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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Nonanoic acid, C16-18-alkyl esters

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/2018	Symrise Pty Ltd	Nonanoic acid, C16-18-alkyl esters	No	< 1 tonne per annum	Cosmetic ingredient

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.

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.

Environmental risk assessment
On the basis of no observed effects to the limits of water solubility and the reported 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 safe work practices to minimise occupational exposure to the notified chemical during reformulation processes:
  - Avoid eye contact

  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.

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;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from 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 provided by the notifier was reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT` AND NOTIFICATION DETAILS

APPLICANT
Symrise Pty Ltd (ABN: 67 000 880 946)
168 South Creek Road
DEE WHY NSW 2099

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
Previous permit – NICNAS

NOTIFICATION IN OTHER COUNTRIES
EU (2012)
China (2017)

2. IDENTITY OF CHEMICAL

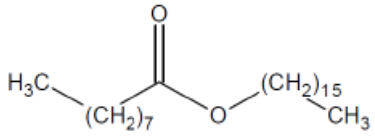
MARKETING NAME
SymMollient S

CAS NUMBER
878027-13-5

CHEMICAL NAME
Nonanoic acid, C16-18-alkyl esters

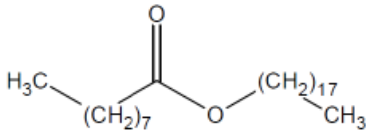
MOLECULAR FORMULA
Main constituent A: $C_{25}H_{50}O_2$
Main constituent B: $C_{27}H_{54}O_2$

STRUCTURAL FORMULA



Main constituent A

Chemical Name	Nonanoic acid, tetradecyl ester		
CAS No.	72934-15-7	*Weight %*	65.2



Main constituent B

Chemical Name	Nonanoic acid, octadecyl ester		
CAS No.	107647-13-2	*Weight %*	29.85

MOLECULAR WEIGHT
Main constituent A: 382.68 g/mol
Main constituent B: 410.73 g/mol

ANALYTICAL DATA
Reference NMR, IR, GC-MS and UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
~ 95%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)

Chemical Name	Nonanoic acid, tetradecyl ester		
CAS No.	72934-14-6	*Weight %*	1.14
Chemical Name	Octanoic acid, 2-methyl-, hexadecyl ester		
CAS No.	287931-73-1	*Weight %*	1.66

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless liquid/solid

Property	Value	Data Source/Justification
Melting Point	22 °C	Measured
Boiling Point	412 - 417 °C at 101.3 kPa	Measured
Density	941 kg/m^3 at 20 °C	Measured
Vapour Pressure	1.45 × 10^{-8} kPa at 20 °C 2.97 × 10^{-8} kPa at 25 °C	Measured
Water Solubility	3.5 x 10^{-6} g/L at 25 °C [A] 1.7 x 10^{-6} g/L at 25 °C [B]	Measured
Hydrolysis as a Function of pH	Not determined	Contains hydrolysable functionalities, but is not expected to hydrolyse under normal environmental conditions (pH 4-9 and ambient temperatures)
Partition Coefficient (n-octanol/water)	log P_{ow} = 11.18 at 25 °C [A] log P_{ow} = 12.16 at 25 °C [B]	Calculated with KOWWIN v1.68
Adsorption/Desorption	log K_{oc} = 6.24* and 7.04$^{\#}$ [A] log K_{oc} = 6.76* and 7.59$^{\#}$ [B]	Calculated using KOCWIN v2.00, from Molecular Connectivity Index (MCI)* and log Kow$^{\#}$. Deemed immobile according to McCall *et al.,* 1980
Dissociation Constant	Not determined	Does not contain any ionisable functionalities
Particle Size	D_{10} = 1.52 µm D_{50} (median) = 2.70 µm D_{90} = 6.54 µm	Measured
Flash Point	198.5 °C at 101.3 kPa	Measured
Flammability	Not highly flammable	Measured
Autoignition Temperature	320 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

A = Main constituent A
B = Main constituent B

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 in the neat form, as a component of a cosmetic blend at ≤ 40% concentration and as a component of finished cosmetic products 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
Sydney

IDENTITY OF RECIPIENTS
Symrise Australia

TRANSPORTATION AND PACKAGING
The notified chemical in the neat form will be imported in 30 L HDPE plastic barrels. The cosmetic blends containing the notified chemical at ≤ 40% concentration will be imported in 25 kg HDPE plastic canisters. The finished cosmetic products will be packaged in containers suitable for retail sale.

USE
The notified chemical will be used as an emollient in cosmetic products such as body lotion, shower gel, hand cream and soap, at ≤ 10% concentration.

OPERATION DESCRIPTION
Reformulation of the notified chemical or cosmetic blends containing the notified chemical at ≤ 40% concentration into finished cosmetic products may vary depending of 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 end-use products into containers of various sizes.

Finished cosmetic products containing the notified chemical at ≤ 10% concentration will be used by consumers and professionals such as beauticians. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

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 warehouse	None	Incidental
Mixer	4	2
Drum handling	4	2
Drum cleaning/washing	4	2
Maintenance	4	2
Quality control	0.5	2
Packaging	4	2
Professional end users (beauticians)	1 - 8	200

EXPOSURE DETAILS
Transport and storage workers may come into contact with the notified chemical in the neat form or at 40% concentration in cosmetic blends, only in the unlikely event of an accidental spill or rupture of packaging.

