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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Gelatins, reaction products with glutaraldehyde

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.

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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/2092	Unilever Australia Trading Ltd and Unilever Asia Private Limited	Gelatins, reaction products with glutaraldehyde	ND*	≤ 1 tonne per annum	Cosmetic ingredient

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the limited available information, the notified polymer cannot be classified using 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.

Based on the available information, when used at ≤ 1% concentration in cosmetic products, the notified polymer is not considered to pose an unreasonable risk to public health.

Environmental Risk Assessment
On the basis of its assumed low hazard and reported use pattern, 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, automated processes, where possible
  - Adequate local exhaust ventilation

- 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 during reformulation:
  - Avoid contact with skin and eyes
  - Avoid inhalation of dusts

- 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:
  - Coveralls
  - Impervious gloves
  - Eye protection
  - Respiratory protection, if inhalation exposure may occur

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.

Emergency procedures

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

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.

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;
- the concentration of the notified polymer exceeds, or is intended to exceed, 1% in cosmetic products;

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.

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)
Unilever Australia Trading Ltd (ABN: 65 136 885 651)
219 North Rocks Road
NORTH ROCKS NSW 2151

Unilever Asia Private Limited (ABN 29 142 738 538)
Level 17, 2 Park Street
SYDNEY NSW 2000

NOTIFICATION CATEGORY
Limited-small volume: Biopolymer (1 tonne or less per year)

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details exempt from publication include: marketing name, structural formulae, molecular weight, analytical data, degree of purity, polymer constituents, residual monomers, impurities, additives/adjuvants and identity of manufacturer.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Schedule data requirements are varied for all physico-chemical endpoints.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA (2019)

2. IDENTITY OF CHEMICAL

CAS NUMBER
68410-46-8

CHEMICAL NAME
Gelatins, reaction products with glutaraldehyde

OTHER NAME
Gelatin Crosspolymer (INCI name)

MOLECULAR FORMULA
$(C_5H_8O_2.\text{Unspecified})_x$

MOLECULAR WEIGHT
Number average molecular weight (Mn) is > 10,000 g/mol.

ANALYTICAL DATA
Reference IR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
Nominally > 95%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: solid

Property	*Value*	*Data Source/Justification*
Melting Point/Freezing Point	Not determined	Not expected to melt/freeze under normal use conditions
Boiling Point	Not determined	Expected to be high based on the high molecular weight
Density	Not determined	Expected to be denser than water based on the polymer structure
Vapour Pressure	Not determined	Expected to be low based on the high molecular weight
Water Solubility	Not determined	Insoluble. The notified polymer is a high molecular weight gelatinous cross-linked polymer.
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionality but is expected to be stable within the environmental pH 4-9
Partition Coefficient (n-octanol/water)	Not determined	The notified polymer is insoluble in water.
Adsorption/Desorption	Not determined	Not expected to be mobile in soil or sewage sludge
Dissociation Constant	Not determined	Does not contain dissociable functionality
Particle Size*	0.55%: < 10 µm < 10%: 24.37 µm < 25%: 34.91 µm < 50%: 46.43 µm < 75%: 57.34 µm < 90%: 67.23 µm Mean: 46.16 µm Medium: 46.43 µm	Measured
Flash Point	Not determined	Expected to be high based on the polymer structure
Autoignition Temperature	Not determined	Not expected to auto-ignite based on the polymer structure
Explosive Properties	Not determined	Contains no functional groups that imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that imply oxidising properties

* Property of the imported solid product containing the notified polymer.

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 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 either in a formulation at < 15% concentration for reformulation into cosmetic products or in finished cosmetic products at ≤ 1% concentration.

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

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

PORT OF ENTRY
Sydney and Melbourne

TRANSPORTATION AND PACKAGING
The products containing the notified polymer will be transported primarily by road to cosmetic blenders in bulk packaging or to retail stores in packages suitable for retail sale.

USE
The notified polymer will be used in leave-on and rinse-off cosmetic products (including aerosols) at ≤ 1% concentration.

OPERATION DESCRIPTION
The notified polymer will be imported in a formulation at < 15% concentration for reformulation into cosmetic products.

