File No: LTD/1879

June 2016

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

L-Ascorbic acid, 3-O-ethyl- (INCI Name: 3-O-ethyl ascorbic acid)

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.

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/1879	L'Oreal Australia Pty Ltd and Ceechem Australia Pty Ltd	L-Ascorbic acid, 3-O-ethyl- (INCI Name: 3-O-ethyl ascorbic acid)	ND*	≤ 1 tonne per annum	Component of cosmetic products

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Human health risk assessment
Provided that the recommended controls are being adhered to, 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
Based on the assumed low hazard and the assessed use pattern, the notified chemical 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 chemical during reformulation:
  - Enclosed, automated processes, where possible
  - Adequate general ventilation and 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 chemical during reformulation:
  - Avoid contact with skin and eyes

- 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:
  - Coveralls
  - Safety glasses or goggles
  - Impervious gloves
  - Respiratory protection if necessary

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 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.

Public Health

- Use of the notified chemical in cosmetic products applied topically may result in skin depigmentation. It is recommended that these products are labelled appropriately in order to inform consumers. This recommendation is consistent with the requirement of the Australian Consumer Law that all representations made in relation to the supply of consumer goods and services must be truthful, including not omitting information that would be relevant to consumers.

- Formulators should exercise due care when using the notified chemical in cosmetic products given its potential ability to cause pro-oxidant activity and eye irritation effects.

- As the notified chemical may potentially also be present in products meeting the definition of a therapeutic good, this report will be referred to the Therapeutic Goods Administration for their consideration.

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 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 of the chemical is intended to exceed 10% in cosmetic products;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of cosmetic products, 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.

(Material) Safety Data Sheet
The (M)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 (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANTS
L'Oreal Australia Pty Ltd (ABN: 40 004 191 673)
564 St Kilda Road
MELBOURNE VIC 3004

Ceechem Australia Pty Ltd (ABN: 61 081 398 192)
227a Belmore Road
RIVERWOOD NSW 2210

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: other names, analytical data, degree of purity, impurities and use details

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for flash point, hydrolysis as a function of pH and dissociation constant.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (2015)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Et-VC™

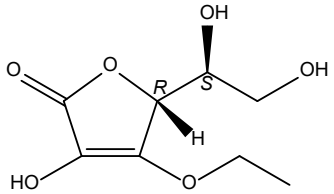
CAS NUMBER
86404-04-8

CHEMICAL NAME
L-Ascorbic acid, 3-O-ethyl-

OTHER NAME
3-O-Ethyl Ascorbic Acid (INCI Name)

MOLECULAR FORMULA
$C_8H_{12}O_6$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
204.18 Da

ANALYTICAL DATA
Reference FTIR, HPLC and UV-Vis spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 99%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: white crystalline powder

Property	Value	Data Source/Justification
Melting Point	112 °C	Measured
Boiling Point	214 ± 5 °C at 98.7 kPa	Measured
Density	1,410 kg/m^3 at 27.2 °C	Measured
Vapour Pressure	3.1 × 10^{-10} kPa at 25 °C	Calculated (SWISSI, 2013)
Water Solubility	778 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Does not contain hydrolysable functionalities
Partition Coefficient (n-octanol/water)	log Pow = -0.71 at 20 °C	Measured
Surface Tension	69.2 mN/m	Measured
Adsorption/Desorption	log K_{oc} = -0.447 at 20 °C	Estimated (US EPA EPI Suite™ v EPIWIN WSKOW v.I.41)
Dissociation Constant	Not determined	The notified chemical does not contain any functional groups that are expected to dissociate in water
Particle Size	Inhalable fraction (< 100 µm): 51.1% Respirable fraction (< 10 µm): 7.89% d_{50} = 95.9 µm	Measured
Flash Point	> 93 °C	(M)SDS
Flammability (Solid)	Not highly flammable	Measured
Autoignition Temperature	Not determined	Solid with melting point ≤ 160 °C
Explosive Properties	Not explosive	Measured
Oxidising Properties	Not oxidising	Based on chemical structure

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

Reactivity
The notified chemical 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 chemical 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 chemical will not be manufactured in Australia. The notified chemical will be imported as a neat chemical for local formulation into end-use cosmetic products at ≤ 10% concentration. The notified chemical will also be imported as a component of finished cosmetics at ≤ 10% 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
Melbourne and Sydney

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a neat chemical in 0.5 kg or 5 kg aluminium-plastic bags. Finished cosmetic products containing the notified chemical at ≤ 10% concentration will be imported in containers suitable for retail sale such as plastic bottles or tubes up to the size of 500 g. The notified chemical and finished cosmetic products containing the chemical will be transported by road or rail for distribution to industrial customers and retailers.

USE
The notified chemical will be used as a component of leave-on and rinse-off cosmetic products at ≤ 10% concentration. The categories of the end use products may include:

- leave-on face products including face only sunscreens;
- makeup and lipstick products;
- leave-on body products; and
- leave-on and rinse off hair products.

No aerosol spray products containing the notified chemical are proposed.

