File No: LTD/2021

July 2018

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Zinc, bis(5-oxo-L-prolinato-κN^1,κO^2)-, (*T*-4)- (INCI Name: Zinc PCA)

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

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2021	L'Oreal Australia Pty Ltd	Zinc, bis(5-oxo-L-prolinato-kN^1,kO^2)-, (*T*-4)- (INCI Name: Zinc PCA)	Yes	≤ 1 tonne per annum	Cosmetic ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Eye Irritation (category 2A)	H319 – Causes serious eye irritation

The environmental hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute (category 2)	H401 – Toxic to Aquatic life

Human health risk assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
On the basis of the PEC/PNEC ratio, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  – Eye Irritation (Category 2A): H319 – Causes serious eye irritation

  The above should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present.

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 handling of the notified chemical during reformulation:
  - Avoid contact with skin and eyes
  - Avoid inhaling 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 chemical during reformulation:
  - Protective goggles
  - Coveralls
  - Impervious gloves
  - Respirator for dust

  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 chemical 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.

- As the notified chemical is introduced as a powder for reformulation and it contains zinc, workplace exposure should be as low as reasonably practicable. Zinc oxide dust has an Australian exposure standard of 10 mg/m^3 time-weighted average (TWA) (SWA, 2018)

Disposal

- Where reuse or recycling are not 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 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 importation volume exceeds one tonne per annum notified chemical;

- the use concentration exceeds or is intended to exceed 4.9% in cosmetic products;

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a cosmetic ingredient, or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical 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 chemical and products containing the notified chemical provided by the notifier were 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
L'Oreal Australia Pty Ltd (ABN: 40 004 191 673)
564 St Kilda Road
MELBOURNE VIC 1145

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less per year)

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: specified other name, degree of purity, use details, identity of manufacturer, and identity of test facilities.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all physico-chemical properties, except for water solubility and flammability.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Zinc PCA

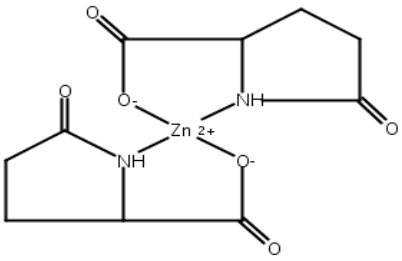
CAS NUMBER
15454-75-8

CHEMICAL NAME
Zinc, bis(5-oxo-L-prolinato-kN^1,kO^2)-, (*T*-4)-

OTHER NAMES
L-Proline, 5-oxo-, zinc complex
Zinc PCA (INCI Name)

MOLECULAR FORMULA
$C_{10}H_{12}N_2O_6Zn$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
321.4 g/mol

ANALYTICAL DATA
Reference IR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 97%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

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

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: White to cream powder

Property	Value	Data Source/Justification
Melting Point	> 300 °C	Measured (supplier communication)
Boiling Point	Expected to decompose before boiling	Estimated
Density	Not determined	-
Vapour Pressure	Not determined	Ionic solid
Water Solubility	168 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Expected to be hydrolytically stable under environmental conditions (pH 4-9, 25 °C)
Partition Coefficient (n-octanol/water)	Not determined	Expected to be low based on water solubility
Adsorption/Desorption	Not determined	The notified chemical is a salt and is expected to adsorb to soil, sediment or sludge, through metal ion exchange and chelation
Dissociation Constant	Not determined	The notified chemical is a salt that will dissociate under environmental conditions (pH 4-9).
Particle Size	Mean particle size > 300 µm	Measured
Flash Point	> 200 °C	Estimated
Flammability	Not flammable	Measured
Autoignition Temperature	Not determined	Not expected to autoignite
Explosive Properties	Not determined	Contain no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contain no functional groups that would imply oxidising properties

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

Reactivity
The notified chemical 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 chemical cannot be 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 chemical will not be manufactured in Australia. The notified chemical will be imported into Australia neat for reformulation into cosmetic products, or as a component of finished cosmetic products at ≤ 4.9% concentration. The notified chemical may also be imported in the future as a component of a premix at < 100% concentration for reformulation 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
Sydney and Melbourne

TRANSPORTATION AND PACKAGING
The notified chemical will be imported neat packed in 10 kg or 25 kg cardboard canisters with double bags. Finished cosmetic products containing the notified chemical at ≤ 4.9% concentration will be imported in containers suitable for retail sale.