Reformulation
When reformulated, the notified polymer will be blended into end-use cosmetic products at customer sites. Procedures will vary depending on the nature of the consumer product being formulated. Both manual and automated steps will likely be involved. For example, a chemist will sample and test the notified polymer for QA purposes manually; a compounder will weigh an appropriate amount of the formulation containing the notified polymer into a container and then add the amount directly into a mixing tank, with periodic sampling for quality control purposes also carried out during the reformulation process. Automated processes may include mixing and filling of end-use containers with finished products.

End-use
Finished cosmetic products containing the notified polymer at ≤ 1% concentration will be used by the public and may also be used by professionals such as hairdressers and workers in beauty salons. Depending on the nature of the product, these could be applied by hand or by using an applicator (including spray applicator).

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, warehouse and retail workers	4	12
Compounding	8	12
Quality control	3	12
Packaging	8	12
Professional users – (e.g. hairdressers and beauty salon workers)	Unspecified	Unspecified

EXPOSURE DETAILS

Transport and storage
Transport and storage workers may come in contact with the notified polymer either at < 15% concentration in imported products or at ≤ 1% concentration in consumer products, only in the event of an unlikely accidental rupture of containers.

Reformulation
During reformulation into consumer products, dermal, ocular and inhalation exposure of workers to the notified polymer at < 15% concentration may occur. Exposure is expected to be minimised through the use of exhaust ventilation and/or automated/enclosed systems as well as through the use of personal protective equipment (PPE) such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate).

End use
Exposure to the notified polymer in end-use products at ≤ 1% concentration may occur in professions where the services provided involve the application of cosmetic products for clients (e.g. hair dressers and 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 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

Although there will be widespread and repeated contact of the public with the notified polymer through the use of a variety of cosmetic products, systemic exposure is expected to be limited given the high molecular weight of the notified polymer (> 50,000 g/mol with estimated 0% low molecular species of < 1,000 g/mol).

6.2. Human Health Effects Assessment

No toxicity studies were submitted for the notified polymer. The results from a key event assay in the Adverse Outcome Pathway (AOP) for skin sensitisation conducted on cosmetic beads containing < 15% notified polymer are summarised in the following table. For full details of the study, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Skin sensitisation – *in vitro* ARE-Nrf2 luciferase test	negative

The primary monomer used in the synthesis of the notified polymer is gelatin (CAS name gelatins, CAS No. 9000-70-8 (generic)) which is hydrolysed from the protein collagen, which is the major structural protein in both vertebrates and invertebrates (Liu *et al*., 2015). Gelatin is a common ingredient in food and is also used in pharmaceuticals and therapeutic treatments (Haug and Draget, 2011). Gelatin is a Generally Recognised as Safe (GRAS) food ingredient (type 1 conclusion) and is therefore not expected to contribute to systemic toxicity (NTRL; US FDA). In randomised controlled six month long trials in humans oral doses up to 10 g/day of collagen hydrolysate were considered to be "safe and well tolerated" (Benito-Ruiz *et al*., 2009). Additionally in a range of animals studies via the oral and dermal routes using either collagen or gelatin there were no adverse findings related to the test materials (CIR, 2017).

Human health effects of the minor monomer pentanedial (CAS No. 111-30-8) were not used to estimate the toxicity of the notified polymer as the aldehyde groups on the pentanedial will react to form imine bonds when cross linking with the gelatin and subsequently the notified polymer will have a significantly lower potential for reactivity than the pentanedial monomer. Additionally the vastly different molecular weight of the polymer vs pentanedial mean that the potential for systemic exposure is also expected to be different with very low dermal absorption predicted for the notified polymer as discussed below in the toxicokinetics section.

Toxicokinetics

No information on the toxicokinetics of the notified polymer was provided. For dermal absorption, molecular weights below 500 g/mol are favourable for absorption and molecular weights above 1,000 g/mol do not favour absorption (ECHA, 2017). Based on the high molecular weight of the notified polymer (> 10,000 g/mol with estimated 0% low molecular species of < 1000 g/mol or < 500 g/mol), dermal absorption is expected to be limited. Gelatin has been reported as having a high oral bioavailability (CIR, 2017).

Irritation

No information was submitted on skin and eye irritation of the notified polymer.

Sensitisation

No skin sensitisation data were submitted on the notified polymer. One *in vitro* cell based assay (ARE-Nrf2 Luciferase Assay) conducted on cosmetic beads containing < 15% notified polymer was provided (OECD TG 442d). This assay is part of an Integrated Approach to Testing and Assessment (IATA) which addresses specific key events of the Adverse Outcome Pathway (AOP) leading to development of skin sensitisation (OECD, 2012).