OPERATION DESCRIPTION
The notified chemical will be imported as a neat chemical for formulation of cosmetic products, or as a component of finished cosmetic products at ≤ 10% concentration that are to be sold to the public in the finished form as imported.

Reformulation
The procedures for incorporating the notified chemical into end-use products will vary depending on the nature of the cosmetic product being formulated, and both manual and automated steps will likely be involved. However, in general, it is expected that for the reformulation process, the notified chemical will be weighed and added to the mixing tank where it will be blended with additional additives to form the finished cosmetic products. This will be followed by automated filling of the reformulated products into containers of various sizes. The blending operations are expected to be highly automated and use closed systems and/or adequate ventilation. During the formulation process, samples of the notified chemical and the finished cosmetic products will be taken for quality control testing.

End-use
Finished cosmetic products containing the notified chemical at ≤ 10% 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 will be applied by hand or by using 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 workers	4	12
Production compounders	8	12
Chemists	3	12
Packers (for dispensing)	8	12
Store persons	4	12
Professional end users	8	365

EXPOSURE DETAILS

Transport and storage

Transport and storage workers are not expected to come into contact with the notified chemical when handling the packaged notified chemical or products containing the chemical unless accidental breach of sealed packaging occurs.

Reformulation

During reformulation into cosmetic products, dermal, ocular and inhalation exposure of workers to the notified chemical at various concentrations up to 100% 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 chemical in end-use products at ≤ 10% concentration may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. hair dressers, workers in beauty salons). The principal route of exposure will be dermal while ocular exposure may also be possible. Such professionals may use some PPE to minimise repeated exposure, but this is not expected to occur in all workplaces. However, 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 less extent than that experienced by consumers using the products containing the notified chemical.

6.1.2. Public Exposure

The notified chemical is proposed to be formulated in a range of leave-on or rinse-off cosmetic products. There will be widespread and repeated exposure of the public to the notified chemical through the use of the cosmetic products at ≤ 10% concentration. The principal route of exposure will be dermal while ocular exposure is also possible. Based on its low vapour pressure with no use in aerosol spray products proposed, inhalation exposure to the notified chemical is not expected.

Based on the use information available for the notified chemical, a combined internal dose of 9.827 mg/kg bw/day was estimated using data on typical use patterns for cosmetic product categories in which the notified chemical may be used (SCCS, 2012; specific use details of the notified chemical are considered as exempt information). This estimation assumed a worst case scenario and is for a person who is a simultaneous user of a selection of cosmetic products that may contain the notified chemical.

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 (QSAR calculation)	estimated LD50 = 5,903.13 mg/kg bw; low toxicity
Skin irritation (*in vitro* reconstructed human *Epidermis* test)	non-irritating
Skin irritation (*in vitro* reconstructed human *Epidermis* test with penetration)	non-irritating; penetration rate = 2.13% in 8 h at 32 °C when tested at 2.06% concentration

Endpoint	*Result and Assessment Conclusion*
Human, skin irritation (patch test at 2%)	non-irritating
Eye irritation potential (*in vitro* NRR test at 10 %)	non-cytotoxic
Eye irritation (*in vitro* HET-CAM at 3%)	moderately irritating
Human, skin sensitisation – RIPT (100%)	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution
No toxicokinetic data were provided on the notified chemical. The notified chemical is a derivative of L-ascorbic acid (vitamin C, CAS RN 50-81-7) with only the addition of an ethyl group to the molecule. If systemically absorbed, the notified chemical is expected to undergo metabolic pathways similar to those of vitamin C.

Based on its low molecular weight, passive diffusion of the notified chemical across the gastrointestinal tract is likely to occur. However, based on its high water solubility and low partition coefficient (log Pow = -0.71), dermal absorption may be limited. This is supported by the low dermal penetration rate (2.13% in 8 hours at 32 °C) obtained from an *in vitro* test.

L-ascorbic acid has an important relationship with the oxidation of transition metals such as iron or copper at enzyme active sites and in food. It is readily and reversibly oxidised to L-dehydroascorbic acid and both forms exist in equilibrium in the body. In alkaline solution, L-dehydroascorbic acid is hydrolysed to L-diketogulonic acid and this reaction is not reversible (CIR, 2005).

Available information indicates that, after an intraperitoneal injection of ^{14}C-labelled ascorbic acid into rats, 19% to 29% was converted to CO_2 and only 0.4% was excreted as oxalic acid in the urine within 24 hours. In guinea pigs, about 48% to 63% of ingested ascorbic acid was eliminated in the urine, 0.2% to 0.43% in the faeces, and 5.5% in expired air. In guinea pigs, distributions of ascorbic acid in organs or tissues were mainly found in adrenals, lungs, and bones (CIR, 2005).

Biochemical action
As a close derivative of L-ascorbic acid, the notified chemical is expected to biochemically function in a similar way to vitamin C. In cosmetic formulations, vitamin C is typically known to function as an antioxidant and pH adjuster (CIR, 2005). It is also known to be used on skin for functions of photoprotection, neocollagenesis, inhibition of melanogenesis and improvement in inflammatory skin disorders (Stamford, 2012).