Reformulation
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical in its neat form or at ≤ 40% concentration may occur during handling of drums, during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. The notifier states that exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems, and through the use of PPE such as protective clothing, eye protection and suitable gloves.

End-use
Exposure to the notified chemical at ≤ 10% concentration in end-use products may occur in professions where the services provided involve the application of cosmetic products to clients (e.g. workers in beauty salons). The principal route of exposure will be dermal, while ocular exposure is also possible. Such professionals may use some PPE to minimise repeated exposure and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the same products containing the notified chemical.

6.1.2. Public Exposure
Public exposure to the notified chemical is expected to be widespread and frequent through daily use of cosmetic products containing the notified chemical at ≤ 10% concentration. The principal route of exposure will be dermal, while ocular exposure is also possible.

Data on typical use patterns of product categories in which the notified chemical may be used are shown in the following table (SCCS, 2012; ACI, 2010). For the purposes of the exposure assessment via the dermal route, Australian use patterns for the various product categories were assumed to be similar to those in Europe. In the absence of dermal absorption data, a dermal absorption (DA) rate of 100% was assumed for the notified chemical (ECHA, 2014). A lifetime average female body weight (BW) of 64 kg (enHealth, 2012) was used for calculation purposes.

Product type	**Amount** (mg/day)	**C** (%)	**RF** (unitless)	**Daily systemic exposure** (mg/kg bw/day)
Body lotion	7820	10.000	1.000	12.2188
Face cream	1540	10.000	1.000	2.4063
Hand cream	2160	10.000	1.000	3.3750
Shower gel	18670	10.000	0.010	0.2917
Hand wash soap	20000	10.000	0.010	0.3125
Total				**18.6042**

C = concentration (%); RF = retention factor.
Daily systemic exposure = (Amount × C × RF × dermal absorption)/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 table that contain the notified chemical. This would result in a combined internal dose of 18.6 mg/kg bw/day.

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 > 2000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Human, skin sensitisation – RIPT (100%)	no evidence of sensitisation
Rat, combined oral repeated dose oral toxicity with reproduction/developmental screening test	NOAEL (parental) = 1,000 mg/kg bw/day NOAEL (reprod/develop) = 1,000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian chromosome aberration test	non genotoxic
Genotoxicity – *in vitro* mammalian gene mutation test	non genotoxic

Toxicokinetics

Given the low molecular weight of the notified chemical (382 - 410 g/mol), absorption across the respiratory or gastrointestinal tract may occur. However, based on the low water solubility and high lipophilicity of the notified chemical, dermal absorption is expected to be limited.

Acute toxicity

The notified chemical was found to be of low acute oral and dermal toxicity in studies conducted in rats.

Irritation and sensitisation

Based on studies conducted in rabbits, the notified chemical is not irritating to skin and slightly irritating to eyes.

In the eye irritation study, moderate conjunctival irritation was noted in all animals 1 hour after treatment. This was reduced to minimal conjunctival irritation at the 24 hour time point. By the 48 hour time point, all treated eyes appeared normal. No corneal or iridial effects were noted during the study.

The notified chemical was not a skin sensitiser in a guinea pig maximisation test. The notified chemical also tested negative in a human repeat insult patch test when tested at 100% concentration.

Repeated dose toxicity and toxicity for reproduction

In a combined oral repeated dose toxicity study with reproduction/developmental screening in rats, the notified chemical was administered daily by gavage for 28 days in males, approx. 7 weeks in females (14 days prior to mating, during mating and gestation, up to day 4 post-partum) and 39 days in recovery animals followed by a 14-day recovery period. The dose levels were 100, 300 and 1,000 mg/kg bw/day. The only noted treatment related effect was salivation at the high dose. No reproduction or developmental toxicity was observed up to the highest dose tested.

The No Observed Adverse Effect Level (NOAEL) of 1,000 mg/kg bw/day was established for parental toxicity and reproduction/developmental toxicity.

Mutagenicity/Genotoxicity

The notified chemical tested negative in a bacterial reverse mutation assay, in an *in vitro* mammalian cell chromosome aberration test in human lymphocytes and in an *in vitro* mammalian cell gene mutation test in Chinese hamster lung fibroblast (V79) cells.

Health 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.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Based on the toxicological information provided, the notified chemical is of low hazard presenting only as a slight eye irritant. The notified chemical has the potential to cross biological membranes; however, the parental and reproductive/developmental toxicity of the notified chemical following repeated exposure is very low.

Reformulation

During reformulation, workers may be at risk of slight eye irritation effects. 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 and eye protection) will also be used to limit worker exposure.

End-Use

Workers involved in professions where the services involve application of cosmetic products containing the notified chemical to clients (e.g. beauty salon workers) may be exposed to the notified chemical at ≤ 10% concentration. Dermal, and to a lesser extent, ocular exposure may occur. PPE may be employed by workers 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 for consumers using the various products containing the notified chemical.

Therefore, under the occupational settings described, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

6.3.2. Public Health

Based on the toxicological information provided, the notified chemical is of low hazard presenting only as a slight eye irritant. At the proposed use concentration (≤ 10%) in cosmetic products, irritation effects are not expected.