The ARE-Nrf2 Luciferase Assay aims to address the second key event (KE) assay (keratinocyte activation) of the AOP by measuring the expression of a report luciferase gene under the control of a promoter from the antioxidant response element (ARE), a responding gene known to be upregulated by contact sensitisers. The notified polymer showed negative responses in the ARE-Nrf2 luciferase assay. However, this result needs to be considered in combination with other two KE assays of the AOP for skin sensitisation (*in chemico* Direct Peptide Reactivity Assay (DPRA) and *in vitro* h-CLAT assay) which were not conducted.

Hydrolysed collagen (30% solution in water; fish scale sourced; MW ~400 Da) was considered to be non-sensitising in a guinea pig maximization test and formulations containing 20% hydrolysed collagen produced no sensitization effects in a human repeated insult patch test (CIR 2017). Therefore, the notified polymer is not expected to be a sensitiser at least up to 30% concentration.

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

6.3. Human Health Risk Characterisation
Based on the available information, the notified polymer is expected to be of low systemic toxicity. Local effects such as skin and eye irritation are not expected at low end-use concentrations (≤ 1%).

Give the high molecular weight of the notified polymer, systemic exposure from dermal absorption is expected to be limited. As the notified polymer has a major component derived from hydrolysed collagen and based on the available information on hydrolysed collagen, skin sensitisation is not expected for the notified polymer at concentrations of ≤ 1%. Inhalation of the notified polymer is not expected, unless it is aerosolised, given its estimated low vapour pressure.

6.3.1. Occupational Health and Safety

Reformulation
During reformulation, dermal, ocular and inhalation exposure of workers to the notified polymer at < 15% concentration may occur. It is stated by the notifier that engineering controls such as enclosed and automated processes and local ventilation will be implemented where possible, and appropriate PPE (coveralls, imperious gloves, eye protection and respiratory protection) will be used to limit worker exposure.

Therefore, under the occupational settings described, the risk to the health of 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, beauty salon workers) may be exposed to the notified polymer at concentrations up to 1%. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, the risk to such workers is expected to be of a similar or lesser extent than that experienced by consumers using the various products containing the notified polymer.

6.3.2. Public Health
Cosmetic products containing the notified chemical at ≤ 1% concentration will be available to the public. The main route of exposure is expected to be dermal and inhalation (if aerosol products are used), with some potential for accidental ocular or oral exposure.

The notified polymer is expected to be of low systemic toxicity, due to expected low dermal absorption. The low use concentration of ≤ 1% will further reduce the potential for systemic exposure and any local effects such as skin and eye irritation.

Therefore, based on the information available, the risk to the public associated with use of the notified polymer at ≤ 1% concentration in cosmetic 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 made in Australia. The notified polymer will be either imported as a raw material and blended into finished cosmetic products or imported in finished cosmetic products. Accidental spills of the notified polymer during import, transport or storage are expected to be adsorbed onto a suitable material and collected for disposal in accordance with local 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 notifier estimates that ≤1% of the notified polymer may remain as residues in raw material containers. Other wastes containing the notified polymer generated during reformulation such as equipment wash water and spilt material are also expected to be disposed of in accordance with local regulations, including to sewer via trade waste.

RELEASE OF CHEMICAL FROM USE

It is expected that the majority of the annual import volume of the notified polymer will be released to sewer across Australia as a result of consumer use in leave-on rinse-off cosmetic products. A small proportion of the notified polymer is expected to remain as residues in empty end-use containers and be disposed of to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

The notifier estimates that a small proportion (approximately ≤3%) of the notified polymer may remain as residues within end use containers. These containers are expected to be recycled or disposed of to landfill, with the notified polymer being disposed of to sewer via trade waste or disposed of to landfill.

7.1.2. Environmental Fate

A biodegradability study on the notified polymer as part of the final product indicated that it was considered to be readily biodegradable (63% biodegradation after 14 days). Details of the study is summarised in Appendix C. Following its use as an ingredient in cosmetic products, the majority of the notified polymer is expected to enter the sewer system before potential release to surface waters nationwide. In water, the notified polymer is highly insoluble and expected to be hydrolytically stable in environmental conditions, therefore the notified polymer is expected to partition to sludge and sediment. Also, based on the high molecular weight of the notified polymer, it is not expected to bioaccumulate.