As a photoprotectant, L-ascorbic acid has been shown to decrease UV-B induced photooxidation on human sebum, stabilise the plasma membranes and mitochondrial membrane potential to prevent UV-A induced apoptosis (Xiao *et.al*, 2009), and suppress the elevation of intracellular peroxide after UV-B irradiation (Ochiai *et.al*, 2006). L-ascorbic acid has also shown the ability to stimulate collagen production in human fibroblasts and enhance mRNA transcription levels of collagen genes (CIR, 2005).

In inhibition of melanogenesis, L-ascorbic acid interacts with copper ions at the tyrosinase active site, acting as an anti-oxidative agent at various oxidation steps of melanin formation (Sarkar *et.al*, 2013). However, the effects of L-ascorbic acid in the skin were still not fully understood (Michels, 2011).

Depigmentation effects
Pigmentation in the skin is caused by enhanced melanin production or melanocyte proliferation (Maeda and Fukuda, 1991). L-ascorbic acid has been reported to inhibit the production of melanin (Parvez *et.al*, 2006) and used as an active whitening component in cosmetics that prevents melanin synthesis. The notified chemical is expected to have similar skin depigmentation effects when used topically.

Available data showed that, if skin depigmentation is caused by cytotoxicity, irreversible hypopigmentation may occur on the skin (Maeda and Fukuda, 1991). It has been reported that L-ascorbic acid is cytotoxic *in vitro* at high concentrations (Siddique *et.al*, 2009). Cytotoxic effects have also been described when L-ascorbic acid and the ascorbyl radical have undergone auto-oxidation (Eberlein-Konig *et.al,* 2005). Therefore, when used topically at high concentration, the potential for the notified chemical to cause cytotoxic effects leading to irreversible skin depigmentation cannot be ruled out.

Potential for pro-oxidant activity
The notified chemical is proposed to have antioxidant activity. At high concentrations or under special conditions, almost all antioxidants have pro-oxidant effects *in vitro*; however, the relevance of these effects *in*

vivo is not currently known (Eberlein-Konig *et.al*¸ 2005). It has been demonstrated that L-ascorbic acid had dose-dependent antioxidant or pro-oxidant effects in rats after hepatic ischemia/perfusion (Seo and Lee, 2002), and extracellular antioxidant activity and intracellular pro-oxidant activity may be simultaneously occurring (Osiecki *et. al*, 2010). Pro-oxidation activity of a chemical *in vivo* is known to generate oxidative damages to biomolecules such as proteins, DNA and lipids that may further lead to cell death or genotoxicity (Aruoma, 2003; CIR, 2005).

It has been shown that L-Ascorbic acid may contribute to pro-oxidant activity by reducing metal ions which further are capable of converting hydrogen peroxide to hydroxyl radicals through a Fenton type reaction (Duarte and Lunec, 2005). Metal ions are widely present in cosmetic products at trace concentrations that may penetrate into or through human skin to produce systemic exposure after applications (Bocca *et.al*, 2014).

In light of the incomplete knowledge regarding the pro-oxidation potential of L-ascorbic acid and ascorbic acid derivative chemicals, and the likelihood that metals will be present in cosmetics containing the notified chemical, its potential for pro-oxidation cannot be ruled out.

Acute toxicity
No acute toxicity study data were provided for the notified chemical.

QSAR modelling using *Toxicity Estimation Software Tool* (version 4.1, US EPA) predicted that the notified chemical is of low toxicity via the oral route (KVD/TG, 2013). This prediction is supported by the low acute oral toxicity (> 5,000 mg/kg bw in most cases) obtained for L-ascorbic acid in a range of species (OECD SIDS, 1994; CIR, 2005).

Irritation and sensitisation
Test results of the notified chemical using the *in vitro* reconstructed human *Epidermis* model suggested that the chemical is non-irritating to skin. This is supported by test results on human volunteers using patches of the notified chemical at 2% concentration. The notified chemical did show skin irritation effects in the patch test.

In an *in vitro* eye irritation study, the notified chemical at 10% concentration was not cytotoxic to fibroblast cells of rabbit cornea. However, an *in vitro* eye irritation study using the HET-CAM model indicated that the notified chemical at 3% concentration was moderately irritating. Based on the latter study, the notified chemical is likely to be irritating to the eyes. It is also noted that the notified chemical is classified as a Category 2 eye irritant in the MSDS provided by the notifier.

In a human repeat insult patch test (HRIPT) completed on the skin of 56 volunteers, the notified chemical at 100% concentration was considered by the study authors to be non-sensitising. This result is supported by observations on L-ascorbic acid (CIR, 2005), showing non-sensitising properties via the dermal route in a study of 103 human subjects using an opaque cream at 5% concentration, and a maximisation assay on 26 human subjects using a facial treatment containing 10% L-ascorbic acid.

Repeated dose toxicity
No repeated dose toxicity data were provided for the notified chemical.

Information on the repeat dose toxicity of L-ascorbic acid is available (CIR, 2005) which generally indicates the absence of effects deemed toxicologically adverse at doses ≤ 1,000 mg/kg bw/day.