Within Australia the neat notified chemical (in powder form) and premixes containing the notified chemical at < 100% concentration will be transported by road to the warehouse for storage and later distributed to industrial customers for reformulation into finished cosmetic products by road. Finished cosmetic products containing the notified chemical will be transported primarily by road to retail stores in packages suitable for retail sale.

USE
The notified chemical will be used as a cosmetic ingredient in a variety of products at a proposed usage concentration of ≤ 4.9%.

OPERATION DESCRIPTION
Reformulation
Reformulation of the neat notified chemical and premixes containing the notified chemical at < 100% concentration into finished cosmetic products may vary depending on the type of product, and may involve both automated and manual transfer steps. Typically, reformulation processes may incorporate blending operations that are highly automated and occur in a fully enclosed/contained environment, followed by automated filling of the reformulated cosmetic products into containers of various sizes.

End-use
Finished cosmetic products containing the notified chemical at ≤ 4.9% concentration will be used by consumers and professionals (such as beauticians and hairdressers). Depending on the nature of the product, application of the products could be by hand, sprayed or through the use of an 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 and storage	4	12
Compounders	8	12
Quality controller	3	12
Packers	8	12
Store persons	4	12
End-users	8	365

EXPOSURE DETAILS

Transport and storage

Transport and storage workers may come into contact with the notified chemical at ≤ 100% concentration, only in the unlikely event of accidental rupture of containers.

Reformulation

During reformulation, dermal, ocular and inhalation exposure of workers to the notified chemical at ≤ 100% concentration may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. The notifier stated that exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems, and through the use of personal protective equipment (PPE) such as protective clothing, eye protection, impervious gloves and respiratory protection.

End-use

Exposure to the notified chemical in end-use products (at ≤ 4.9% concentration) may occur in professions where the services provided involve the application of cosmetics to clients (e.g. hair dressers and workers in beauty salons). The principal route of exposure will be dermal, while ocular and inhalation exposure are also possible depending on the product type and application procedure. 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 the products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical at ≤ 4.9% concentration through the use of a wide range of leave-on and rinse-off cosmetic products. The main route of exposure will be dermal, while ocular and inhalation exposure are also possible, particularly if products are applied by spray.

Data on typical use patterns of product categories in which the notified chemical may be used are shown in the following tables (SCCS, 2010; Cadby et al., 2002; Loretz *et al.,* 2006). For the purposes of the exposure assessment, Australian use patterns for the various product categories are assumed to be similar to those in Europe. A dermal absorption (DA) rate of 100% was assumed for the notified chemical for calculation purposes. For the inhalation exposure assessment, a 2-zone approach was used (Steiling *et al*., 2014; Rothe *et al*., 2011; Earnest, Jr, 2009). An adult inhalation rate of 20 m^3/day (enHealth, 2012) was used and it was conservatively assumed that the fraction of the notified chemical inhaled is 50%. A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used for calculation purposes.

