File No: LTD/1802

March 2015

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

PEG/PPG/Polybutylene Glycol- 8/5/3 Glycerin

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/1802	L'Oreal Australia Pty Ltd	PEG/PPG/Polybutylene Glycol-8/5/3 Glycerin	ND*	1 tonne per annum	Ingredient in cosmetics

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified polymer is not recommended for hazard classification according to the *Globally Harmonised System for the 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 the PEC/PNEC ratio and the assessed use pattern, the notified chemical is not expected 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 safe work practices to minimise occupational exposure during reformulation of the notified polymer :
  - Avoid skin and eye 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 during reformulation:
  - Safety glasses
  - Gloves
  - Coveralls

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

- 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 for the 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 available or appropriate, dispose of the notified chemical 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 chemical 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 is intended to exceed 5% in leave-on cosmetic products or 10% in rinse-off cosmetic products

or

(2) Under Section 64(2) of the Act; if
- the function or use of the polymer has changed from ingredient in cosmetics 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 one 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)
L'Oreal Australia Pty Ltd (ABN: 40004191673)
564 St Kilda Road, Melbourne VIC 3004

NOTIFICATION CATEGORY
Limited-small volume: Synthetic polymer with Mn < 1,000 Da (1 tonne or less per year).

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Boiling point, Vapour pressure, Water Solubility, Hydrolysis as a function of pH, Partition coefficient, Absorption/desorption, Dissociation constant, Particle size, Flammability, Auto ignition temperature, Explosive properties, Oxidising properties, Reactivity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
China

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
PEG/PPG/Polybutylene Glycol- 8/5/3 Glycerin (INCI name)

MOLECULAR WEIGHT
< 1000 Da.

3. COMPOSITION

DEGREE OF PURITY
>90%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
All hazardous impurities (and residual monomers) are present at below the relevant cut offs for classification of the notified chemical (polymer) as a hazardous substance

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa:
Colourless to pale yellow transparent viscous liquid with slight specific odour

Property	**Value** *[or 'not determined']*	**Data Source/Justification**
Melting Point/Freezing Point	< 0°C	SDS
Boiling Point	No boiling point determined as the notified chemical decomposes before boiling	SDS
Density	Approximately 1040 kg/m^3	SDS

Vapour Pressure	Not determined.	Expected to be low, based on average molecular weight.
Water Solubility	25.47 g/L at 25°C	SDS QSAR (2014) Calculated (WSKOW v1.42)
Hydrolysis as a Function of pH	Not determined.	Not expected as the notified chemical does not contain readily hydrolysable functionalities.
Partition Coefficient (n-octanol/water)	Log K_{ow} = -1.82 at 25°C	QSAR (2014) Calculated (KOWWIN v1.68)
Adsorption/Desorption	Log K_{oc} = -1.539 at 25 °C	QSAR (2014) Calculated (KOCWIM v2.00).
Dissociation Constant	Not determined	No dissociable functionality
Particle Size	Not determined	The notified polymer is a liquid at room temperature.
Flash Point	246°C at 101 kPa	SDS (Cleveland Open Cup method).
Flammability limits	Not determined.	-
Autoignition Temperature	Not determined.	Expected to be high, based on flash point.
Explosive Properties	Not determined	Not expected to have explosive properties, based on structure.
Oxidising Properties	Not determined	Not expected to have oxidising properties, based on structure

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 for the 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 a component of finished cosmetic products at up to 10%. It may also be imported as the chemical itself, for formulation in Australia into cosmetic products.

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

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

PORT OF ENTRY
Melbourne or Sydney.

TRANSPORTATION AND PACKAGING
Products containing the notified polymer in packages up to 500 mL are generally shipped to Australia by sea in containers. The products are packed in dozens inside a shipper, with multiple shippers per pallet and multiple pallets per container. The containers are taken from the wharf in Melbourne or Sydney and transported by road to the appropriate central distribution centres. They are then picked into individual orders for delivery to the warehouses of major retailers. The containers may be bottles or tubes made mainly from high density polyethylene (HDPE). Where the notified polymer is imported for reformulation in Australia, it will be

transported to the reformulation sites in 18 kg drums. The cosmetic products manufactured will then be packaged and distributed as above.