Therefore, based on the information available, the risk to the public associated with use of the notified chemical at ≤ 10% 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 in its neat form, as a component of cosmetic blends or as a component of finished cosmetic products. There is unlikely to be any significant release of the notified chemical to the environment from transport and storage, except in the case of accidental spills and leaks. In the event of spills, the products containing the notified chemical is expected to be collected with absorbents, and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve blending operations that will be highly automated, and is expected to occur within a fully enclosed environment followed by automated filling of the reformulated end-use products into containers of various sizes. Wastes containing the notified chemical generated during reformulation include equipment wash water (estimated to be < 1% of the import volume by the notifier), residues in empty import containers and spilt materials. Wash waters are expected to be released to on-site waste water treatment processes, or sewers in a worst case scenario. Empty import containers and residues are expected to be recycled or disposed of through licensed waste management services.

Release of Chemical from Use

The notified chemical is expected to be released to the aquatic compartment through sewers during its use in cosmetic products across Australia.

RELEASE OF CHEMICAL FROM DISPOSAL

Only a small amount of residue is expected to remain in containers upon disposal. Wastes and residues of the notified chemical in empty end-use containers are likely to either share the fate of the container and be disposed of to landfill, or be released to the sewer system when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified chemical is expected to be released to sewers on a nationwide basis. The submitted biodegradation studies indicate that the notified chemical is expected to be rapidly degraded in sewage treatment plants (STPs). For the details of the environmental fate studies please refer to Appendix C.

Fate in air is not considered important for exposure because the notified chemical is only slightly volatile, and hence is expected to be present in air at very low levels. Any notified chemical released to the atmospheric compartment is not expected to persist [$t_{1/2}$ ~ 4 hours (AOPWIN v1.92, US EPA 2012)].

In STPs, where most of the chemical is likely to end up, a significant proportion of the notified chemical is expected to be associated with sewage sludge phase, based on its low water solubility and lipophilicity. Therefore, a significant proportion of the notified chemical may be removed during sewage treatment, thus reducing its release to surface waters. A proportion of the notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. The notified chemical is not expected to be immobile in soil and sludge.

The notified chemical has the potential to bioaccumulate based on the log Pow of its main constituents. For purposes of determining bioaccumulative potential and in the absence of any measured BCF or BAF, a log Pow > 4.2 indicates that the notified chemical has the potential to bioaccumulate. However, there is increased uncertainty in predicting the bioaccumulation using log Pow > 6 (EPHC, 2007).

The notified chemical is expected to degrade via biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume the worst case scenario with 100% release of the notified chemical into sewer systems nationwide over 365 days per annum. Based on the estimated log Pow of its two main notified chemical constituents, as well as its ready biodegradability, it was assumed there will be 89% removal of the notified chemical during sewage treatment processes. The resultant PEC in sewage effluent on a nationwide basis is estimated as follows:

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:	2.7	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	24.4	million
Removal within STP	89 %	
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.062	µg/L
PEC - Ocean:	0.0062	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 0.062 µg/L may potentially result in a soil concentration of approximately 4.1 x 10^{-4} mg/kg.

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 4.4 mg/kg (dry weight). Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1,500 kg/m^3 and a soil-mixing zone of 10 cm, the concentration of the notified chemical may approximate 0.029 mg/kg in applied soil. The notified chemical is not expected to accumulate in soil after irrigation or biosolids application due to its ready biodegradability.

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*
Fish Toxicity	96h LC50 > 0.1 mg/L	Not toxic to fish up to water solubility limit
Daphnia Toxicity	21 d NOEC = 5 µg/L	Not toxic to aquatic invertebrates up to water solubility limit
Algal Toxicity	72 h ErC50 > 0.0044 mg/L	Not toxic to algae up to water solubility limit
Inhibition of Bacterial Respiration	3h EC50 > 1,013 mg/L	Not inhibitory to microbial respiration
Earthworm toxicity	14 d LC50 > 1,000 mg/kg dry weight	Not toxic to earthworms

Based on the acute ecotoxicological endpoints, the notified chemical is not expected to be toxic to aquatic organisms to the limits of water solubility. Therefore, the notified chemical cannot be classified according to the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations 2009).

Taking into account that the notified chemical is likely to rapidly biodegrade it has not formally classified as a long-term aquatic hazard.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentrations (PNEC) for the notified chemical have not been derived as no effects could be established below the limit of water solubility of the notified chemical.

7.3. Environmental Risk Assessment

No risk quotients were determined for discharge of effluents containing the notified chemical to the aquatic environment as no effects could be established below the limit of water solubility of the notified chemical. The notified chemical has bioaccumulation potential based on its log Pow. However, the notified chemical is expected to biodegrade rapidly, and will partition to sludge and soil. Thus the notified chemical is unlikely to persist in the environment or be bioavailable. Therefore, based on the assessed use pattern as a component of cosmetic products, the fate of the notified chemical in the STP, and on no observed toxic effects to the limits of water solubility, the notified chemical is not expected to pose an unreasonable risk to the aquatic environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point 22 °C

Method	OECD TG 102 Melting Point/Melting Range (1995) EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature
Remarks	Determined by differential scanning calorimetry.
Test Facility	Siemens (2010a)

Boiling Point 412 - 417 °C at 101.3 kPa

Method	OECD TG 103 Boiling Point (1995) EC Council Regulation No 440/2008 A.2 Boiling Temperature
Remarks	Determined by differential scanning calorimetry.
Test Facility	Siemens (2010a)

Density 941 kg/m^3 at 20 °C

Method	OECD TG 109 Density of Liquids and Solids (1995) EC Council Regulation No 440/2008 A.3 Relative Density
Remarks	Gas comparison pycnometer method.
Test Facility	Siemens (2010b)

Vapour Pressure 1.45×10^{-8} kPa at 20 °C
2.97×10^{-8} kPa at 25 °C
7.59×10^{-7} kPa at 50 °C

Method	OECD TG 104 Vapour Pressure (2006) EC Council Regulation No 440/2008 A.4 Vapour Pressure
Remarks	Vapour pressure balance (effusion) method. Vapour pressure measurements were below the point of detection at temperatures < 51 °C. Vapour pressures at 20, 25 and 50 °C were calculated from the measured values obtained above 51 °C.
Test Facility	Siemens (2010c)

Water Solubility 3.5×10^{-6} g/L at 25 °C (Main constituent A)
1.7×10^{-6} g/L at 25 °C (Main constituent B).