Cosmetic products (Dermal exposure):

Product type	Amount (mg/day)	C (%)	RF (unitless)	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	4.9	1	0.5987
Face cream	1540	4.9	1	0.1179
Hand cream	2160	4.9	1	0.1654
Fine fragrances	750	4.9	1	0.0574
Deodorant spray	1430	4.9	1	0.1148
Shampoo	10460	4.9	0.01	0.0080
Conditioner	3920	4.9	0.01	0.0030
Shower gel	18670	4.9	0.01	0.0143
Hand soap	20000	4.9	0.01	0.0153
Hair styling products	4000	4.9	0.1	0.0306
Total				**1.1255**

C = maximum intended concentration of notified chemical; RF = retention factor.
Daily systemic exposure = (Amount × C × RF × DA)/BW

Hairspray (Inhalation exposure):

Product type	Amount	C	Inhalation rate	Exposure duration zone 1	Exposure duration zone 2	Fraction inhaled	Volume zone 1	Volume zone 2	Daily systemic exposure
	(g/use)	(%)	(m^3/day)	(min)	(min)	(%)	(m^3)	(m^3)	(mg/kg bw/day)
Hairspray	20	4.9	20	1	20	50	1	10	**0.1578**

C = maximum intended concentration of notified chemical

Total daily systemic exposure = Daily systemic exposure in Zone 1 [(amount × C × inhalation rate × exposure duration (zone 1) × fraction inhaled)/(volume (zone 1) × body weight)] + Daily systemic exposure in Zone 2 [(amount × C × inhalation rate × exposure duration (zone 2) × fraction inhaled)/(volume (zone 2) × body weight)]

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical at the maximum intended concentration specified by the notifier in various product types. This would result in a combined internal dose of 1.2833 mg/kg bw/day for the notified chemical. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic (in addition to hair spray) may occur. However, it is considered that the combination of the conservative hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% dermal absorption rate, is sufficiently protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic products with low exposure.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	slightly irritating
Guinea pig, skin irritation – 14 day repeat application	slightly irritating
Rabbit, eye irritation	irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics

Given the low molecular weight (321.4 g/mol), the notified chemical may be absorbed across the respiratory or gastrointestinal tract. The notified chemical is a salt with a moderate water solubility, hence dermal absorption is expected to be limited. This is supported from the result of an *in vitro* percutaneous absorption study with an analogue chemical, Sodium PCA. In this study the percutaneous absorption of 5, 10 and 20% Sodium PCA through human skin was 5.97, 6.78 and 5.89%, respectively (CIR, 1999).

Acute toxicity

The notified chemical was found to be of low acute oral toxicity in rats.

No studies were submitted for acute dermal and acute inhalation toxicity of the notified chemical.

Irritation and sensitisation

The notified chemical is slightly irritating to the skin based on studies conducted in rabbits (single application) and guinea pigs (14 day repeat application).

The notified chemical is irritating to the eyes based on a study conducted in rabbits. Irritation effects included conjunctival irritation (max. grade 3), corneal opacity (max. grade 2) and iridial inflammation (max. grade 1). At the end of the study period (day 7), slight conjunctival irritation (redness) (grade 1) remained in 3/6 animals. Effects on the cornea and iris were resolved in all animals by Day 4.

In a guinea pig maximisation test the notified chemical was found not to be a skin sensitiser. Similarly, an analogue chemical (sodium PCA) at 5% concentration was determined not to be a skin sensitiser in guinea pigs (CIR, 1999).

Repeated dose toxicity

No studies were submitted for repeated dose toxicity of the notified chemical.

In a 26 week study in rats fed with diets containing up to 8% of an analogue chemical (Sodium PCA), no adverse effects were observed (CIR, 1999).

Reproductive and developmental toxicity

No studies were submitted for reproductive and developmental toxicity of the notified chemical.

An analogue chemical, Sodium PCA, was not a developmental or reproductive toxicant in rats. In the oral (gavage) reproductive and developmental toxicity study, the No Observed Adverse Effect Level (NOAEL) was 1,000 mg/kg bw/day (the highest dose tested) (CIR, 2015).

Mutagenicity/Genotoxicity

The notified chemical was negative in a bacterial reverse mutation assay.

Health hazard classification

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

Hazard classification	***Hazard statement***
Eye Irritation (category 2A)	H319 – Causes serious eye irritation

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Based on the toxicological information provided, the notified chemical is an eye irritant.

