File No: LTD/2019

April 2018

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

2*H*-2,4a-Methanonaphthalene, 1,3,4,5,6,7-hexahydro-7-methoxy-1,1,5,5-tetramethyl-

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:

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX:	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

TABLE OF CONTENTS

SUMMARY

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2019	Symrise Pty Ltd	2*H*-2,4a-Methanonaphthalene, 1,3,4,5,6,7-hexahydro-7-methoxy-1,1,5,5-tetramethyl-	No	≤ 1 tonne per annum	Fragrance 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.

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

Hazard classification	*Hazard statement*
Chronic aquatic toxicity (Category 2)	H411: Toxic to aquatic life with long lasting effects

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

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

Environmental risk assessment
On the basis of the PEC/PNEC ratio 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 safe work practices to minimise occupational exposure to the notified chemical during reformulation processes:
  - Avoid eye contact
- A copy of the SDS should be easily accessible to employees.
- If products and mixtures containing the notified chemical is 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 fragrance 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
Low Volume Chemical Permit (NICNAS)

NOTIFICATION IN OTHER COUNTRIES
EU (2008), Philippines (2016)

2. IDENTITY OF CHEMICAL

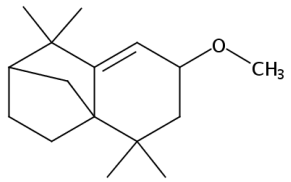
MARKETING NAME
SymRoxane

CAS NUMBER
676125-00-1

CHEMICAL NAME
2*H*-2,4a-Methanonaphthalene, 1,3,4,5,6,7-hexahydro-7-methoxy-1,1,5,5-tetramethyl-

MOLECULAR FORMULA
$C_{16}H_{26}O$

STRUCTURAL FORMULA



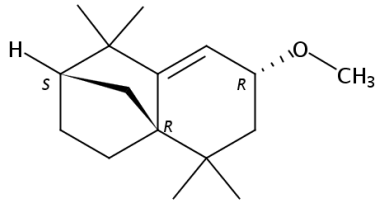
MOLECULAR WEIGHT
234.38 g/mol

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

3. COMPOSITION

DEGREE OF PURITY
~95%

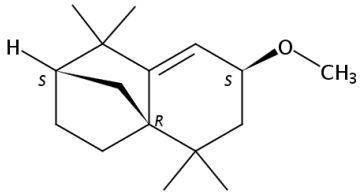
The notified chemical is comprised of the following isomers:



(65-80%)

Relative stereochemistry

2*H*-2,4a-Methanonaphthalene, 1,3,4,5,6,7-hexahydro-7-methoxy-1,1,5,5-tetramethyl-, (2*S*,4a*R*,7*R*)-*rel*



(15-25%)

Relative stereochemistry

2*H*-2,4a-Methanonaphthalene, 1,3,4,5,6,7-hexahydro-7-methoxy-1,1,5,5-tetramethyl-, (2*S*,4a*R*,7*S*)-*rel*

IMPURITIES/RESIDUAL MONOMERS
The notified chemical contains three impurities by GC-MS at concentrations of 0.57%, 1.08% and 2.5%. The impurities have not been identified.

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Clear liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -80 °C	Measured
Boiling Point	287 - 288.5 °C at 101.3 kPa	Measured
Density	970 kg/m^3 at 20 °C	Measured
Vapour Pressure	4.2×10^{-3} kPa at 25 °C	Measured
Water Solubility	6.61 x 10^{-3} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Stable at pH 7 and pH 9 At pH 4 $t_{½}$ = < 1 day at 25°C	Measured
Partition Coefficient (n-octanol/water)	log Pow = 4.51 at 21.5 ± 1 °C	Measured
Adsorption/Desorption	log K_{oc} = 3.85 - 4.99 at 21.5 °C	Measured
Dissociation Constant	Not determined	No dissociable functionality
Flash Point	134 °C at 101.3 kPa	Measured
Flammability	Not determined	Not expected to be flammable based on measured flash point
Autoignition Temperature	235 °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

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 into Australia mostly as a component of fragrance oil at ≤ 50% concentration. The notified chemical may also be imported into Australia in its neat form or as a component of finished consumer products such as fine fragrances, other cosmetic products and household cleaning products at ≤ 7.5% 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

TRANSPORTATION AND PACKAGING
The notified chemical will be imported as a component of finished products at a concentration of ≤ 7.5% packed in containers suitable for retail sale; in neat form in 25 kg closed blue steel barrels or as fragrance oil at ≤ 50% concentration in 30 L and 216 L tightly closed lacquered metal drums and 30 L HDPE/EVOH canisters. Within Australia the drums will be transported by road to the warehouse for storage and later distributed to the industrial customers by road. Finished consumer products containing the notified chemical will be transported primarily by road to retail stores in packages suitable for retail sale.

