not determined in the study.

RESULTS

Test material	*EC_{50} Value (+ UV) [µg/mL]*	*EC_{50} Value (- UV) [µg/mL]*	*PIF*
Positive control	1.08	26.8	24.9
Test substance	> 0.032%	> 0.032%	1.0
Negative control	0.813	0.766	-

Remarks - Results

No dose dependent phototoxic response was observed after treatment of cells with the notified polymer in both the presence and absence of irradiation with artificial sunlight.

The controls gave responses within the expected range, confirming the validity of the test system.

CONCLUSION

According to the PIF model and classification criteria used, the notified polymer was not considered to have phototoxic potential on BALB/c 3T3 cells, under the test conditions.

TEST FACILITY

Laboratory 2 (2006)

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