USE
The notified polymer will be used in leave-on cosmetic products at up to 5% and rinse-off products at up to 10%.

OPERATION DESCRIPTION
Where the notified polymer will be imported in finished cosmetic products, the products will be stored at the notifier's warehouse in Melbourne or Sydney, before being distributed to warehouses and shops for retail sale to consumers.

The notified polymer may also be imported as the polymer itself, and in this case the formulation process will take place in Australia. At the reformulation sites, production compounders will weigh an appropriate amount of the raw material into a separate container then add the amount directly into a flame proof mixing tank with other ingredients. Mixing and dispensing will be carried out in a closed system with flame proof mixers and pumps designed not to create aerosols or a dust hazard and earthed for static discharges. Quantities of the cosmetic products containing the notified chemical will be sampled and tested by a chemist for quality control purposes. They will then be distributed for retail sale.

Products containing the notified chemical (up to 10%) may also be used in professions where the services involve the application of cosmetic products to clients (e.g. hairdressing or beauty salons).

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
Professional compounder	8	12
Chemist	3	12
Packers (Dispensing & Capping)	8	12
Store Persons	4	12
Salon workers	8	365

Exposure Details
Transport and storage
Transport and storage workers may come into contact with the notified polymer, as a component of the imported products or end-use products, only in the event of an accidental rupture of containers.
Reformulation
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified polymer (at 100% or up to 10% concentration) may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. Mixing and dispensing is expected to carried out in a closed system with flame proof mixers and pumps designed not to create aerosols or a dust hazard and earthed with static discharges. Exposure is expected to be minimised through the use of adequate ventilation, exhausted hoods, and through the use of personal protective equipment (PPE) such as safety glasses with side shields, Goggles, face shields, appropriate respirators (in case of inadequate ventilation), gloves, apron or coverall (also full face protection if potential exists for direct exposure to aerosols or splashes).
End use
Exposure to the notified chemical in end-use products (at up to 10% concentration) may occur in professions where the services provided involve the application of cosmetic and personal care products to clients (e.g. hair dressers, workers in beauty salons). Application of products could be by hand or through the use of an applicator. The principal route of exposure will be dermal, while ocular exposure is also possible. Inhalation exposure is not expected. Such professionals may use some 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 chemical.

6.1.2. Public Exposure

Public exposure to the notified polymer is expected to be widespread and frequent through daily use of personal care products containing the notified polymer at concentrations up to 5% in leave-on products and up to 10% in rinse-off products. The principal route of exposure will be dermal, while ocular exposure is also possible. As the notified polymer is not proposed to be used in spray products, inhalation exposure is not anticipated.

For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. An adult bodyweight of 60 kg was used for calculation purposes. Dermal absorption was conservatively assumed to be 100%, in the absence of data for the notified polymer.

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products that contain the notified polymer. This would result in a combined internal dose of 13.129 mg/kg bw/day. Specific use details of the notified polymer are considered as exempt information.

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 A.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2500 mg/kg bw; low toxicity
Rabbit, skin irritation	Non-irritating
Rabbit, skin irritation (Cumulative)	Non-irritating
Rabbit, eye irritation	Non-irritating
Guinea pig, skin sensitisation – Maximisation test	No evidence of sensitisation
Human, skin irritation	Non-irritating
Mutagenicity–bacterial reverse mutation Assay	Non mutagenic
Genotoxicity – in vitro – Chromosome Aberration	Non clastogenetic

No information on the toxicokinetics of the notified polymer was provided. However, data on analogous compounds are available from the safety assessments of the Polyethylene Glycols (PEGs) (CIR, 2010) and Polypropylene Glycols (PPGs) (CIR, 2005, 2012). Animal studies using PPGs with average molecular weights of 425-2025 indicated that PPGs are readily absorbed from the GI tract and excreted in the urine and feces. It is noted that there is potential for some PPG derivatives to enhance the dermal penetration of other molecules, however no information is available on the notified polymer. Dermal absorption for both PEG and PPG derivatives is expected to be enhanced where skin is damaged.