USE
The notified chemical will be used as a fragrance ingredient in cosmetic and household products. The proposed usage concentration of the notified chemical in various consumer products will be:

Finished Consumer Product	*Final Concentration of the Notified Chemical (%)*
Fine fragrance	0.0013 – 7.5
Other cosmetic products	0.00014 – 0.2
Household cleaning products	0.00001 – 0.25

OPERATION DESCRIPTION
Reformulation of the notified chemical or fragrance mixtures containing the notified chemical at ≤ 50% concentration into finished consumer goods 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.

End-use products containing the notified chemical (at ≤ 7.5% concentration) will be used by consumers and professionals such as hairdressers, beauticians and cleaners. 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
End users (professionals)	1- 8	200

EXPOSURE DETAILS

Transport and storage

Transport, storage and warehouse workers may come into contact with the notified chemical in its neat form or at ≤ 50% concentration in fragrance oil formulation or at ≤ 7.5% concentration (in final formulated products), only in the event of accidental rupture of containers. If such an event occurs, workers may be exposed through dermal, ocular or perhaps inhalation exposure. Exposure should be minimised through the stated use by the notifier of personal protective equipment (PPE) including protective coveralls, impervious gloves and eye protection.

Reformulation

During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical in its neat form or at ≤ 50% 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 impervious gloves.

End-use

Exposure to the notified chemical in end-use products (at ≤ 7.5% concentration) may occur in professions where the services provided involve the application of cosmetics to clients (e.g. hair dressers and workers in beauty salons), or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such professionals may use some PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical at ≤ 7.5% concentration through the use of a wide range of cosmetic and household products. The main route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

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

Cosmetic products (Dermal exposure):

Product type	Amount (mg/day)	C (%)	RF (unitless)	Daily systemic exposure (mg/kg bw/day)
Body lotion	7820	0.2	1	0.2444
Face cream	1540	0.2	1	0.0481
Hand cream	2160	0.2	1	0.0675
Fine fragrances	750	7.5	1	0.8789
Deodorant spray	1430	0.2	1	0.0469
Shampoo	10460	0.2	0.01	0.0033
Conditioner	3920	0.2	0.01	0.0012
Shower gel	18670	0.2	0.01	0.0058
Hand soap	20000	0.2	0.01	0.0063
Hair styling products	4000	0.2	0.1	0.0125
Total				**1.3149**

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

Household products (Indirect dermal exposure - from wearing clothes):

Product type	Amount (g/use)	C (%)	Product Retained (PR) (%)	Percent Transfer (PT) (%)	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	230	0.25	0.25	10	0.0085
Fabric softener	90	0.25	0.25	10	0.0033
Total					**0.0119**

C = maximum intended concentration of notified chemical
Daily systemic exposure = (Amount × C × PR × PT × DA)/BW

Household products (Direct dermal exposure):

Product type	Frequency (use/day)	C (%)	Contact Area (cm^2)	Product Use C (g/cm^3)	Film Thickness (cm)	Time Scale Factor	Daily systemic exposure (mg/kg bw/day)
Laundry liquid	1.43	0.25	1980	0.01	0.01	0.007	0.0001
Dishwashing liquid	3	0.25	1980	0.0093	0.01	0.03	0.0006
All-purpose cleaner	1	0.25	1980	1	0.01	0.007	0.0054
Total							**0.0061**

C = maximum intended concentration of notified chemical
Daily systemic exposure = (Frequency × C × Contact area × Product Use Concentration × Film Thickness on skin × Time Scale Factor × DA)/BW

Hairspray (Inhalation exposure):