Mutagenicity/Genotoxicity
The notified chemical was not mutagenic in a bacterial reverse mutation study.

For L-ascorbic acid, the weight of evidence from assays in bacteria and mammalian cells *in vitro* indicate the absence of ability to produce gene mutations. Some positive results were noted in the *in vitro* assays for unscheduled DNA synthesis (UDS) and sister chromatid exchanges (SCE), but were considered to be due to formation of hydrogen peroxide and reactive oxygen species at very high concentrations which would not be expected to be relevant to the *in vivo* situation. Negative results were obtained *in vivo* for both clastogenicity and SCE induction. Ascorbic acid has been considered to have no significant mutagenic potential (OECD SIDS, 1994).

Toxicity for reproduction
No reproductive/developmental toxicity data were provided for the notified chemical.

A number of developmental studies for L-ascorbic acid have been published (OECD SIDS, 1994; CIR, 2005). All the studies showed that high doses of L-ascorbic acid (1,000 mg/kg bw/day) had no effect on development of the offspring or on breeding, pregnancy, parturition or lactation in the maternal animals.

Observations on human exposure
No human exposure observation information for the notified chemical was submitted.

According to *Nutrient Reference Values for Australia and New Zealand* (NRV, 2005), the recommended daily intake (RDI) for vitamin C (L-ascorbic acid) is 45 mg/day with a prudent upper level limit of 1,000 mg/day for an average adult. Gastrointestinal effects were the most common adverse effects associated with acute, high doses given over a short period of time. Other reported effects included metabolic acidosis, changes in prothrombin activity and low ingestion in pregnancy conditioning the need for higher amounts in the infant. It has also been suggested that consumption of L-ascorbic acid may increase oxalate excretion. However, studies in humans have not revealed a substantial increase in urinary oxalate stones with high intakes of L-ascorbic acid. The studies concluded that L-ascorbic acid is not associated with significant adverse effects (NRV, 2005).

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

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the available information, the notified chemical has potential to cause eye irritation effects. As an antioxidant used in cosmetics, the notified chemical may present topical depigmentation effects on skin which sometimes may not be reversible. Under complex combination of topical conditions, the notified chemical may produce pro-oxidant activity leading to adverse cytotoxicity.

Reformulation
Dermal, ocular and inhalation exposure of workers to the notified chemical at various concentrations up to 100% may occur during formulation of cosmetics. As stated by the notifier, the use of PPE such as coveralls, eye protection, impervious gloves and respiratory protection (as appropriate), and engineering controls including automated/enclosed blending processes and local exhaust ventilation should minimise the risk for workers. Provided that the protective measures and engineering controls proposed are implemented, the use of the notified chemical is not expected to pose an unreasonable risk to workers under the occupational conditions described.

End use
Store persons and professional end users may come into contact with cosmetic products containing the notified chemical at ≤ 10% concentration. These products will also be available to the public. The risk to workers who regularly handle these products is expected to be of a similar or lesser extent than that experienced by consumers using products containing the notified polymer (for details of the public health risk assessment, see Section 6.3.2).

6.3.2. Public Health
The notified chemical is a derivative of L-ascorbic acid. Use of ascorbic acid and its derivatives in cosmetic products has been reviewed by Cosmetic Ingredient Review Expert Panel (CIR, 1999 and 2005).

In Europe, ascorbic acid derivatives have been used as skin depigmenting agents at concentrations of 2-3% (Prakash *et.al*, 2009) and in cosmetic water/oil emulsions as antioxidants at ≤ 2% (CIR, 1999). It has been reported (CIR, 2005) that there were 431 cosmetic formulations containing L-ascorbic acid from 10 ppm to 10% from various product categories based on information from US Food and Drug Administration (US FDA). Various ascorbic acid derivatives have also been previously used in Australia at concentrations ≤ 5% (typically in the range of 0.01 to 2% as an antioxidant and ≤ 5% in specialised skin care products as skin lightening agent).

There will be widespread and repeated exposure of the public to the notified chemical through the use of the cosmetic products at proposed concentrations of ≤ 10% in individual products. The principal route of exposure

will be dermal, while ocular exposure is also possible. Inhalation exposure to the notified chemical is not expected based on proposed use scenario and its low vapour pressure.

Eye irritation
The notified chemical has potential to cause eye irritation. However, at the proposed use concentrations of ≤ 10% in cosmetic products, significant eye irritation effects of the notified chemical are not expected. The eye irritation risk may be further minimised by the inclusion of appropriate labelling and directions for use to warn consumers against eye contact.

Risk of repeated exposure
Estimation of repeated dose toxicity potential of the notified chemical using the worst case exposure scenario from the use of multiple products would result in a combined internal dose of 9.827 mg/kg bw/day (see Section 6.1.2). Using a NOAEL of 1,000 mg/kg bw/day based on the results of studies conducted on L-ascorbic acid, the margin of exposure (MoE) was estimated to be 102. A MoE value greater than or equal to 100 is generally considered acceptable to account for intra- and inter-species differences. Based on the above estimation, the notified chemical is unlikely to cause systemic or reproductive/development toxicity by normal use of the cosmetic products containing the chemical.