Method	OECD TG 105 Water Solubility (modification): Slow stirring method (1995) EC Council Regulation No 440/2008 A.6 Water Solubility (2008)
Remarks	Both of the standard methods (Flask and Column Elution) were tested and found to be unsuitable due to low water solubility. The slow stirring method is a modified shake flask method, involving continuously stirring the test item, introduced on top of the water phase in a thin layer until equilibrium was reached. Samples were taken by constant circulation of the saturated solution through a HPLC pump and subsequent online extraction using a reversed phase chromatographic column. The validity criteria of the test guideline were met in spite of modifications, and it is unlikely that deviations from the standard methodology would have significantly affected the reliability of test results. Very slightly water soluble according to Mensink *et al*., 1995.
Test Facility	U N-LAB (2011a)

Partition Coefficient (n-octanol/water) Could not be measured

Method	OECD 123 Partition Coefficient (n-octanol/water): Slow-Stirring Method
Remarks	After stirring for 35 days, the concentration of test item in saturated n-octanol was 916.22 mg/L, and that in saturated water was below the limit of detection. The method is not suitable for compounds with a log P_{ow} of < 8.2. It was estimated (with EPI Suite software (KOWWIN vl.68)) that the log P_{ow} of the two main constituents of the notified chemical are 11.18 and 12.16 for main constituent A and main constituent B, respectively.
Test Facility	PTLSY (2017a)

Particle Size

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

Diameter (μm)	*Percentage of particles below diameter*
1.52	10
2.70*	50
6.54	90

* Median diameter

Remarks Laser scattering/diffraction method. The test substance was dispersed in water using sonication.
Test Facility PTLSY (2017b)

Flash Point 198.5 °C at 101.3 kPa

Method EC Council Regulation No 440/2008 A.9 Flash Point
Remarks Closed cup method.
Test Facility Siemens (2010d)

Flammability Not highly flammable

Method EC Council Regulation No 440/2008 A.10 Flammability (Solids)
Remarks The study authors noted that the test substance pile could not be ignited with a flame during the preliminary test. The test item was noted to have melted into a white liquid when the flame was applied. No continuous combustion or smoulder was observed after flame removal. No main test was performed.
Test Facility PTLSY (2017c)

Autoignition Temperature 320 °C

Method EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Remarks None
Test Facility Siemens (2010e)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD

OECD TG 420 Acute Oral Toxicity – Fixed Dose Procedure (2001)
EC Council Regulation No 440/2008 B.1 bis Acute toxicity (oral) fixed dose method

Species/Strain	Sprague-Dawley Rat / CD
Vehicle	300 mg/kg bw – arachis oil BP 2000 mg/kg bw - none
Remarks - Method	No significant protocol deviations. A preliminary test was performed on one female animal with 300 mg/kg bw of the test substance. As no mortality was observed, the test dose was increased to 2000 mg/kg bw.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5F	2000	0/5

LD50	> 2000 mg/kg bw
Signs of Toxicity	Noted signs of toxicity after treatment with 300 mg/kg bw of the test substance included ataxia, hunched posture, pilo-erection and tiptoe gait. These signs were observed from 4 hours after treatment until 1 day after treatment. No signs of systemic toxicity were noted after dosing with 2000 mg/kg bw of the test substance.
Effects in Organs	No abnormalities detected at post-mortem.
Remarks - Results	All animals made expected body weight gains throughout the study.

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

TEST FACILITY: Harlan (2009a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE: Notified chemical

METHOD

OECD TG 402 Acute Dermal Toxicity – Limit Test (1987)
EC Council Regulation No 440/2008 B.3 Acute Toxicity (Dermal) - Limit Test

Species/Strain	Sprague-Dawley Rat / CD
Vehicle	None
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5F	2000	0/5
2	5M	2000	0/5

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	None observed during the study.
Signs of Toxicity - Systemic	None observed during the study.
Effects in Organs	No abnormalities detected at post-mortem.
Remarks - Results	All males and two female animals showed expected gains in body weight during the study. Three female animals showed either minimal or no

bodyweight gain during the first week after treatment. Three female animals displayed bodyweight loss during the second week after treatment.

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

TEST FACILITY Harlan (2008a)

B.3. Irritation – skin

TEST SUBSTANCE Notified chemical

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion (2002)
EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation)

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations

RESULTS

Remarks - Results No signs of dermal irritation were noted during the observation period after treatment with the test substance.

All animals showed expected gains in body weight during the study.

CONCLUSION The notified chemical is non-irritating to the skin.