Product type	Amount (g/use)	C (%)	Inhalation rate (m^3/day)	Exposure duration zone 1 (min)	Exposure duration zone 2 (min)	Fraction inhaled (%)	Volume zone 1 (m^3)	Volume zone 2 (m^3)	Daily systemic exposure (mg/kg bw/day)
Hairspray	20	0.2	20	15	20	50	1	10	**0.0064**

C = maximum intended concentration of notified chemical

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

The worst case scenario estimation using these assumptions is for a person who is a simultaneous user of all products listed in the above tables that contain the notified chemical at the maximum intended concentrations specified by the notifier in various product types. This would result in a combined internal dose of 1.3393 mg/kg bw/day for the notified chemical. It is acknowledged that inhalation exposure to the notified chemical from use of other cosmetic and household products (in addition to hair spray) may occur. However, it is considered that the combination of the conservative hair spray inhalation exposure assessment parameters, and the aggregate exposure from use of the dermally applied products, which assumes a conservative 100% absorption rate, is sufficiently protective to cover additional inhalation exposure to the notified chemical from use of other spray cosmetic and household products with low exposure.

6.2. Human Health Effects Assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,500 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	not irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation at up to 100%
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation at up to 100%
Rat, repeat dose oral toxicity – 28 days	NOAEL > 1,000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian chromosome aberration test	non genotoxic

Toxicokinetics

Given the low molecular weight (234.38 g/mol) the notified chemical may be absorbed across the respiratory or gastrointestinal tract. However, based on the low water solubility (6.61 mg/L at 20 °C) and high partition coefficient (log Pow = 4.51 at 21.5 °C), indicating a reasonably high lipophilicity, percutaneous absorption is expected to be limited.

Acute toxicity

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

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

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.

Two guinea pig maximisation tests for skin sensitisation were submitted for the notified chemical.

In the first study, discrete or patchy erythema (grade 1) was observed in two animals during challenge at 75% concentration and in three animals at 100% concentration at the 24 hour observation. These skin reactions were not apparent at the 48 hour observation and were therefore not attributed to contact sensitisation by the study authors. In the second study, no signs of allergic skin reactions were observed at challenged with 75% and 100% topical concentrations. The notified chemical is therefore not considered a skin sensitiser.

Repeated dose toxicity

In a 28-day repeated dose oral toxicity study in rats, the notified chemical was administered daily by gavage at dose levels of 100, 300, and 1,000 mg/kg bw/day. A treatment related increase in absolute and relative liver weights were observed in males and females treated at 300 mg/kg bw/day or 1,000 mg/kg bw/day (statistically significant for the relative liver weights in males at 300 mg/kg bw/day [20.6% increase] and 1,000 mg/kg bw/day [24.1% increase], and in females at 1,000 mg/kg bw/day [25.1% increase]). These findings, however, were not accompanied by associated clinical pathology or histopathological findings and therefore not considered to be toxicologically significant.

Hyaline droplet formation was observed in the tubular epithelium of males at all dose levels. The study authors attributed this effect to an excessive accumulation of alpha-2-globulin in the P2 segment cells of renal proximal tubules, resulting in droplets formation as a manifestation of protein overload. This phenomenon is rat specific and therefore not relevant to humans.

Based on the absence of toxicologically significant effects at any dose tested, the No Observed Adverse Effect Level (NOAEL) is established as greater than 1,000 mg/kg bw/day.

Mutagenicity/Genotoxicity
The notified chemical was negative in a bacterial reverse mutation assay and in an *in vitro* chromosomal aberration test in human lymphocytes.

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 with potential for slight eye irritation.

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 provided involve the application of cosmetic and household products containing the notified chemical to clients (*e.g.*, hairdressers, beauty salon workers and cleaners) or the use of household products in the cleaning industry may be exposed to the notified chemical at ≤ 7.5% concentration. Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, the risk to such workers is expected to be of a similar or lesser extent than that experienced by consumers using the various products containing the notified chemical.

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

6.3.2. Public Health
Based on the toxicological information provided, the notified chemical is of low hazard except for slight eye irritation. At the proposed use concentration (≤ 7.5%) in cosmetics and household products, eye irritation is not expected.