Reformulation

During reformulation, workers may be at risk of eye irritation effects when handling the notified chemical as a powder at ≤ 100% concentration. Zinc oxide dust has an Australian workplace exposure standard of 10 mg/m^3 TWA (SWA, 2018). The notifier anticipates that worker exposure will be limited through the use of engineering controls such as enclosed systems, automated processes and mechanical ventilation. The use of appropriate PPE (coveralls, imperious gloves, respiratory protection for dusts and eye protection) will also be used to limit worker exposure.

End-use

Workers involved in professions where the services provided involve the application of cosmetic products containing the notified chemical to clients (*e.g.*, hairdressers and beauty salon workers) may be exposed to the notified chemical at ≤ 4.9% concentration. 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 chemical.

Therefore, under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

6.3.2. Public Health

Members of the public will experience widespread and frequent exposure to the notified chemical at ≤ 4.9% concentration through daily use of cosmetic products. The main route of exposure is expected to be dermal, while ocular and inhalation exposure are also possible, particularly if products are applied by spray.

Irritation

The notified chemical is a slight skin irritant and an eye irritant. Given the proposed use concentration (≤ 4.9%) irritation effects are not expected.

Repeated dose toxicity
No repeated dose toxicity studies were submitted for the notified chemical. An analogue chemical (Sodium PCA) up to 8% showed no adverse effects in a 26 week oral toxicity study in rats.

Zinc is an essential element playing an important role in many processes in the body. However excess exposure over natural background levels can lead to adverse effects mainly related to its ability to induce copper deficiency. Water soluble zinc salts, like the notified chemical, are restricted for use in cosmetic products in the EU based on a maximum of 1% zinc (equivalent to 4.9% notified chemical) (EU Cosmetics Regulation 1223/2009 Annex III).

PCA is a cyclic organic compound commonly known as pyroglutamic acid (CIR, 1999). It is an internal amide of L-glutamic acid found in vegetables, fruits, grasses and molasses (Budavari, 1989). PCA is a naturally occurring component of mammalian tissue (CIR, 1999).

Overall, based on the available information, systemic toxicity from use of the notified chemical at ≤ 4.9% concentration in cosmetic products is not expected.

Therefore, the risk associated with use of the notified chemical at ≤ 4.9% 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 chemical will be imported into Australia neat for reformulation into cosmetic products, or as a component of finished cosmetic products at ≤ 4.9% concentration. The notified chemical may also be imported in the future as a component of a premix at < 100% concentration for reformulation into cosmetic products. Significant release to the environment from transport and storage is not expected. In the event of accidental spillage, spills containing the notified chemical are expected to be collected by inert absorbent material, and be disposed of to landfill in accordance with local government regulations.

The reformulation process will involve blending operations and may involve both automated and manual transfer steps. Release of the notified chemical from reformulation is expected to be minimal. The notifier has indicated that wastes containing the notified chemical generated during reformulation may be collected and released to sewers, or disposed of to landfill in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The majority of the notified chemical is expected to be released to sewer as a result of its use in cosmetic products.

RELEASE OF CHEMICAL FROM DISPOSAL

It is estimated by the notifier that a maximum of 1%, or up to 10 kg per annum of the notified chemical, may remain in import containers, and a maximum of 3%, or up to 30 kg per annum, in end-use containers once the consumer products are used up. Wastes and residue of the notified chemical in empty containers will either share the fate of the container and be disposed of to landfill, or be released to sewer when containers are rinsed, before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in personal care products, the majority of the notified chemical is expected to enter the sewer system. Hydrolysis is not expected to be significant under environmental conditions based on structure but the notified chemical is readily biodegradable (99% in 28 days). For the details of the environmental fate studies please refer to Appendix C.