TEST FACILITY Safepharm (2008a)

B.4. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion (2002)
EC Directive 2004/73/EC B.5 Acute Toxicity (Eye Irritation)

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	72 hours
Remarks - Method	No significant protocol deviations. The test substance was applied undiluted.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.33	0.33	0.33	2	< 48 h	0
Conjunctiva: chemosis	0	0	0.33	2	< 48 h	0
Conjunctiva: discharge	0	0	0	1	< 48 h	0

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

Remarks - Results No corneal or iridial effects were noted during the study. Moderate conjunctival irritation was noted in all animals 1 hour after treatment. This was reduced to minimal conjunctival irritation at the 24 hour time point. By the 48 hour time point, all treated eyes appeared normal.

All animals showed expected body weight gain during the study.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Safepharm (2008b)

B.5. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation – Guinea Pig Maximisation Test (1992)
EC Directive 96/54/EC B.6 Skin Sensitisation - Guinea Pig Maximisation Test

Species/Strain Guinea pig/ Dunkin Hartley

PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: > 10%
topical: 10 %

MAIN STUDY

Number of Animals Test Group: 10 Vehicle Control Group: 5

Vehicle Sesame oil

Positive control Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using 2% benzocaine solution.

INDUCTION PHASE Induction Concentration:
intradermal: 10% (in sesame oil)
topical: 50% (in sesame oil)

Signs of Irritation

CHALLENGE PHASE

1st challenge topical: 10% (in sesame oil)

Remarks - Method No significant protocol deviations. In the preliminary study, the topical treatment at 50% concentration did not induce irritation. In the main study therefore, the skin of each animal was coated with sodium lauryl sulfate the day before the topical induction stage in order to induce local irritation.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*	
		48 h	*72 h*
Test Group	10%	0/10	0/10
Control Group	10%	0/5	0/5

Remarks - Results No skin reactions were observed after challenge with the test substance in any of the animals. The positive control performed as expected, confirming the validity of the test system.

Body weight gains were comparable to those seen in the control group animals.

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

TEST FACILITY LPT (2008)

B.6. Skin sensitisation – human volunteers

TEST SUBSTANCE Notified chemical

METHOD Repeated insult patch test with challenge

Study Design Induction Procedure: Patches containing 0.2 g test substance were applied 3 times per week (Monday, Wednesday and Friday) for a total of 9 applications. Patches were removed by the applicants after 24 hours and graded after an additional 24 h (or 48 h for patches applied on Friday).

Rest Period: approx. 14 days
Challenge Procedure: A patch was applied to a naïve site. Patches were

	removed by the applicants after 24 h. Sites were graded immediately following and 48 h post-patch removal.
Study Group	83 F, 32 M; age range 18 - 70 years
Vehicle	None
Remarks - Method	Occluded patches were used. The test substance was spread on ¾ inch × ¾ inch patches.

RESULTS

Remarks - Results	106/115 subjects completed the study. The authors of this study note that the remaining subjects discontinued their participation for various reasons, which were not related to the application of the test material. No visible skin reaction was observed on any of the subjects during the induction or challenge phases.

CONCLUSION	The notified chemical was non-sensitising under the conditions of the test.
TEST FACILITY	Consumer Product Testing Co. (2009)

B.7. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (1996) OPPTS (EPA) Guideline 870.3650 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (2000)
Species/Strain	Rat/Wistar (Han:Rcc)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days for main group males (2 weeks prior to mating, during mating and up to the day prior to scheduled necropsy) and Approx. 7 weeks for main group females (2 weeks prior to mating, during mating, gestation, and up to the 4th day post-partum) 39 days for recovery animals - both sexes Dose regimen: 7 days per week Post-exposure observation period: 2 weeks
Vehicle	Peanut oil
Remarks - Method	No significant protocol deviations. Dose levels were selected as based on the results of a dose-range finding study performed previously (Harlan Laboratories Study C76932).

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
control	10M / 10F	0	0/20
low dose	10M / 10F	100	0/20
mid dose	10M / 10F	300	0/20
high dose	10M / 10F	1000	0/20
control recovery	10M / 10F	0	0/20
high dose recovery	10M / 10F	1000	0/20

Mortality and Time to Death
No unscheduled mortality occurred during the study period.

Clinical Observations
No test substance-related effects on locomotor activity, food consumption, body weight or body weight gain were observed.

At the dose level of 1000 mg/kg bw/day, salivation was observed in main group females and in males and females of the recovery group during treatment and on the first day of the recovery period.

Laboratory Findings – Clinical Chemistry, Haematology
No test substance-related effects were noted on haematology and biochemical parameters

Reproductive/developmental findings
No test substance related effects were observed on mating performance, fertility, corpora lutea count, implantation rate and post-implantation loss, litter size or postnatal loss.

Effects in Organs
No test substance-related effects on absolute or relative organ weights, macroscopical findings or histopathological changes were noted.

Remarks – Results
The only test substance-related effect was salivation. The authors of this study however, considered this a sign of discomfort and not an adverse effect.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) for parental toxicity and reproduction/developmental toxicity was established as 1000 mg/kg bw/day in this study.

TEST FACILITY Harlan (2010)

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

Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	S9 fraction from phenobarbital/β-napthoflavone-induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 50 - 5000 µg/plate b) Without metabolic activation: 50 – 5000 µg/plate
Vehicle	Acetone
Remarks - Method	In the preliminary test, only the TA100 strain was tested.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5000	> 5000	≥ 1500	Negative
Test 2		> 5000	≥ 1500	Negative
Present				
Test 1	> 5000	> 5000	≥ 1500	Negative
Test 2		> 5000	≥ 1500	Negative

Remarks - Results No substantial increase in revertant colony numbers of any of the five tester strains was observed following treatment with the test substance at any dose level, in the presence or absence of metabolic activation. Positive controls performed as expected, confirming the validity of the test system.