Depigmentation and pro-oxidant effects
As an antioxidant used in cosmetics, the notified chemical has the potential to cause skin depigmentation that may be irreversible. The extent of this effect depends on many factors, including the type of cosmetic product, and the type and frequency of application. Therefore it is recommended that products containing the notified chemical be labelled to warn consumers of the possibility of such unintended consequences.

Under certain complex topical use conditions, the notified chemical may also produce pro-oxidant activity. It has been recommended that formulators of the cosmetics should ensure vitamin C and its derivatives acting as antioxidants in the formulations avoid possible pro-oxidant activity (CIR, 2005).

Based on the available information, with appropriate labelling regarding risks associated with eye irritation, skin depigmentation and possible adverse effects caused by pro-oxidant activity of the chemical, the risk to the public from use of the notified chemical at ≤ 10% in cosmetics 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 not be manufactured in Australia; therefore there is no release of the notified chemical to the environment from this activity. Environmental release during importation, transport and distribution may occur as a result of accidental spills. In the event of a spill, the notified chemical is expected to be contained and collected in an inert absorbent material and disposed of in accordance with local regulations.

The notified chemical will be blended with other ingredients in automated/enclosed facilities to produce cosmetic products. Release from blending is expected to be very low. A total of up to < 1% of the import volume is estimated to be generated as waste from residues in empty containers and spills during blending. Empty containers containing the notified chemical will either be recycled or disposed of through an approved waste management facility.

RELEASE OF CHEMICAL FROM USE
The majority of the notified chemical is expected to be released to sewers across Australia as a result of its use in cosmetic products, which are washed off the hair and skin of consumers and disposed of to the sewer.

RELEASE OF CHEMICAL FROM DISPOSAL
It is expected that about 3% (30 kg) of the product containing the notified chemical will remain in end-use containers. The containers are expected be disposed of through domestic garbage disposal and will enter landfill, or be subjected to recycling processes.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified chemical is expected to enter the sewer system through its use as a component of cosmetics before potential release to surface waters nationwide. The notified chemical is not readily biodegradable (38% after 28 days) in the environment and is not expected to hydrolyse under environmental conditions. Therefore, the notified chemical has the potential to persist in the aquatic compartment. However, in surface waters the notified chemical is expected to disperse and degrade into water and oxides of carbon. For details of the environmental fate studies, please refer to Appendix C. Upon release to the aquatic environment in effluent from sewage treatment plants (STPs), the notified chemical is expected to remain in the water column due to very high water solubility, low vapour pressure and low n-octanol/water partition coefficient (log K_{OW}). The notified chemical is expected to leach through soil and sediments given its low adsorption/desorption coefficient (log K_{OC}). Given the notified chemical's low log K_{OW}, it is not expected to bioaccumulate.

The half-life of the notified chemical in air is calculated to be 1.749 hours based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2011). Therefore, in the event of release to atmosphere, the notified chemical is not expected to persist in the atmospheric compartment.

The majority of the notified chemical will be released to sewer after use. A small proportion of notified chemical may be applied to land when effluent is used for irrigation, or disposed of to landfill as waste. Notified chemical residues in landfill and soils are expected to leach through soil and sediments based on its low soil adsorption coefficient. In the aquatic and soil compartments, the notified chemical is expected to degrade through biotic and abiotic processes to form water and oxides of carbon.

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 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	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.61	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 1,000 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 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.6 µg/L may potentially result in a soil concentration of approximately 4.03 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of the notified chemical in the applied soil in 5 and 10 years may be approximately 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	EC50 (48 h) > 100 mg/L	Not harmful to aquatic invertebrates

Endpoint	*Result*	*Assessment Conclusion*
Algal Toxicity	E_rC50 (72 h) > 100 mg/L	Not harmful to algae

Based on the endpoints for toxicity of the notified chemical to aquatic organisms, the notified chemical is not considered to be harmful to aquatic organisms under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009). Therefore, the notified chemical is not formally classified under the GHS. Based on its measured acute toxicity, lack of ready biodegradability and expected low bioaccumulation potential, the notified chemical is not formally classified under the GHS for the chronic hazard.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has not been calculated for the notified chemical as no significant adverse effects were observed in any of the ecotoxicity tests submitted.