The notified chemical a metal salt and is highly soluble in water (solubility = 168 g/L in water). After being released to sewer system following its use, the notified chemical is expected to partition to water column. There it is likely to degrade, based on its ready biodegradability, or exchange ions. Both of these mechanisms will result in the release of zinc. Zinc is a naturally occurring element, which can exist in the environment in many different forms. It may exist in a bioavailable form in the environment and be consumed or absorbed by biota.

The notified chemical is expected to be largely removed by biodegradation at the sewage treatment plants (STP). The notified chemical may be applied to soil when effluent from STP is used for irrigation, or when sewage sludge is used for soil remediation, or disposed of to landfill as collected spills and empty container residue. In surface water, soils or landfill, the notified chemical is not expected to persist based on its ready biodegradability. The notified chemical will eventually degrade to form water, oxides of carbon and nitrogen and inorganic salts.

The notified chemical is not expected to bioaccumulate based on its high water solubility and readily biodegradability.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume a worst case scenario, with 100% release of the notified chemical into sewer systems nationwide and no removal within sewage treatment plants (STPs).

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	200.0	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

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 0.56 µg/L may potentially result in a soil concentration of approximately 3.74 µg/kg. It is not expected to accumulate in soil based on its ready biodegradability.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations for Daphnia are summarised in the table below. Details of this study can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 = 8.85 mg/L	Toxic to aquatic invertebrate

Based on the above ecotoxicological data for the notified chemical, it is considered to be acutely toxic to daphnids. Therefore, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009), the notified chemical is formally classified as "Category 2, Toxic to aquatic life". The notified chemical is rapidly biodegradable and is not expected to bioaccumulate. Therefore, the notified chemical is not formally classified under the GHS for its long-term hazard.

The notified chemical contains elemental zinc metal. At low concentrations it is essential to the functioning of organisms, but may become toxic at higher concentrations (ANZWG, 2000). The worst case release of the notified chemical is 0.56 and 0.06 µg/L in river and marine water (see above), corresponding to 0.11 and 0.01 µg/L zinc in river and marine water. These values indicate that the release of the zinc metal due to the assessed use of the notified chemical in Australia are far below the abundance of elemental zinc in the ocean (2 µg/L) and stream water (20 µg/L; Porterfield, 1984). Therefore, zinc metal from the use of the notified chemical is not expected to cause hazardous effects to the environment.

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated based on the measured ecotoxicity data from daphnia (48 hours EC50 = 8.85 mg/L) and a safety factor of 1000. A safety factor of 1000 was used as acute data is only available for one trophic level.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment	
EC50 (Invertebrate, 48 h)	8.85 mg/L
Assessment Factor	1000
PNEC:	8.85 µg/L

7.3. Environmental Risk Assessment

Based on the above PEC and PNEC values, the following Risk Quotient (Q) has been calculated:

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.56	8.85	**0.06**
Q - Ocean	0.06	8.85	**0.006**

The risk quotient for discharge of treated effluents indicates that the notified chemical is not expected to reach ecotoxicologically significant concentrations in the aquatic environment based on the worst-case estimate of exposure. The notified chemical has a low potential for bioaccumulation and is unlikely to persist in surface waters or soils.

The release of the zinc from the use of the notified chemical in Australia is not expected to significantly increase the background concentration of this element in environmental waters. Accordingly only the release of the notified chemical requires consideration in determining the risk to the aquatic environment.

Therefore, on the basis of the PEC/PNEC ratio, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility 168 g/L at 20 °C

Method In-house method
Remarks Flask Method
Test Facility Exempt Information (11)

Particle Size Mean particle size > 300 µm

Method Not stated

Range (µm)	*Mass (%)*
< 300	2.2
< 150	0.2
< 106	0.0

Remarks Determined using a mechanical sieve
Test Facility Exempt Information (1)

Flammability Flammable

Method Not stated
Remarks The test item in dust form was dispersed by a blast of compressed air in a 1L vertical Hartmann tube in the presence of an energetic continuous high-voltage arc (10 kV). Ignition was observed at ≥ 2 g mass dispersed.
Test Facility Exempt Information (2)