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

TEST FACILITY Harlan (2008b)

B.9. Genotoxicity – *in vitro* mammalian chromosome aberration

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test (1998) EC Directive 2000/32/EC B.10 Mutagenicity - *In vitro* Mammalian Chromosome Aberration Test (2008)
Species/Strain	Human
Cell Type/Cell Line	Lymphocyte
Metabolic Activation System	S9 fraction from phenobarbital/β-napthoflavone induced rat liver
Vehicle	Acetone
Remarks - Method	No significant deviations from the protocol. A preliminary experiment was conducted to determine the dose range for the main test. As the preliminary test fulfilled the requirements for cytogenic evaluation, the preliminary test was designated as Test 1.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	25.4, 44.5, 77.9, 136.3, 238.5, 417.4, 730.5, 1278.4*, 2237.1*, 3915.0*	4 h	22 h
Test 2	77.9, 136.3, 238.5, 417.4, 730.5, 1278.4*, 2237.1*, 3915.0*	22 h	22 h
Present			
Test 1	25.4, 44.5, 77.9, 136.3, 238.5, 417.4, 730.5, 1278.4*, 2237.1*, 3915.0*	4h	22 h
Test 2	417.4, 730.5, 1278.4*, 2237.1*, 3915.0*	4h	22 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 3915.0	-	> 3915.0	Negative
Test 2	-	> 3915.0	> 3915.0	Negative
Present				
Test 1	> 3915.0	-	> 3915.0	Negative
Test 2	-	> 3915.0	> 3915.0	Negative

Remarks - Results	In the presence and absence of metabolic activation, there were no biologically relevant increases in structural chromosomal aberrations after treatment with the test substance. However in Test 1 with metabolic activation statistically significant increases were observed after treatment with 2237.1 and 3915.0 µg/mL. The values were within the historical solvent control range and were not confirmed in Test 2 with metabolic activation. Therefore these values were considered by the study authors to be biologically irrelevant. In the presence and absence of metabolic activation, there were no biologically relevant increases in polyploid cells after treatment with the test substance. The solvent and positive controls performed as expected, confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to human lymphocytes treated *in vitro* under the conditions of the test.
TEST FACILITY	Harlan CCR (2010a)

B.10. Genotoxicity – *in vitro*

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test (1997) EC Directive 2000/32/EC B.17 Mutagenicity - *In vitro* Mammalian Cell Gene Mutation Test (2008)
Species/Strain	Chinese hamster
Cell Type/Cell Line	Lung fibroblast/ V79
Metabolic Activation System	S9 fraction from phenobarbital/β-napthoflavone induced rat liver
Vehicle	Acetone
Remarks - Method	Only minor deviations to the study plan were noted. The authors of this study state that these deviations have no detrimental impact upon the study outcome. The V79 cells were tested with the test substance for potential to induce mutations at the HPRT locus. Preliminary experiments were conducted to determine the dose range for the main study. Each test consisted of two cultures run in duplicate.

Preliminary Test

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	30.6, 61.2, 122.3, 244.7, 489.4, 978.8, 1957.5, 3915.0#	4 h	7 days	8 days
Test 2	30.6, 61.2#, 122.3#, 244.7#, 489.4#, 978.8#, 1957.5#, 3915.0#	24 h	7 days	8 days
Present				
Test 1	30.6, 61.2, 122.3, 244.7#, 489.4#, 978.8#, 1957.5#, 3915.0#	4 h	7 days	8 days
Test 2	-	-	-	-

#Precipitation

Main Test

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	122.3, 244.7*, 489.8*, 978.8*, 1957.5*, 3915.0*	4 h	7 days	8 days
Test 2	15.3, 30.6, 61.2, 122.3, 244.7*, 489.4*, 978.8*, 1957.5*, 3915.0*	24 h	7 days	8 days
Present				
Test 1	30.6, 61.2*, 122.3*, 244.7*, 489.8*, 3915.0*	4 h	7 days	8 days
Test 2	244.7*, 489.4*, 978.8*, 1957.5*, 3915.0*	4 h	7 days	8 days

*Cultures selected for mutation analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 3915.0	> 3915.0	> 3915.0	Negative
Test 2	> 3915.0	> 3915.0	≥ 978.8	Negative
Present				
Test 1	> 3915.0	> 3915.0	> 3915.0	Negative
Test 2	-	> 3915.0	> 3915.0	Negative

Remarks - Results	In the presence and absence of metabolic activation, there were no biologically relevant increases in mutant colonies after treatment with the

	test item. The negative and positive controls performed as expected, confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to the HRPT locus in Chinese hamster V79 lung fibroblasts treated *in vitro* under the conditions of the test.
TEST FACILITY	Harlan CCR (2010b)

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 from a sewage treatment plant fed mainly with municipal wastewater.
Exposure Period	28 and 35 days
Auxiliary Solvent	None.
Analytical Monitoring	Oxygen demand was measured continuously using a SAPROMAT respirometer.
Remarks - Method	The purity of the test item was 95% (62.4% and 29.8% of constituents A and B, respectively). No significant deviation from the test guidelines were reported. Sodium benzoate was used as a reference item. An inoculum blank, a toxicity control (105.2 mg/L SymMollient S, and 100 mg/L sodium benzoate) and an abiotic control (105.2 mg/L SymMollient S and sterilising agent) were also included in the test design. Test item treatments (in duplicate) were 25, 50 and 105.2 mg/L, corrected for uptake by the blank inoculum.