Therefore, the risk associated with use of the notified chemical at ≤ 7.5% concentration in cosmetics and household cleaning 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 neat or as a component of fragrance formulations, for reformulation into finished cosmetic formulations and household 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 are expected to be collected with adsorbents, 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. Therefore, significant release of the notified chemical from this process to the environment is not expected. The process will be followed by automated filling of the formulated products into containers of various sizes suitable for retail and end-use. Waste containing the notified chemical generated during reformulation includes equipment wash water, residues in empty import containers and spilt materials. It is estimated by the notifier that up to 1% of the import volume of the notified chemical (or up to 8 kg) may be released from reformulation processes. These will be collected and released to on-site waste water treatment processes, or released to sewers in a worst case scenario. Empty import containers are expected to be recycled or disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The notified chemical is expected to be released to the aquatic compartment through sewers during its use in various cosmetic formulations and household products.

RELEASE OF CHEMICAL FROM DISPOSAL

A small proportion of the notified chemical may remain in end-use containers once the consumer products are used up. Wastes and residues of the notified chemical in empty 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 cosmetic formulations and household products in Australia, the majority of the notified chemical will be released to sewer after use. Based on its low water solubility (6.61 mg/L) and high calculated adsorption coefficient (log K_{OC} = 3.85 – 4.99), most of the notified chemical released to sewer is expected to be removed at sewage treatment process by partitioning to sludge or sediment. Limited amount of the notified chemical remaining in effluent from sewage treatment plants may enter to surface waters.

The notified chemical is highly volatile from water (vapour pressure = 2.9×10^{-3} kPa at 20 °C and Henry's Law constant of 104 Pa m^3/mole) and is expected to volatilise to air during sewage treatment. The half-life of the notified chemical in air is calculated to be 1.18 hours, based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2011). Therefore, the notified chemical is not expected to persist in the air compartment.

Based on the result of biodegradability study, the notified chemical is not considered readily biodegradable (24.8% in 28 days). For details of the environmental fate studies, please refer to Appendix C.

The notified chemical has the potential to be bioaccumulative based on its partition coefficient (log K_{OW} = 4.51), small molecular size and lack of ready biodegradability. However, the notified chemical is not expected to be released to surface waters in significant quantities.

The notified chemical in water, landfill, soil, and sludge is expected to eventually degrade through 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 a worst case scenario, with 100% release of the notified chemical into sewer systems nationwide and no removal within sewage treatment plants (STPs).

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0%	
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	

PEC - River:	0.56	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.56 µg/L may potentially result in a soil concentration of approximately 0.0037 mg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 0.018 mg/kg and 0.037 mg/kg, respectively.

7.2. Environmental Effects Assessment

The results from an ecotoxicological investigation conducted on the notified chemical are summarised in the table below. Details of this study can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 1.73 mg/L	Toxic to fish
Daphnia Toxicity	48 h EC50 = 3.91 mg/L	Toxic to aquatic invertebrates
Algal Toxicity	72 h EC50 > 6.61 mg/L	Not harmful to algae up to water solubility limit
Inhibition of Bacterial Respiration	3 h EC50 > 100 mg/L	Not inhibitory to microbial respiration

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is considered to be toxic to fish and aquatic invertebrates. On the basis of its lack of ready biodegradability, the notified chemical is classified 'Chronic Category 2: Toxic to aquatic life with long lasting effects'.

7.2.1. Predicted No-Effect Concentration

The predicted no-effects concentration (PNEC) has been calculated from the available endpoint for fish. A safety factor of 100 was used given acute endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Fish, 96 h)	1.73	mg/L
Assessment Factor	100	
Mitigation Factor	1.00	
PNEC:	17.3	µg/L

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has been calculated based on the predicted PEC and PNEC.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q – River	0.56	1.73	**0.32**
Q – Ocean	0.056	1.73	**0.032**

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters, based on its maximum annual importation quantity. The notified chemical has a potential for bioaccumulation. However, the notified chemical is not expected released to surface waters in significant quantities.