Autoignition Temperature Not ignitable

Method Not stated
Remarks The test item in dust form was dispersed in the explosion vessel and sparked (10 kV and 500 mJ) with a known energy are passed through the dust cloud. No ignition was observed at ≤ 15 g mass dispersed at 10 to 20 dispersions.
Test Facility Exempt Information (1)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD
- Species/Strain: Rat/Sprague-Dawley
- Vehicle: Water
- Remarks - Method: No protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5M/5F	2,000	2F/10

- LD50: > 2,000 mg/kg bw
- Signs of Toxicity: Two females were found dead at the 24 hour observation.

  Sedation was observed in all treated animals 15 minutes after the administration of the test substance which persisted in all animals at the 6 hour observation. Two males and a female showed sedation at the Day 2 observation.

  Swelling of the face was observed in all treated animals at the 1 hour observation which persisted in all the treated animals at the 6 hour observation. The symptom persisted in two males and one female at the 72 hour observation.

  Piloerection and tremor were observed in all treated animals at the 4- and 6-hour observations which persisted in two males and one female at the 24 hour observation.

  Three males and two females showed hypokinesia at the 24 hour observation.

  All clinical signs were resolved at the 96 hour observation.
- Effects in Organs: No abnormalities were noted at necroscopy in the animals found dead during the study or animals sacrificed at the end of the study.
- Remarks - Results: Weight loss was noted in 2 out of 5 males between Day 1 and Day 5 with normal weight recovery on Day 8. The body weight gain of the surviving females was normal throughout the duration of the study.

CONCLUSION: The notified chemical is of low acute oral toxicity via the oral route.

TEST FACILITY: Exempt Information (3)

B.2. Irritation – skin

TEST SUBSTANCE: Notified chemical

METHOD
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 6M
- Vehicle: None
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive
- Remarks - Method: Skin reaction observations were made at 24-hour and 72-hour after the administration of the test substance.

RESULTS

Lesion	*Mean Score**						*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3	4	5	6			
Erythema/Eschar	0.5	0.0	0.0	0.5	0.0	0.0	1.0	< 72 h	0.0
Oedema	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0

* Calculated on the basis of the scores at 24 and 72 hours for EACH animals

Remarks - Results: Slight erythema (grade 1) was observed in two animals at the 24-hour observation which was resolved at the 72-hour observation. No signs of irritation were observed in the remaining test animals.

CONCLUSION: The notified chemical is slightly irritating to the skin.

TEST FACILITY: Exempt Information (5)

B.3. Irritation – skin (14 day repeat application)

TEST SUBSTANCE: Notified chemical

METHOD: Repeated application skin irritation test (in-house method)

Species/Strain	Guinea Pigs/Hartley Albino Charles River
Number of Animals	5M/5F
Vehicle	Moistened with distilled water
Observation Period	15 days
Exposure Information	Total exposure days: 14 days Application: 7 days per week
Type of Dressing	Nil
Remarks - Method	The test substance (0.05 g) moistened with distilled water was applied on the skin of guinea pigs once daily for 14 consecutive days. A daily mean irritation index was calculated by adding scores obtained for the erythema and oedema and dividing the total by the number of animals. Weekly mean irritation index was obtained by calculating the weekly mean of the daily indices. Weekly mean indices of ≤ 0.5, 0.5 to ≤ 2, 2 to ≤ 5 and 5 to ≤ 8 were considered as non-irritant, slightly irritant, irritant and very irritant, respectively. Histopathological examination was conducted on day 15.

RESULTS

Remarks - Results: In week 1, 2 males and 2 females displayed slight erythema (grade 1) at Day 8. In week 2, 8 animals out of 10 displayed slight and transient erythema with one animal displaying well-defined erythema on Day 13. All signs of irritation were resolved at the end of the study period (Day 15), except for one male which still had a slight erythema.