RESULTS

Test substance – Run 2			*Sodium benzoate*	
Day	*% Degradation (Mean ± SD)*		*Day*	*% Degradation (Mean ± SD)*
	25 mg/L	*50 mg/L*		
14	86 ± 3.9	76 ± 2.9	14	81.4 ± 0
28	92.9 ± 2.9	89.1 ± 0.5	28	86.2 ± 0.4

Remarks - Results	All validity criteria were met. No inhibitory effects were observed for the test item (toxicity control). After 28 days biodegradation of > 60% was observed at the test item concentrations of 25 mg/L and 50 mg/L. No significant abiotic degradation was observed.
CONCLUSION	The notified chemical is readily biodegradable.
TEST FACILITY	IME (2010a)

C.1.2. Inherent biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD 302 C Inherent Biodegradability: Modified MITI Test (II)
Inoculum	Activated sludge the sources of which included a combination of sewage treatment works, rivers, lakes, etc.
Exposure Period	28 days
Auxiliary Solvent	None.
Analytical Monitoring	Biochemical Oxygen Demand (BOD) was measured by a respirometer system.
Remarks – Method	The purity of the test item was 99.5%, but no information was provided on the proportion of the two main constituents A and B. No significant deviation from the test guidelines were reported. Sodium benzoate was used as a reference item. Blank inoculum control and an abiotic control (31.26 mg/L SymMollient S and sterilised deionised water) were also included in the test design. The concentration of the test item treatment was 30.54 mg/L and performed in triplicate.

RESULTS

Test substance		*<Reference Substance>*	
Day	*% Degradation (mean)*	*Day*	*% Degradation*
14	72.6	14	88.4
28	87.4	28	90.2

Remarks – Results: All validity criteria were met. No inhibitory effects were observed for the abiotic control, i.e., no significant abiotic degradation was observed. Based on the calculation for BOD, the percentage biodegradation after treatment of 28 days averaged 87.4% (> 70%).

CONCLUSION: The notified chemical is inherently and ultimately biodegradable.

TEST FACILITY: SYRICI (2017a)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 203 Fish, Acute Toxicity Test – semi static
EC Council Regulation No 440/2008 C.1 Acute Toxicity for Fish - semi static

Species: *Oncorhynchus mykiss*
Exposure Period: 96 hours
Auxiliary Solvent: Dimethylformamide
Water Hardness: 140 mg $CaCO_3$/L
Analytical Monitoring: High performance liquid chromatography mass spectrometry (HPLC-MS).
Remarks – Method: Test item was 96.3% purity; 64.5% and 31.8% constituent A and B, respectively. A limit test was conducted based on the results of a range finding test, where fish were exposed to the test item at a nominal concentration of 0.090 and 0.90 mg/L. A test item of 0.10 mg/L (mean measured of centrifuged test media concentration), a control and a solvent control (100 µL/L of dimethylformamide in dechlorinated tap water) group were included in the limit test design. The test involved daily renewal of the test preparations.

Temperature (14°C to 16°C) and dissolved oxygen levels [≥ 9.8 mg O_2/L (95% of the air saturation value)] were kept relatively stable throughout the test.

All validity criteria for the test were satisfied. The test preparations were observed to be clear, colourless solutions for all test media throughout the test.

RESULTS

Treatment	*Actual Concentration (mg/L)*	*No. Fish*	*Mortality*				
			3 h	*24 h*	*48 h*	*72 h*	*96 h*
Control	0	7	0	0	0	0	0
Solvent control	0	7	0	0	0	0	0
Test item – Replicate 1	0.10	7	0	0	0	0	0
Test item – Replicate 2	0.10	7	0	0	0	0	0

LC50: > 0.10 mg/L at 96 hours
Remarks – Results: Concentrations in the fresh media ranged from 61 % to 117% of nominal for the untreated samples at 0, 24, 48 and 72 hours. In old media samples taken at 24, 48, 72 and 96 hours there was a decline in measured concentrations (39% to 85% of nominal) with an exception attributed to

sampling error or analytical variation.

There were no sub-lethal effects of exposure observed in 14 fish exposed to a geometric mean measured test concentration of 0.10 mg/L for a period of 96 hours.

CONCLUSION The notified chemical is not toxic to fish to the limits of water solubility.

TEST FACILITY Harlan (2009b)

C.2.2. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 211 *Daphnia magna* Reproduction test – semi static
EC Council Regulation No 440/2008 C.2 Acute Toxicity for *Daphnia*

Species *Daphnia magna*
Exposure Period 21 d
Auxiliary Solvent Methanol
Water Hardness 144 – 182 mg $CaCO_3$/L in control and treatment vessels measured on days 0, 1, 7, 8, 15 and 16.
Analytical Monitoring Ultra-performance liquid chromatography - tandem mass spectrometer (UPLC-MS/MS)
Remarks - Method The purity of the test item was 96.3% (64.5% and 31.8% of constituents A and B, respectively).