7.3. Environmental Risk Assessment

The majority of the notified chemical will be disposed of to the sewer, based on its use as a component in cosmetic products. The notified chemical has a low potential for bioaccumulation and is not expected to be harmful to aquatic organisms. Therefore, on the basis of the assessed use pattern in cosmetic products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point 112 °C

Method	OECD TG 102 Melting Point/Melting Range EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature
Remarks	Capillary method
Test Facility	Exempt Information (2013a)

Boiling Point 214 ± 5 °C at 98.7 kPa

Method	OECD TG 103 Boiling Point EC Council Regulation No 440/2008 A.2 Boiling Temperature
Remarks	Siwoloboff test method. At boiling point the test substance turned from clear to brown indicating a sign of decomposition.
Test Facility	Exempt Information (2013a)

Density 1,410 kg/m^3 at 27.2 °C

Method	OECD TG 109 Density of Liquids and Solids EC Council Regulation No 440/2008 A.3 Relative Density
Remarks	Determined with a helium pycnometer
Test Facility	Exempt Information (2013a)

Vapour Pressure 3.1×10^{-10} kPa at 25 °C

Method	OECD TG 104 Vapour Pressure EC Council Regulation No 440/2008 A.4 Vapour Pressure
Remarks	Calculated with EPI Suite 4.10 using measured melting point and boiling point. Modified grain method.
Test Facility	Exempt Information (2013a)

Water Solubility 778 g/L at 20 °C

Method	OECD TG 105 Water Solubility. EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks	Flask Method
Test Facility	Exempt Information (2013a)

Partition Coefficient (n-octanol/water) log Pow = - 0.71 at 20 °C

Method	OECD TG 117 Partition Coefficient (n-octanol/water). EC Council Regulation No 440/2008 A.8 Partition Coefficient.
Remarks	Flask Method
Test Facility	Exempt Information (2013a)

Surface Tension 69.2 mN/m at 20 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions. EC Council Regulation No 440/2008 A.5 Surface Tension.
Remarks	Concentration: 1 g/L
Test Facility	Exempt Information (2013a)

Particle Size d_{50} = 95.9 µm

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

Range (µm)	*Mass (%)*
< 10	7.89

Range (μm)	*Mass (%)*
< 50	36.0
< 100	51.1

Remarks Laser diffraction method was used.
Test Facility Exempt Information (2013a)

Flammability – Solids Not highly flammable

Method EC Council Regulation No 440/2008 A.10 Flammability (Solids).
Remarks Propagation time for combustion over 200 mm of a mould powder train of 250 (L) × 20 (W) × 10 (H) mm was > 4 minutes.
Test Facility Exempt Information (2013a)

Explosive Properties Not explosive

Method EC Council Regulation No 440/2008 A.14 Explosive Properties.
Remarks Thermal stability was determined by DSC (Differential Scanning Calorimetry). The exothermic decomposition energy was determined to be 518 kJ/kg between 30 °C and 400 °C which is slightly above the limit of 500 kJ/kg for exclusion under the guidelines. However, the notified chemical is not expected to be explosive based on the chemical structure.
Test Facility Exempt Information (2013a)

Oxidizing Properties Not oxidising

Method EC Council Regulation No 440/2008 A.17 Oxidizing Properties (Solids).
Remarks Based on chemical structure
Test Facility Exempt Information (2013a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral (QSAR calculation)

TEST SUBSTANCE	Notified chemical
METHOD	QSAR (Toxicity Estimation Software Tool, version 4.1, US EPA)
Species	Rat
Remarks - Method	The notified chemical is within the applicability domain of the training data set.
RESULTS	
LD50	5903.13 mg/kg bw
Remarks - Results	Validation of the prediction resulted in a correlation (R^2) value of 0.626 and a coverage of 0.984 for the consensus. Further weight of evidence was required to support the prediction.
CONCLUSION	The notified chemical was predicted to be of low toxicity via the oral route.
TEST FACILITY	Exempt Information (2013b)

B.2. Irritation – skin (*in vitro* reconstructed human *Epidermis* test)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method EC Commission Regulation No 761/2009 B.46. *In vitro* Skin Irritation - Reconstructed Human *Epidermis* Test Method
Vehicle	None, skin model was moistened with phosphate buffered saline.
Remarks - Method	No significant deviation of the protocol was noted. 25 mg of the test substance was applied directly to the skin model with a surface area of 0.6 cm^2. 5% SDS was used as positive control.

RESULTS

Test material	*Mean OD_{570} of triplicate tissues*	*SD of mean OD_{570}*	*Relative mean viability (%)*
Negative control	2.271	0.142	100
Test substance	2.243	0.079	98.8
Positive control	0.086	0.004	3.8

OD = optical density; SD = standard deviation

Remarks - Results	The relative mean viability of the test substance was > 50%, the cut-off value for a skin irritant.
CONCLUSION	The notified chemical was non-irritating to the skin under the conditions of the test.
TEST FACILITY	Exempt Information (2013c)

B.3. Irritation – skin (*in vitro* reconstructed human *Epidermis* test with penetration)

TEST SUBSTANCE	Cosmetic product containing 2% notified chemical
METHOD	Similar to OECD TG 439 *In vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method
Vehicle	None, test substance applied directly
Remarks - Method	Penetration test 26.3 mg/cm^2 test substance (containing 0.542 mg/cm^2 notified chemical)

was applied to the top of epidermis. Receptor fluids were collected every hour for 8 hours at 32 °C and analysed using HPLC/DAD for the notified chemical that reached receptor fluids.

Irritation test
MTT assay and IL-1α release quantitatively measured using OD_{595} and ELISA, respectively, were utilised to determine the irritation potential of the test substance.