Weekly mean indices of 0.06 and 0.34 were obtained for the treated animals in week 1 and week 2, respectively. As the weekly mean indices were < 0.5, the study authors concluded the notified chemical is not a skin irritant.

At necroscopy, slight thickening of epidermis was observed in all control and treated animals. Very slight to slight focal or diffuse inflammatory reaction in mononuclear cells was observed in treated (2 females and 1 male) and control (1 male and 2 females) animals.

No abnormal bodyweight changes were observed during the study. No unscheduled mortality was observed.

CONCLUSION The notified chemical is slightly irritating to the skin with repeated exposure.

TEST FACILITY Exempt Information (10)

B.4. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD Similar to OECD TG 405 Acute Eye Irritation/Corrosion
Species/Strain Rabbit/New Zealand White
Number of Animals 6M
Observation Period 7 days
Remarks - Method Distilled water was used as vehicle.

RESULTS

Lesion	*Mean Score**						*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3	4	5	6			
Conjunctiva: redness	1.7	2.3	1.7	1.7	1.3	1.7	3.0	> 7 days	1.0
Conjunctiva: chemosis	1.3	2.3	2.0	1.7	0.7	1.0	3.0	< 6 days	0.0
Conjunctiva: discharge	1.3	2.7	1.7	1.0	0.7	0.0	3.0	< 4 days	0.0
Corneal opacity	0.0	1.3	1.0	0.3	0.0	0.0	2.0	< 4 days	0.0
Iridial inflammation	0.3	0.7	0.7	0.3	0.0	0.0	1.0	< 3 days	0.0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animals

Remarks - Results Conjunctival irritation (grades 1-3) was observed in all animals from the 24-hour observation. Conjunctival discharge and chemosis were resolved by Day 6; however, slight conjunctival redness (grade 1) persisted in 3/6 animals at the end of the observation period (Day 7).

Corneal opacity (grade 1-2) was observed in 3/6 animals at the Day 1 observation which resolved in all animals at the Day 4 observation.

Iridial inflammation (grade 1) was observed in 4/6 animals at the Day 1 observation which resolved in all animals at the Day 6 observation.

CONCLUSION The notified chemical is irritating to the eye.

TEST FACILITY Exempt Information (6)

B.5. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD Similar to OECD TG 406 Skin Sensitisation - maximisation test (Magnusson/Kligman).
Species/Strain Guinea pig/Albino/Dunkin Hartley
PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal:6.25%

MAIN STUDY
Number of Animals Test Group: 10F Control Group: 5F
Vehicle Distilled water
Positive control Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using 1-chloro-2,4 dinitro benzene.

INDUCTION PHASE	Induction Concentration: intradermal: 50% topical: 100%
Signs of Irritation	Not reported.
CHALLENGE PHASE	
1st challenge	topical: 50% (day 25)
2nd challenge	not conducted
Remarks - Method	10 % sodium laurylsulfate was applied on the day prior (day 7) to topical induction.

RESULTS

Remarks - Results	The following symptoms were observed during challenge phase: Eight out of 10 test animals showed slight erythema (grade 1 similar to the vehicle control group) and two out of 10 animals showed mild erythema (grade 2) at the 24 hour observation. Slight erythema was observed in four animals at the 48 hour observation similar to the vehicle control group. These skin reactions were not apparent at the 72 hour observation.