Some of the notified polymer may remain as residues within end use containers and is expected to either be recycled or disposed of to landfill. 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. The notified polymer in landfill, soil and sludge is expected to eventually degrade by biotic and abiotic processes to form amino acids and ultimately water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

A predicted environmental concentration (PEC) worst case scenario has been calculated. It was assumed that 100% of the annual import quantity of the notified polymer is released to the sewer from its use in cosmetic products over 365 days/year, with no removal of the notified chemical by sewage treatment plant (STP) processes. The extent to which the notified chemical is removed from the effluent in STP processes based on the properties of the notified chemical has not been considered for the worst-case scenario:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1000	kg/year
Proportion expected to be released to sewer	100.0	%
Annual quantity of chemical released to sewer	1000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0	%
Daily effluent production:	4,877	ML
Dilution Factor – River	1.0	
Dilution Factor – Ocean	10.0	
PEC – River:	0.56	µg/L
PEC – Ocean:	0.06	µg/L

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. However, polymers without significant ionic functionality are generally of low concern to the environment. Therefore, the notified chemical is not formally classified under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) (United Nations, 2009) for acute and chronic toxicities.

7.2.1. Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) for the aquatic compartment has not been calculated as the notified polymer has not been tested on aquatic life or organisms.

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) for the aquatic compartment has not been calculated as a PNEC value is not available. However, the polymer is likely to be of low concern to the environment. The majority of the notified polymer is expected to enter the sewer system as a result of its use in cosmetics, but based on its low assumed hazard it's unlikely to reach ecotoxicologically significant concentrations. In water, the notified polymer is highly insoluble, stable and due to its extremely high molecular weight, it is not expected to cross biological membranes and therefore not expected to bioaccumulate. In soils and landfills, the notified polymer is expected to eventually degrade via biotic and abiotic processes to form amino acids, and ultimately water and oxides of carbon and nitrogen.

On the basis of its assumed low hazard and assessed use pattern as a cosmetic ingredient, the notified polymer is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Particle Size Mean: 46.16 µm; Medium: 46.43 µm

Method OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions

Range (µm)	*Mass (%)*
< 10	0.55
24.37	< 10
34.91	< 25
46.43	< 50
57.34	< 75
67.23	< 90

Remarks The test substance was cosmetic beads containing < 15% notified polymer.
Test Facility Manufacturer (2019a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Skin Sensitisation – *In Vitro* ARE-Nrf2 Luciferase Test

TEST SUBSTANCE	Cosmetic beads containing < 15% notified polymer
METHOD	OECD TG 442d *In Vitro* Skin Sensitisation Assays Addressing the AOP Key Event on Keratinocyte Activation (2015) - The ARE-Nrf2 luciferase KeratinoSens™ test method (Appendix IA)
Vehicle	Cell culture medium containing 4% dimethylsulfoxide (DMSO)
Remarks – Method	The test substance was not freely soluble in DMSO and this preferred solvent according the SOP could thus not be used. Test substance was therefore dissolved in cell culture medium containing 4% DMSO at a final concentration of 6.4 mg/L. This solution was further diluted 4-fold upon addition to the cells to reach the top concentration tested (1600 µg/ml in cell culture medium containing 1% DMSO). Positive control and negative control were cinnamic aldehyde and dimethylsulfoxide respectively.

RESULTS

Sample	*Mean EC 1.5*	*Mean IC50 (µg/mL)*	*Maximal Induction (I_{max})*
Test substance	> 1,600 µg/mL	291.2	1.16
Positive Control	19.17 µM	not provided	not provided

EC1.5 - concentration for an induction of luciferase activity 50% above vehicle control
IC50 - concentration leading to 50% cell viability compared to vehicle control

Remarks – Results	No induction of luciferase above the Imax threshold of 1.5 was observed for all 3 repetitions. The positive and vehicle controls were reported to have performed as expected.
CONCLUSION	The test substance was negative in the second key event (keratinocytes response) of the adverse outcome pathway (AOP) for skin sensitisation as defined in the test guideline.
TEST FACILITY	Manufacturer (2019b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready Biodegradability

TEST SUBSTANCE	Cosmetic beads containing < 15% notified polymer
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test
Inoculum	Activated Sludge
Exposure Period	28 Days
Auxiliary Solvent	None
Analytical Monitoring	Biological Oxygen Demand
Remarks – Method	The study was not performed in accordance with GLP. The test was conducted on a mixture that contained the notified polymer. The majority of the mixture contained a cosmetic ingredient that was known to not degrade under the conditions of the test so any resultant degradation could be attributed to the substance containing the notified polymer.