No percutaneous absorption data is available for the notified polymer or its analogues. Estimated properties (i.e., averaging molecular weight < 1000 Da, expected to contain a proportion of low molecular weight species, and modelled log Kow of -1.82), suggest that the notified polymer has limited dermal penetration potential; however, in the absence of measured data the extend of dermal absorption is uncertain.

Acute toxicity

The notified polymer was of low acute oral toxicity in a study conducted via the oral route in rats to OECD guidelines (Calculated LD50 >2500 mg/kg bw).

No acute dermal or inhalation toxicity data were provided for the notified polymer. The results in a dermal irritation study in rabbits indicate that the notified polymer is not acutely toxic via the dermal route.

Irritation and sensitisation

The notified polymer was non-irritating to the rabbit eye in a study similar to OECD TG405. It was non-irritating to the skin after single and multiple applications in rabbits. A single application patch test in humans (45 volunteers) did not show any signs of irritation.

The notified polymer was not sensitising in a guinea pig Maximisation test.

Repeated dose toxicity
Repeated dose toxicity information on the notified polymer was not provided. A study on PEG8, that contains some of the same components as the notified polymer was cited in CIR (2010). The NOEL from the 13 week gavage treatment in Fischer-344 rats was 1.1g/kg/ day, based on renal toxicity.

Mutagenicity/Genotoxicity
The notified polymer was negative in an *in vitro* bacterial reverse mutation study, and in an *in vitro* chromosome aberration test using Chinese hamster lung fibroblasts.

Health hazard classification

Based on the available information, the notified polymer is not recommended for classification according to the *Globally Harmonised System for the 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

Reformulation
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified polymer (up to 100%) may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. Based on available information, the potential for skin and eye irritation is low. The notifier has stated that enclosed, automated processes and PPE (impervious gloves, goggles, coveralls and respiratory protection, if significant inhalation exposure is expected) will be used, which is expected minimise the potential for exposure.
In the scenarios described, the risk to workers from use of the notified polymer is not considered to be unreasonable.

End-use
Workers involved in professions where the services provided involve the application of cosmetic products containing the notified polymer to clients (e.g., hairdressers and beauty salon workers) may be exposed to the notified polymer. The risk to these workers is expected to be of a 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

Members of the public will experience widespread and frequent exposure to the notified chemical through daily use of leave-on cosmetic products at up to 5% concentrations and rinse-off cosmetic products at up to 10% concentration.

The potential systemic exposure to the public from the use of the notified polymer in cosmetic products was estimated to be 13.129 mg/kg bw/day. Using a NO(A)EL of 1100 mg/kg bw/day, which was derived from a repeated dose toxicity study on an analogue polymer, the margin of exposure (MOE) was estimated to be 83.78. A MOE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences. However, it is acknowledged that the calculations are conservative, given the assumption of 100% dermal absorption for the notified polymer. Furthermore, the assumption that an adult consumer will use daily a large number of cosmetics containing the notified chemical at up to 10% concentration, is conservative, and likely to overestimate exposure under realistic use scenarios. Therefore, the MOE is considered to be acceptable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified polymer will be imported as a component of finished cosmetic products or as a raw material for local reformulation. Accidental spills during transport or reformulation are expected to be collected with inert material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified polymer is a component in rinse-off and leave-on cosmetic products. Therefore, it is expected that the majority of the imported quantity of notified polymer will be released to sewer.