CONCLUSION	The notified chemical showed skin reactions similar to the vehicle control (distilled water) group indicating it to be a non-sensitiser.
TEST FACILITY	Exempt Information (7)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test (March, 1996)
Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100 and TA102 *Escherichia coli*: WP2uvrA
Metabolic Activation System	S9 mix from Aroclor 1254 induced rat liver
Concentration Range in Main Test	<u>Test 1 and 2:</u> a) With metabolic activation: 312.5, 625, 1,250, 2,500 and 5,000 µg/plate b) Without metabolic activation: 156.25, 312.5, 625, 1,250, 2,500 and 5,000 µg/plate <u>Test 3</u> a) Without metabolic activation: 1,250, 2,500, 3,000, 4,000 and 5,000 µg/plate
Vehicle	Distilled water
Remarks - Method	A preliminary test at a concentration range of 10 to 5,000 µg/plate (with and without metabolic activation) was conducted on TA98, TA100, TA102 and WP2uvrA. The plate incorporation method was used for the preliminary toxicity test, all experiments without metabolic activation and Test 1 with metabolic activation. The preincubation method was used for Test 2 with metabolic activation. Negative control: distilled water Positive control: With metabolic activation: 2-anthramine (all strains) Without metabolic activation: sodium azide (TA1535 and TA100), 2-nitro-fluorene (TA98), 9-amino-acridine (TA1537), mitomycin C (TA102) and N-ethyl-N-nitro-nitrosoguanidine (WP2uvrA) No significant protocol deviations.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 500	≥ 312.5	> 5,000	Negative
Test 2		≥ 156.25	> 5,000	Negative
Test 3		> 5,000	> 5,000	Negative
Present				
Test 1	> 5,000	> 5,000	> 5,000	Negative
Test 2		> 5,000	> 5,000	Negative

Remarks - Results

In Test 2 without metabolic activation, a slight increase (2.19 fold) in the number of revertant colonies was observed with the WP2uvrA tester strain at 5,000 µg/mL. As this increase was not observed in Test 1 or the preliminary test, a confirmatory test with the tester strain WP2uvrA (Test 3) was conducted. As no significant increase in the number of revertants was observed at any dose level in the confirmatory test, the study authors concluded the increase observed in Test 2 with tester strain WP2uvrA was not biologically relevant.

No significant increases in the frequency of revertant colonies were recorded, in Test 1 and Test 2, for any of the remaining tester strains at any dose level either with or without metabolic activation.

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

CONCLUSION

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

TEST FACILITY

Exempt Information (4)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 A Ready Biodegradability: DOC Die-Away Test
Inoculum	Activated Sludge
Exposure Period	28 Days
Auxiliary Solvent	None
Analytical Monitoring	TOC analyser to determine dissolved organic carbon
Remarks - Method	The test was conducted according to the above OECD test guideline, no significant deviation from the protocol. A toxicity control was also run.

RESULTS

Test substance		*Sodium Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
1	8.7	1	93.2
6	99.1	6	96.9
14	100.2	14	99
21	99.7	21	99
28	99.7	28	99.4

Remarks - Results	The difference of extremes of replicate values of the degradation at the end of the test and at the end of the 10-day window was less than the threshold of 20% and the degradation of the toxicity control on day 14 was 99.7%. All validity criteria for the test were satisfied
CONCLUSION	The notified chemical is readily biodegradable.
TEST FACILITY	Exempt Information (8)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test - Static
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	140-250 mg $CaCO_3$/L
Analytical Monitoring	TOC analyser to determine the total organic carbon
Remarks - Method	Following the range finding test, the definitive tests were conducted at five different concentrations of the test substance for a total period of 48 hours. The test was conducted according to the above OECD test guideline. No significant deviation from the protocol was reported.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	-	20	0	0
9.53	Not determined	20	2	10

17.15	Not determined	20	11	16
30.86	Not determined	20	13	19
55.55	Not determined	20	13	19
100	Not determined	20	19	20

EC50	8.852 mg/L at 48 hours
Remarks - Results	Although the test substance is readily biodegradable, the test substance was determined to be stable during this test, remaining 80-120% of the concentration at the beginning of the test. The results were based on nominal concentrations. The concentration of dissolved oxygen in the test solution is greater than 3 mg/L. All validity criteria for the test were satisfied.
CONCLUSION	The notified chemical is determined to be toxic to aquatic invertebrates.
TEST FACILITY	Exempt Information (9)

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