RESULTS

Test Substance		*Sodium Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	62	7	87
28	55	28	97

Remarks – Results	The activity of the inoculum material was verified with the degradation of the reference material exceeding 40% after 7 days and 65% after 14 days. The test substance reached a maximum of 63% biodegradation after 14 days but dropped to 55 % after 28 days. It was suggested that the drop in the biodegradation from day 23 was due to the high concentration of the main cosmetic material, leading to reduced intrinsic respiration after the substance which contained the notified polymer had degraded.
CONCLUSION	The test substance is readily biodegradable.
TEST FACILITY	Manufacturer (2010)

BIBLIOGRAPHY

Benito-Ruiz, P., Camacho-Zambrano, M.M., Carrillo-Arcentales, J.N., Mestanza-Peralta, M.A., Vallejo-Flores, C.A., Vargas-López, S.V., Villacís-Tamayo, R.A., and Zurita-Gavilanes, L.A. (2009) A randomized controlled trial on the efficacy and safety of a food ingredient, collagen hydrolysate, for improving joint comfort. International Journal of Food Sciences and Nutrition, 60(S2): 99-113. https://doi.org/10.1080/09637480802498820

CIR (2017) Safety Assessment of Skin and Connective Tissue-Derived Proteins and Peptides as Used in Cosmetics. Cosmetic Ingredient Review. https://www.cir-safety.org/sites/default/files/tsupep092017final.pdf

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

Haug, I.J., and Draget, K.I. (2011) Gelatin. Handbook of Food Proteins, Woodhead Publishing Series in Food Science, Technology and Nutrition, 92-115. https://doi.org/10.1533/9780857093639.92

IMAP (1994) Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for Glutaradehyde. National Industrial Chemicals Notification and Assessment Scheme (NICNAS).

Liu, D., Nikoo, M., Boran, G., Zhou, P., and Regenstein, J.M. (2015) Collagen and Gelatin. Annual Review of Food Science and Technology, 6:527-557. https://doi.org/10.1146/annurev-food-031414-111800

Manufacturer (2010) Ready biodegradability of [Cosmetic Beads Containing the Notified Polymer] (Study No. 10-E003/P, April, 2010) (Unpublished report submitted by the notifier).

Manufacturer (2019a) The Expert Statement on the Size Distribution of the [Cosmetic Beads Containing the Notified Polymer] (May, 2019) (Unpublished report submitted by the notifier).

Manufacturer (2019b) KeratinoSens™ Assay: Test Report on [Beads Containing the Notified Polymer] (Study No. RCR 153865, May, 2019) (Unpublished report submitted by the notifier).

National Technical Reports Library (NTRL), United Stated Department of Commerce, Evaluation of the Health Aspects of Gelatin as a Food Ingredient, 1975. Accession Number: PB254527. https://ntrl.ntis.gov/NTRL/dashboard/searchResults.xhtml?searchQuery=PB254527#

NICNAS (1994) Priority Existing Chemical No. 3, Glutaraldehyde, Full Public Report. https://www.nicnas.gov.au/__data/assets/word_doc/0005/34808/PEC3-glutaraldehyde.docx

OECD (2012) The Adverse Outcome Pathway for Skin Sensitisation Initiated by Covalent Binding to Proteins. Part 1: Scientific Evidence. Series on Testing and Assessment No. 168, OECD, Paris.

SIDS (1995) SIDS Assessment Report for Glutaradehyde, OECD SIDS, Paris, France.

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2019. https://www.legislation.gov.au/Details/F2019L00685

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

United States Food and Drug Administration (US FDA), Select Committee on GRAS Substances (SCOGS) Opinion: Gelatin, https://www.fda.gov/food/generally-recognized-safe-gras/gras-substances-scogs-database; http://wayback.archive-it.org/7993/20171031062708/https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm261307.htm.