RELEASE OF CHEMICAL FROM DISPOSAL

As the notified polymer is used in cosmetics it is expected that the majority of the annual import volume will be released to the sewer through consumer use. A small proportion (estimated to be ≤3%) may remain as residues within end use containers. It is expected that end use containers containing residues of the notified polymer will either be recycled or disposed of as domestic garbage and end up in landfill sites.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified chemical is expected to enter the sewer system before potential release to surface waters on a nationwide basis. Biodegradability, persistence and bioaccumulation were estimated using QSAR (2014) Biowin (Ultimate) data. The notified chemical is not readily biodegradable and, based on its calculated adsorption coefficient (log Koc = -1.53), partial partitioning to sludge is expected. In surface waters, the notified chemical is expected to disperse and degrade through biotic and abiotic processes to form water and oxides of carbon.

Based on the calculated bioconcentration factor of 0.87 L/kg and Log Pow (-1.82) the notified polymer is neither persistent nor bioaccumulative. The QSAR data indicates that the notified polymer may be persistent in sediment with a calculated half-life of 18 months. In air the notified polymer is not persistent with calculated atmospheric half-life of less than a day. Therefore, the notified polymer does not have the potential to be transported in the atmosphere and not expected to persist in the air compartment.

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 uses in cosmetic products, it is conservatively assumed that 100% of the notified chemical will be released to sewer on a nationwide basis over 365 days per year. It is also assumed that under a worst-case scenario that there is no removal of the notified chemical during STP processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
PEC - River:	0.61	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and

accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.61 µg/L may potentially result in a soil concentration of approximately 4.04 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 20.2 µg/kg and 40.4 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity measured data is available. However, ecotoxicity effects of the notified chemical have been modelled using QSAR (2014).

Endpoint	Result	Assessment Conclusion
Acute Toxicity		
Fish	96 h LC50 > 100 mg/L	Not harmful to fish
Daphnia	48 h EC50 > 100 mg/L	Not harmful to aquatic invertebrates
Algal	96 h EC50 > 100 mg/L	Not harmful to alga

Based on the above endpoints, the notified chemical is not considered to be harmful to aquatic organisms. Based on the toxicity to aquatic biota the notified chemical is not classified under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) on acute and chronic bases.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) was calculated for the notified chemical using the common lower limit of the endpoint (100 mg/L) for fish, alga and *Daphnia*. A safety factor of 100 is used since ecotoxicity data for three trophical levels of aquatic organisms are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LL50/EL50/E_rC50	> 100	mg/L
Assessment Factor	100	
PNEC:	>1,000	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	0.61	> 1000	< 0.001
Q - Ocean:	0.06	> 1000	< 0.0001

The risk quotient (Q = PEC/PNEC) for discharge of effluents containing the notified chemical to the aquatic environment, assuming a worst case with no removal during sewage treatment plant (STP) processes, indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters based on its maximum annual use quantity. The risk quotient, Q was calculated to be < 0.001. The notified chemical has a low potential for bioaccumulation and is not expected be persistent in the environment. Therefore, on the basis of the PEC/PNEC ratio, maximum annual use volume and assessed use pattern, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified Polymer
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat - Sprague-Dawley CD strain
Vehicle	None
Remarks - Method	Treatment of the animals in groups was sequential. Dosing was by gavage. The animals were observed for deaths or overt signs of toxicity ½, 1, 2 and 4 hours after dosing and subsequently once daily for fourteen days. At the end of the observation period, the animals were killed by cervical dislocation and all animals were also subjected to gross pathological examination.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3, female	2000	None
2	3, female	2000	None

LD50	Estimated >2500 mg/kg bw
Signs of Toxicity	No evidence
Effects in Organs	No effect
Remarks - Results	No deaths or signs of systemic toxicity were seen. All animals showed expected gains in the bodyweight over the study period and no abnormalities were noted at necroscopy.
CONCLUSION	The notified polymer is not toxic via the oral route.
TEST FACILITY	Safe Pharm (2004a)

B.2. Irritation-skin (translation)

TEST SUBSTANCE	Notified polymer
METHOD	In-house method.
Species/Strain	Japanese white rabbit; conventional, female
Number of Animals	Three
Vehicle	Water (for the diluted samples)
Observation Period	48 h
Type of Dressing	Occlusive.
Remarks - Method	It was stated that the method was according to OECD TG404; however the exposure period in this test was longer (24 h instead of 4 h in TG404). Three rabbits were used in a 24 hours closed patch test on abraded and non-abraded skin. 0.5 ml test article solution (100%, 50%, 25%, 10%) was applied via an impregnated dossil. Administration sites were rotated. Observations were made 3, 24 and 48 h after patch removal.