On the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic formulations and household products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -80 °C

Method	OECD TG 102 Melting Point/Melting Range EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature
Remarks	Determined using differential scanning calorimetry
Test Facility	Siemens (2002a)

Boiling Point 287 - 288.5 °C at 101.3 kPa

Method	OECD TG 103 Boiling Point EC Council Regulation No 440/2008 A.2 Boiling Temperature
Remarks	Determined using differential scanning calorimetry
Test Facility	Siemens (2002a)

Density 970 kg/m^3 at 20 °C

Method	OECD TG 109 Density of Liquids and Solids EC Council Regulation No 440/2008 A.3 Relative Density
Remarks	Determined using glass pycnometer
Test Facility	Siemens (2002b)

Vapour Pressure 4.2×10^{-3} kPa at 25 °C

Method	OECD TG 104 Vapour Pressure EC Council Regulation No 440/2008 A.4 Vapour Pressure
Remarks	Determined by dynamic method
Test Facility	Siemens (2002a)

Water Solubility 6.61×10^{-3} g/L at 20 °C

Method	OECD TG 105 Water Solubility EC Council Regulation No 440/2008 A.6 Water Solubility
Remarks	Column Elution Method
Test Facility	GAB (2003a)

Hydrolysis as a Function of pH

Method	OECD TG 111 Hydrolysis as a Function of pH EC Council Regulation No 440/2008 C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH

pH	*T (°C)*	$t_{½}$
4	25	< 1 day
7	25	> 1 year
9	25	> 1 year

Remarks	After 5 days under the accelerated conditions of 50 °C the rate of hydrolysis of the test substance was less than 10% at pH 7 and 9. This equates to a half-life at 25 °C of $t_{½}$ > 1 year. At pH 4, a rapid degradation of the test substance was observed under accelerated conditions of 50 °C. This equates to a half-life at 25 °C of $t_{½}$ = 16.8 hours. Therefore, under the conditions of the test, the test substance is expected to be hydrolytically stable under neutral and basic conditions. The test substance is expected to hydrolyse slowly under acidic conditions
Test Facility	GAB (2003b)

Partition Coefficient (n-octanol/water) log Pow = 4.51 at 21.5±1 °C

Method	OECD TG 107 Partition Coefficient (n-octanol/water).
Remarks	Flask Method
Test Facility	GAB (2003c)

Adsorption/Desorption log K_{oc} = 3.85 – 4.99 at 21.5±1 °C

Method	OECD TG 121 Estimation of the Adsorption Coefficient on Soil and on Sewage Sludge
Remarks	HPLC method
Test Facility	GAB (2002a)

Flash Point 134 °C at 101.3 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point
Remarks	Determined using Pensky Martens apparatus
Test Facility	Siemens (2002c)

Autoignition Temperature 235 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases)
Test Facility	Siemens (2002d)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical (94.9% purity)
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method
Species/Strain	Rat/Sprague-Dawley/ Crl:CD
Vehicle	Nil
Remarks - Method	No protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	3M/3F	2,000	0/6

LD50	> 2,500 mg/kg bw
Signs of Toxicity	Diarrhoea was noted in all animals at 4 hours or 1 day observations and all animals appeared normal at the day 2 observation.
Effects in Organs	No abnormalities noted at necroscopy.
Remarks - Results	No unscheduled mortalities occurred during the study. All animals showed expected gains in bodyweight over the observation period. Based on OECD TG 423, the LD50 was estimated to be > 2,500 mg/kg bw.

CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	SafePharm (2000)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical (96.9% purity)
METHOD	OECD TG 402 Acute Dermal Toxicity
Species/Strain	Rat/Sprague-Dawley/Crl:CD
Vehicle	Nil
Type of dressing	Semi-occlusive
Remarks - Method	No protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5M/5F	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	No signs of local toxicity were noted.
Signs of Toxicity - Systemic	No signs of systemic toxicity were noted.
Effects in Organs	No abnormalities were noted during necroscopy.
Remarks - Results	All treated animals showed expected body weight gain during the observation period.