Positive control
Potassium hydroxide (8N).

RESULTS

Penetration

Time (h)	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
Cumulative penetration (µg/cm²)	0.54	1.96	3.23	4.80	6.42	7.85	9.74	11.47
SD of cumulative penetration (µg/cm²)	0.17	0.52	1.06	1.42	1.97	2.33	2.36	2.57
Penetration rate (%)	0.10	0.36	0.60	0.89	1.19	1.46	1.81	2.13

SD = standard deviation

Irritation
Results

Test material	*Relative viability by MTT test (%)*	*IL-1α release (pg/mL)*
Negative control	100	< 50
Test substance	113.97	< 50
Positive control	34.0	< 50

Interpretation Criteria

Criteria	*Interpretation*
Relative viability ≤ 50%	Irritant
Relative viability > 50% AND IL-1α release ≥ 50 pg/mL	Irritant
Relative viability > 50% AND IL-1α release < 50 pg/mL	Non-irritant

Remarks - Results
The test substance did not directly reduce MTT in a pre-test.

The test substance was interpreted to be a non-irritant with notified chemical penetrating at 11.47 ± 2.57 µg/cm² (2.13% of the amount applied) in 8 hours at 32 °C.

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

TEST FACILITY
Exempt Information (undated)

B.4. Irritation – skin (patch test)

TEST SUBSTANCE
Notified chemical (2%)

METHOD
Semi-occlusive patch test on volunteers

Volunteers
11 (8 F/3 M) volunteers aged 19 to 63 years participated.

Vehicle
Unspecified

Application Period
48 hours

Type of Dressing
Semi-occlusive

Remarks - Method
Single application of 0.02 mL of the test substance diluted at 2% was administered on the external side of the arm and maintained for 48 hours under semi-occlusive conditions. Skin reactions including erythema, oedema, papules, vesicles and blisters were observed 30 minutes after the patches were removed.

RESULTS	No significant skin reactions were recoded.
Remarks - Results	All volunteers completed the test.
CONCLUSION	The notified chemical at 2% concentration is non-irritating to the skin under the conditions of the test.
TEST FACILITY	Exempt Information (2009a)

B.5. Irritation – eye (*in vitro* NRR test)

TEST SUBSTANCE	Notifier chemical
METHOD	Reader *et al* (1990) Neutral Red Release (NRR) from Pre-Loaded Cells
Vehicle	Distilled water and 0.9% sodium chloride
Remarks - Method	The test substance was dissolved in distilled water at 10% and further diluted with 0.9% sodium chloride at 5, 15, 25, 35 and 50% by weight to yield 0.5, 1.5, 2.5, 3.5 and 5% final test concentrations. Diluted test substance was put in contact for 60 seconds with fibroblast cells of rabbit cornea marked by neutral red. Cytotoxicity was examined by the percentage of cell death and the IC50 (inhibition concentration of 50% cell survival) determined by measuring the neutral red retained in the cells using OD_{540}. Negative control used was 0.9% sodium chloride. Positive controls were 0.01%, 0.05% and 0.2% SDS in 0.9% sodium chloride.

RESULTS

Dilution (%)	*PC*	*NC*	*5*	*15*	*25*	*35*	*50*
Mean OD_{540}	0.405	1.032	1.037	1.057	1.002	1.021	0.999
Cell death (%)	61	0	0	0	3	1	3

NC = Negative Control (0.9% sodium chloride); PC = Positive Control (0.2% SDS)

Interpretation Criteria

IC50 (% dilution)	*Cell death at 50% dilution (%)*	*Interpretation*
> 50	≤ 20	Negligible cytotoxicity
> 50	> 20 and < 50	Slightly cytotoxic
> 25 and ≤ 50		Moderately cytotoxic
≤ 25		Severely cytotoxic

Remarks - Results	The IC50 for the test substance was determined to be > 50% (equivalent to 5% concentration) with a cell death rate of 3% at 50% dilution, indicating negligible level of cytotoxicity. The IC50 for the positive control substance (SDS) was determined to be 0.16%, indicating expected severe cytotoxicity.
CONCLUSION	The notified chemical at 10% concentration was not cytotoxic under the conditions of the test.
TEST FACILITY	Exempt Information (2009b)

B.6. Irritation – eye (*in vitro* HET-CAM)

TEST SUBSTANCE	Notified chemical (3%)
METHOD	HET-CAM Test - Official Journal of the Republic France (#302, 26 December 1996)
Vehicle	Physiological serum
Remarks - Method	The notified chemical was tested at 3% dilution in 4 eggs. The treated membranes were observed for 5 minutes to record signs of hyperaemia, haemorrhage, coagulation, opacity and/or thrombus.

N-Dodecylsulfobetaine (CAS RN 14933-08-5) in physiological serum was used as a negative control at 0.05% and as a positive control at 0.4% and 3.2%.

RESULTS

Egg No.	*Score*			*Total score*
	Hyperaemia	*Haemorrhage*	*Coagulation, opacity/thrombus*	
1	3	3	0	6
2	3	3	0	6
3	3	3	0	6
4	3	3	0	6

Remarks - Results: Negative and positive controls showed expected results.