RESULTS

No dermal reaction was seen at any concentration of the notified polymer, at any of the observations.

CONCLUSION	The notified polymer was non-irritating under the conditions of the test.
TEST FACILITY	DST (2004d)

B.3. Irritation – skin (cumulative) (translation)

TEST SUBSTANCE	Notified polymer
METHOD	In-house method
Species/Strain	Japanese white rabbit; conventional, female
Number of Animals	Three
Vehicle	Water (for the diluted samples)
Observation Period	14 days
Type of Dressing	Not stated
Remarks - Method	0.5 ml test article solution (100%, 50%, 25%, 10%) was applied to the skin by teflon stick like drawing circle 8 times. Each administration site was individually examined and scored 24 h later. Each animal was dosed once a day for 2 weeks, i.e., 14 times. In order to average the specific reaction by application site, it was changed animal by animal. The exact protocol is not clear from the description.

RESULTS

No dermal reaction was seen at any tested concentration of the notified polymer solution during the test period.

CONCLUSION	The notified polymer was non-irritating after cumulative exposure under the conditions of the test.
TEST FACILITY	DST (2004a)

B.4. Irritation – eye (translation)

TEST SUBSTANCE	Notified polymer
METHOD	Similar to OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Japanese white rabbit; conventional, female
Number of Animals	Three
Observation Period	72 h
Remarks - Method	0.1 ml test liquid was applied to the right eye.

RESULTS

No reaction to the cornea, iris or conjunctiva was observed during the observations at 1, 3, 6, 24, 48 and 72 hours after the dosing

CONCLUSION	The notified polymer was non-irritating to the eye under the conditions of the test.
TEST FACILITY	DST (2004c)

B.5. Skin sensitization (translation)

TEST SUBSTANCE	Notified polymer	
METHOD	Similar to OECD TG 406 Skin Sensitisation - <Guinea Pig Maximisation Test (GPMT)>.	
Species/Strain	Guinea pig/Hartley White, Clean.	
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 0.3% topical: 100%	
MAIN STUDY		
Number of Animals	Test Group: 10 F	Control Group: 5F
INDUCTION PHASE	Induction Concentration: intradermal: 10% topical: 100%	
Signs of Irritation	None after topical application	
CHALLENGE PHASE		

1st challenge	intradermal: none topical: 100, 50, 25, 10%
2nd challenge	topical: None
Remarks - Method	24 h prior to the topical challenge, 10% sodium lauryl sulphate in vaseline was applied to the skin, as the test article itself was non irritating.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	100	0	0	N/A	N/A
		0	0	N/A	N/A
Control Group	0	0	0	N/A	N/A
		0	0	N/A	N/A

Remarks - Results

CONCLUSION There was no evidence of reactions indicative of skin sensitisation to the notified polymer under the conditions of the test.

TEST FACILITY DST (2004b)

B.6. Skin irritation- human volunteers (translation)

TEST SUBSTANCE Notified polymer

METHOD Single application patch test

Study Design The test substance (0.01 g) was placed on a Finn Chamber (Epitest)) and patched to the inner side of forearm of each volunteer for 24 hours under occlusive conditions.
At the end of 24 hours exposure period, the test sample was removed, and skin reactions were evaluated after 1 hour later and 24 hours later.

Study Group 45 volunteers, 21 MF, 24 M; age range 22-56

Vehicle None

Remarks - Method

RESULTS

Remarks - Results 45 volunteers completed the study. In all volunteers, no reaction was observed 24 h or 48 h after removing the test samples, similarly, no reaction was observed in 48 hours after removing the test samples.