CONCLUSION	The notified chemical is of low acute toxicity via the dermal route.
TEST FACILITY	LPT (2002a)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical (purity not reported)
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 (2 M and 1 F)
Vehicle	Nil
Observation Period	72 hours
Type of Dressing	Semi-occlusive
Remarks - Method	No protocol deviations.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0	0	0	0	Nil	0
Oedema	0	0	0	0	Nil	0

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

Remarks - Results	No erythema or oedema was observed in any of the treated animals.
CONCLUSION	The notified chemical is not irritating to the skin.
TEST FACILITY	SafePharm (2001a)

B.4. Irritation – eye

TEST SUBSTANCE	Notified chemical (95.9% purity)
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White
Number of Animals	2 M and 1 F
Observation Period	72 hours
Remarks - Method	No protocol deviations.

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	0.0
Conjunctiva: chemosis	0.0	0.0	0.0	2**	< 24 h	0.0
Conjunctiva: discharge	0.0	0.0	0.0	2**	< 24 h	0.0
Corneal opacity	0.0	0.0	0.0	0	Nil	0.0
Iridial inflammation	0.0	0.0	0.0	0	Nil	0.0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal
** at the 1-hour observation

Remarks - Results	Moderate reddening of the conjunctivae (grade 2) was observed in all animals at the 1-hour observation. Slight reddening (grade 1) was observed at the 24-hour observation in all animals. Moderate chemosis (grade 2) was observed in two animals and slight chemosis (grade 1) was observed in one animal at the 1-hour observation. Moderate discharge (grade 2) was observed in all animals at the 1-hour observation.

All signs of irritation were resolved at the 48-hour observation.

No abnormal body weight changes were observed during the study.

No clinical signs of systemic toxicity were observed.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY SafePharm (2001b)

B.5. Skin sensitisation

TEST SUBSTANCE Notified chemical (purity not reported)

METHOD OECD TG 406 Skin Sensitisation – Guinea pig maximisation test (GPMT)

Species/Strain Guinea pig/Dunkin Hartley/albino

PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: not determined (moderate erythema noted at 1% and 5%)
topical: 100%

MAIN STUDY

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

Vehicle Arachis oil

Positive control Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using 2-mercaptobenzothiazole and α-hexylcinnamaldehyde.

INDUCTION PHASE Induction Concentration:
intradermal: 5%
topical: 100%

Signs of Irritation Intradermal induction: Discrete or patchy to moderate and confluent erythema was observed at the intradermal induction sites of test group and control group animals.

Topical induction: Discrete or patchy (grade 1) to moderate and confluent erythema (grade 2) was observed at the topical induction sites of test group animals.

Discrete or patchy erythema was observed at the topical induction sites of control group animals.

Four out of 10 animals from test group and one animal from the control group showed bleeding from the intradermal induction site at the 1 hour observation.

CHALLENGE PHASE

1st challenge topical: 75% and 100%

2nd challenge not conducted

Remarks - Method A preliminary study was carried out to select suitable concentrations for induction and challenge.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge**	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	75%	2	0	-	-
	100%	3	0	-	-
Control Group	75%	0	0	-	-
	100%	0	0	-	-

*Not conducted

Remarks - Results	No mortality and no clinical signs of toxicity observed in the test animals, with all animals gaining weight during the study. Discrete or patchy erythema (grade 1) was observed in two test group animals at 75% and in three test group animals at 100% concentration at the 24 hour observation. These skin reactions were not apparent at the 48 hour observation and were therefore not attributed to contact sensitisation by the study authors. No skin reactions were noted in control group animals at the 24 or 48 hour observations. The positive control confirmed the sensitivity of the test system.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	SafePharm (2001c)

B.6. Skin sensitisation

TEST SUBSTANCE	Notified chemical (95.9% purity)
METHOD	OECD TG 406 Skin Sensitisation - Guinea pig maximisation test (GPMT)
Species/Strain	Guinea pig/ Dunkin Hartley/albino
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 5% topical: 100%
MAIN STUDY	
Number of Animals	Test Group: 10 M Control Group: 5 M
Vehicle	Arachis oil
Positive control	Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using 2-mercaptobenzothiazole and α-hexylcinnamaldehyde.
INDUCTION PHASE	Induction Concentration: intradermal: 5% topical: 100%
Signs of Irritation	Intradermal induction: Discrete or patchy to moderate and confluent erythema was observed at the intradermal induction sites of test group and control group animals. Topical: Discrete or patchy (grade 1) to moderate and confluent erythema (grade 2) was observed at the topical induction sites of test group animals. Discrete or patchy erythema was observed at the topical induction sites of control group animals. One animal showed bleeding from the intradermal injection site.
CHALLENGE PHASE	
1st challenge	topical: 75% and 100%
2nd challenge	not conducted
Remarks - Method	A preliminary study was carried out to select suitable concentrations for induction and challenge.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge**	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	75%	0	0	-	-

	100%	0	0	-	-
Control Group	75%	0	0	-	-
	100%	0	0	-	-

*Not conducted

Remarks - Results

No mortality and no clinical signs of toxicity observed in the test animals, with all animals gaining weight during the study.