The test substance at 3% dilution resulted in a mean score of 6, indicating moderate irritancy.

CONCLUSION: The notified chemical at 3% concentration was considered to be moderately irritating to the eye under the conditions of the test.

TEST FACILITY: Exempt Information (2009c)

B.7. Skin sensitisation – volunteers

TEST SUBSTANCE: Notified chemical

METHOD: Repeated insult patch test with challenge

Study Design: *Induction Procedure:* 160 mg of the test substance was applied to the back of each subject every Monday, Wednesday and Friday and replaced on every Wednesday, Friday and Monday respectively until 9 applications were reached. Skin reactions were recorded on every replacement.

Rest Period: 2 weeks

Challenge Procedure: The challenge patches were applied to both a previously unpatched site and a patched site. Skin reactions were recorded 20 minutes, 24 hours and 48 hours after patch removal.

Study Group: 46 F, 11 M; age range 19 to 69 years (24 with sensitive skin)

Vehicle: None; the patches were moistened with 160 µL of water before application.

Remarks - Method: Semi-occluded. The test substance was spread on a patch in the size of 4 cm^2.

RESULTS

Remarks - Results: One subject did not return for the challenge procedure due to family reasons. No skin irritation effects were observed during the induction and challenge procedures. No evidence of induced allergic contact dermatitis was recorded during the study.

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

TEST FACILITY: Exempt Information (2013d)

B.8. Genotoxicity – bacteria

TEST SUBSTANCE: Notified chemical

METHOD	OECD TG 471 Bacterial Reverse Mutation Test EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria Plate incorporation procedure (Test 1), repeated with pre incubation procedure (Test 2)
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98 and TA100 *E. coli*: WP2 (pKM101)
Metabolic Activation System	S9 fraction from Aroclor induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 200 – 5,000 µg/plate b) Without metabolic activation: 200 – 5,000 µg/plate
Vehicle	Distilled water
Remarks - Method	No significant deviation of protocol was noted.

RESULTS

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

Remarks - Results	There were no biological significant increases in the number of revertant colonies observed in any of the strains, at any of the concentrations tested, either in the presence or absence of metabolic activation. No dose response was observed in the tested bacterial strains. The positive controls produced satisfactory responses, thus confirming the performance of the test system and the metabolic activation.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Exempt Information (2009d)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None Reported
Analytical Monitoring	Biochemical oxygen demand (BOD)
Remarks - Method	The test was conducted in accordance with the test guideline above with no significant deviation from the protocol reported.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
3	2.67	4	58.51
7	2.67	7	74.47
14	10.00	14	85.11
21	24.67	21	87.77
28	38.00	28	89.76

Remarks - Results	After 28 days, the percent degradation for the notified chemical was 38.0%. The percent degradation calculated in the reference item replicate (procedure control) up to day 28 was 89.76%. In the toxicity control, more than 25% degradation was observed up to day 14.
CONCLUSION	The notified chemical is not readily biodegradable.
TEST FACILITY	Exempt Information (2014)

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 and Reproduction Test - static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None reported
Water Hardness	None reported
Analytical Monitoring	High performance liquid chromatography (HPLC)
Remarks - Method	The test was conducted in accordance with the test guideline without significant deviations. Good Laboratory Practice (GLP) was followed.

RESULTS

Concentration mg/L	*Number of D. magna*	*Number Immobilised*	
Nominal		*24 h*	*48 h*
Control	20	0	0
100	20	0	0

LC50	> 100 mg/L at 48 hours

NOEC	100 mg/L at 48 hours
Remarks - Results	Because significant toxic response was not observed during the preliminary concentration range-finding tests, only one test concentration at 100 mg/L was used in the main study. The deviation from the nominal concentration of the measured concentration was less than 20%.
CONCLUSION	The notified chemical is not harmful to aquatic invertebrates
TEST FACILITY	Exempt Information (2013e)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test. Effects on Biotic Systems, Version 2, 201 Algae Growth Inhibition Test, The China Environment Press. 2013.
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: 100 mg/L
Auxiliary Solvent	None reported.
Water Hardness	None reported.
Analytical Monitoring	High performance liquid chromatography (HPLC)
Remarks - Method	Because significant toxic response was not observed during the preliminary concentration range-finding tests, only one test concentration at 100 mg/L was used in the main study. The test was conducted in accordance with the test guideline without significant deviations. Good Laboratory Practice (GLP) was followed.

RESULTS

Biomass		*Growth*	
E_yC50 (mg/L at 72h)	*NOEC (mg/L at 72h)*	*E_rC50 (mg/L at 72 h)*	*NOEC (mg/L at 72h)*
> 100	100	> 100	100

Remarks - Results	Because significant toxic response was not observed in the preliminary range-finding test at a concentration of 100 mg/L, only this concentration and one control were tested in a limit-test.
CONCLUSION	The notified chemical not harmful to algae.
TEST FACILITY	Exempt Information (2015)

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