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

TEST FACILITY Japan Hair Science Association (2004)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
Plate incorporation method

Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100,
E. coli: WP2uvrA

Metabolic Activation System Rat liver homogenate metabolising system, from rats induced with phenobarbitone/β-naphthoflavone.

Concentration Range in Main Test 50, 150, 500, 1500 and 5000 µg/plate (With/without metabolic activation)

Vehicle	Sterile distilled water
Remarks - Method	A preliminary toxicity test (0, 0.15, 0.5, 1.5, 5, 15, 50, 150, 500, 1500 and 5000 µg/plate) was performed to determine the toxicity of the test material. *Salmonella a*nd *E. coli* strains were treated with the test material using the Ames plate incorporation method at five dose levels, in triplicate, both with and without the addition of a rat liver homogenate metabolising system. The dose range was determined using a preliminary toxicity assay (TA100 and WP2uvrA$^-$only). The plates were incubated for 48 hours. The experiment was repeated on a separate day using the same dose range, fresh cultures of the bacterial strains and fresh test materials. Vehicle and positive controls were used in parallel with the test material.

RESULTS

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

Remarks - Results	In the preliminary toxicity study, the test material was non-toxic to the TA100/WP2uvrA$^-$ strain at 5000 µg/plate, with and without metabolic activation. In the mutation studies, the test material caused no visible reduction in the growth of the bacterial background lawn at any given dose level. The test material was tested up to the maximum recommended dose level of 5000µg/plate. No test material precipitate was observed on the plates at any of the doses tested in either the presence or absence of S9-mix. No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test material, either with or without metabolic activation. The positive controls gave satisfactory responses, confirming the validity of the test system.
CONCLUSION	The notified polymer was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Safe Pharm (2004b)

B.8. Genotoxicity – in vitro- Chromosomal Aberration test (translation)

TEST SUBSTANCE	Notified polymer
METHOD	Similar to OECD TG 473, the tests were performed in accordance with "Guidelines for genotoxicity testing of pharmaceuticals" (Pharmaceutical affairs council notification No. 1604, November 1, 1999).
Cell Type/Cell Line	Chinese hamster lung fibroblast cell line (CHL/IU cells)
Vehicle	Physiological saline (55 mg/ml)
Concentration Range	1. 0.010, 0.020, 0.039, 0.078, 0.156, 0.313, 0.625, 1.250, 2.500 and 5.000 mg/ml: Cell growth inhibition test 2. 1.250, 2.500, 5.000 mg/ml: Chromosomal abnormality test, continuous treatment method, 24 hours and 48 hours (- S9 mix) 3. 1.250, 2.500, 5.000 mg/ml: Chromosomal abnormality test, short time treatment method (- S9 mix and +S9 mix methods)

Remarks - Method	S9 mix was induced with phenobarbital and 5,6-benzoflavone. Physiological saline was used as the negative control. Positive controls used were as follows: Mitomycin C (MMC): Short-time and continuous treatment without S9 mix., N-nitrosodimethylamine (DMN), Short-time treatment with S9 mix.

RESULTS

Remarks - Results	Full results were not presented in the translation - tables were not provided. Results of the short time treatment method tests indicate that for both in the presence and absence of S9, the occurrence frequency of cells with chromosomal structural abnormality and occurrence frequency of polyploid cells were both less than 5% at any test dose. Results of continuous treatment method tests (presumed to be carried out in the absence of S9) indicate that for both 24 h and 48 h methods, the occurrence frequency of cells with chromosomal structural abnormality and occurrence frequency of polyploid cells were less than 5% at any test dose. From the above results it is concluded that this test material has no clastogenic effect on CHL/IU cells. The positive controls gave satisfactory responses, confirming the validity of the test system.
CONCLUSION	The notified polymer was not clastogenic to CHL/IU cells treated in vitro under the conditions of the test.
TEST FACILITY	DST (General Laboratory, BML Inc) (2006)

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