No signs of skin irritation were observed in the test and control animals.

The positive control confirmed the sensitivity of the test system

CONCLUSION

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

TEST FACILITY

SafePharm (2001d)

B.7. Repeat dose toxicity

TEST SUBSTANCE

Notified chemical (96.9% purity)

METHOD

OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents

Species/Strain: Rat/SD/Crl:CD

Route of Administration: Oral – gavage

Exposure Information: Total exposure days: 28 days
Dose regimen: 7 days per week
Post-exposure observation period: 14 days

Vehicle: 0.5% Aqueous hydroxypropyl-methylcellulose gel

Remarks - Method: No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
control	5M/5F	-	0/10
low dose	5M/5F	100	0/10
mid dose	5M/5F	300	0/10
high dose	5M/5F	1,000	0/10
control recovery	5M/5F	-	0/10
high dose recovery	5M/5F	1,000	0/10

Mortality and Time to Death

No unscheduled mortality occurred during the study period.

Clinical Observations

Piloerection was observed in all animals treated at 1,000 mg/kg bw/day from day 14 to day 38.

Statistically significant reduction in body weight in males treated at 1,000 mg/kg bw/day was observed from week 1 to week 3. The body weight normalised during the recovery period but remained lower than control animals.

Statistically significant increase in food consumption was observed in both sexes treated at 1,000 mg/kg bw/day in test week 4. Food intake was within the normal range during the recovery period.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Statistically significant reduction in glucose in males was observed in the 1,000 mg/kg bw/day treatment group.

Effects in Organs

A treatment related increase in absolute and relative liver weights were observed in males and females treated at 300 mg/kg bw/day or 1,000 mg/kg bw/day (statistically significant for the relative liver weights in males at 300 mg/kg bw/day [20.6% increase] and 1,000 mg/kg bw/day [24.1% increase], and in females at 1,000 mg/kg

bw/day [25.1% increase]). However, no corresponding adverse histopathological changes were observed therefore the liver weight increase was not considered to be toxicologically significant. No influence on the absolute or relative organ weights of male and female animals of the recovery group was noted.

Hyaline droplet formation was observed in the tubular epithelium of males at all dose levels. The study authors attributed this effect to an excessive accumulation of alpha-2-globulin in the P2 segment cells of renal proximal tubules, resulting in droplets formation as a manifestation of protein overload. This phenomenon is rat specific and therefore not relevant to humans.

Remarks – Results
Treatment related mild hyperplasia and hyperkeratosis of the epidermis of the skin of males at 300 mg/kg bw/day, and mild hyperplasia and hyperkeratosis of the epidermis of the skin and fore-stomach epithelium of female rats at 300 mg/kg bw/day and 1,000 mg/kg bw/day were observed.

None of the animals of the recovery group revealed any delayed treatment related effects.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as > 1,000 mg/kg bw/day in this study, based on the absence of toxicologically significant effects at any of the doses administered.

TEST FACILITY LPT (2003a)

B.8. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical (96.9% purity)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test Plate incorporation procedure (Test 1) and Pre incubation procedure (Test 2)
Species/Strain	*Salmonella typhimurium*: TA1535, TA1537, TA98, TA100 and TA102
Metabolic Activation System	S9 fraction from Aroclor 1254 induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 0.006 – 0.6 µg/plate b) Without metabolic activation: 0.006 – 0.6 µg/plate
Vehicle	Dimethyl sulfoxide (DMSO)
Remarks - Method	A plate incorporation preliminary test at a concentration range of 0.006 – 200 µg/plate was conducted with tester strain TA100 only. Negative control: DMSO Positive control: With metabolic activation: 2-anthraceneamide (TA98, TA102 and TA1537) and cyclophosphamide (TA100 and TA1535) Without metabolic activation: sodium azide (TA1535 and TA100), 2-nitro-fluorene (TA98), 9-amino-acridine (TA1537) and methyl methane sulfonate (TA102). No significant protocol deviations.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 0.6	0.6	> 0.6	Negative
Test 2		0.6	> 0.6	Negative
Present				
Test 1	≥ 0.6	0.6	> 0.6	Negative
Test 2		0.6	> 0.6	Negative