No significant deviations from the test guidelines were reported. A limit test was conducted at the water solubility limit of the test chemical, where daphnid were exposed to a nominal concentration of the test item of 5.0 µg/L. A control and solvent control (0.05 ml methanol/L dilution water) were also included in the limit test design. The test method was semi-static with a daily renewal of the test solutions. The test item was analysed in the stock solutions used in the test, and were determined to be within 103 to 121% of the nominal concentrations. Ten daphnids were used per test concentration, solvent control and control.

An acute immobilization using a reference item (potassium dichromate) was run less than one month prior to this study being conducted.

Survival of parental daphnids and number of offspring released per female daphnid (*Daphnia magna*)

Test day	A	B	C	D	E	F	G	H	I	J	Number of Adult Daphnids Immobilized	Percent Survival
Total Number of Offspring Released per Daphnid												
21	96	81	88	88	87	80	88	92	90	96	0	100

Nominal loading retested, daphnid survival and cumulative mean number of offspring released, mean total body length and dry weight of daphnids (*Daphnia magna*)

Test Day 21				
Nominal Loading arte (mg/L)	Mean Percent Survival	Mean Number of Offspring Released per female (SD)$^{\alpha}$	Mean Total Body Length in mm (SD)$^{\alpha}$	Mean Dry Weight in mg (SD)
Solvent Control	100	88 (5)	5.08 (0.23)	0.89 (not reported)
Control	100	89 (8)	5.13 (0.23)	1.34 (not reported)
0.005	100	89 (5)	5.10 (0.20)	0.91 (not reported)

Remarks - Results The test was considered valid. No males and ephippia were observed in the respective control or test group. The reference item test had a 24 h EC50 = 1.29 mg/L, which is within the recommended concentration range.

There were no significant effects on reproductive parameters in the test group relative to the control (one-way analysis of variance, Dunnett's method, $\alpha = 0.05$).

No adult mortality or immobilization of parental daphnids was observed in control, solvent control and test solution.

The mean total body lengths of all parental daphnids of the test and control groups were determined at the end of the study, and found not to be significantly different (Kruskal-Wallis one-way analysis of variance on ranks, $\alpha = 0.05$).

CONCLUSION The notified chemical is not toxic to aquatic invertebrates to the limits of water solubility.

TEST FACILITY U N-LAB (2011b)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test - Static
EC Council Regulation No 440/2008 C.3 Algal Inhibition Test

Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 2.0 mg/L Actual: 0.0044 mg/L
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	Gas chromatography coupled with flame ionization detector
Remarks - Method	The purity of the test item was 99.5%, with no information provided on the proportion of main constituents A and B. No significant deviations from the test guidelines were reported. Based on the results of a preliminary test, a limit test was performed where algae were exposed under static conditions to the notified chemical at a concentration of 2.0 mg/L (nominal), 0.0044 mg/L (initial measured concentration) and 0.0011 mg/L (geometric mean of initial and old measured concentration at 0 h, 24 h, 48 h and 72 h). Ten replicates of the test item and a control were included in the test design.

RESULTS

Biomass (inhibition of yield) *EyC50 mg/L at 72 h*	*Growth (inhibition of growth rate)* *ErC50 mg/L at 72 h*
> 0.0044*	> 0.0044*

* initial measured concentration

Remarks - Results All validity criteria for the test were satisfied.

CONCLUSION The notified chemical is not toxic to algae to the limits of water solubility.

TEST FACILITY SYRICI (2017b)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 209 Activated Sludge, Respiration Inhibition Test
EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test

Inoculum	Activated sludge from a wastewater treatment plant fed mainly by municipal wastewater.
Exposure Period	3 hours
Concentration Range	Nominal: 12.5 – 1012.5 mg/L
Remarks – Method	The purity of the test item was 95% (65.2% and 29.8% of constituents A and B, respectively). There were no major deviations from the test guidelines. The test was carried out based on results of a range-finding test. The test item was not measured over the duration of the test. 3,5-dichlorophenol was used as the reference item.
RESULTS	
EC50	> 1012.5 mg/L
NOEC	1012.5 mg/L
Remarks – Results	All validity criteria for the test were satisfied. The EC50 of the reference item 3,5-dichlorophenol for respiration inhibition was between 5.0 and 30.0 mg/L (5.1 mg/L). No important physical-chemical oxygen consumption by the test item was detected after three hours.
CONCLUSION	Not inhibitory to microbial respiration.
TEST FACILITY	IME (2010b)

C.2.5. Acute toxicity to earthworms

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 207 Earthworm, Acute Toxicity Tests
Remarks - Method	The purity of the test item was 99.5%, with no information provided on the proportion of main constituents A and B. A reference substance (chloracetamide) test was conducted ~6 months prior to the testing of the notified chemical. In a limit test, earthworms (*Eisenia foetida*) were exposed to 1,000 mg/kg dry weight of the notified chemical in artificial soil. A control group was run concurrently with the test substance. There were 4 replicates per test treatment and control, and 10 earthworms in each vessel. Mortality was recorded after 7 and 14 days of exposure. The earthworms were keep under continuous light at the test system was kept at a temperature of 19.3 °C - 21.5 °C, and a soil moisture content of 65-85 %.
RESULTS	
Remarks - Results	The 14-d LC50 (95% confidence limits) for the reference substance was 42.36 (37.20 - 48.28) mg/kg dry weight and met the method requirement. No mortalities were observed in the control and test treatment. The 14-days LC50 of the notified chemical was greater >1,000 mg/kg dry weight.
CONCLUSION	The notified chemical is not toxic to earthworms.
TEST FACILITY	SYRICI (2017c)

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