Remarks - Results In Test 1 (in the absence and presence of metabolic activation)

cytotoxicity was observed in TA100, TA1535 and TA1537 at 0.6 µg/mL.

In Test 2 (in the absence of metabolic activation) cytotoxicity was observed in TA1537 at 0.6 µg/mL and in the presence of metabolic activation in TA100 at 0.6 µg/mL.

No significant increases in the frequency of revertant colonies were recorded for any of the strains of bacteria, at any dose level either with or without metabolic activation.

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

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

TEST FACILITY LPT (2002b)

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

TEST SUBSTANCE Notified chemical (96.9% purity)

METHOD OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test

Species/Strain	Human
Cell Type/Cell Line	Peripheral blood lymphocytes
Metabolic Activation System	S9 mix from Aroclor 1254 induced rat liver
Vehicle	DMSO
Remarks - Method	Negative control: DMSO Positive control: without metabolic activation – mitomycin C with metabolic activation - cyclophosphamide

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	7.5, 15.0*, 37.5*, 75.0* and 150.0	4 h	24 h
Test 2	7.5*, 15.0*, 37.5*, 75.0* and 150.0	24 h	24 h
Present			
Test 1	7.5, 15.0*, 37.5*, 75.0* and 150.0	4 h	24 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		≥ 75	> 150	Negative
Test 2	≥ 100	≥ 75	> 150	Negative
Present				
Test 1	≥ 100	150	> 150	Negative

Remarks - Results In all tests, high cytotoxicity was observed in cells treated at 150 µg/mL.

Increases in chromosomal aberrations outside the normal range of 0 - 5.0% were observed without metabolic activation at 150 µg/mL in Test 1 (8.4%) and at 75 µg/mL in Test 2 (6.9%). However these results were considered as artefacts by the study authors due to the high cytotoxicity at these test concentrations. Only 12 of 200 and 117 of 200 metaphases could be

	analysed, respectively, at mitotic indices of 0.05 and 0.39. No significant increases in chromosomal aberrations were observed at all other test concentrations either with or without metabolic activation. The positive controls gave satisfactory responses, confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to human peripheral blood lymphocytes treated *in vitro* under the conditions of the test.
TEST FACILITY	LPT (2003b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE: Notified chemical (94.9% purity)

METHOD: OECD TG 301 D Ready Biodegradability: Closed Bottle Test

Inoculum	Activated sewage sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Oxygen Demand (ThOD)
Remarks - Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Test substance		*Toxicity control*		*Sodium benzoate*	
Day	*% Degradation*	*Days*	*% Degradation*	*Day*	*% Degradation*
7	11.2	7	54.1	7	99.4
14	28.7	14	69.7	14	131.5
21	24.0	21	65.2	21	130.3
28	24.8	28	68.8	28	128.1

Remarks - Results: All validity criteria for the test were satisfied. The percentage degradation of the reference compound attained the threshold level of > 60% by 8 days. Therefore, the tests indicate the suitability of the inoculum. The percentage degradation of the toxicity control surpassed the threshold level of 25% by 21 days (65.2% in 28 days), showing that toxicity was not a factor inhibiting the biodegradability of the test substance.

The degree of degradation of the test substance after 28 days was 24.8%. Therefore, the test substance is not considered to be readily biodegradable according to the OECD (301 D) guideline.

CONCLUSION: The notified chemical is not readily biodegradable.

TEST FACILITY: GAB (2001)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE: Notified chemical (purity not reported)

METHOD: OECD TG 203 Fish, Acute Toxicity Test – Semi Static

Species	Zebra Fish *(Brachydanio rerio)*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	High Pressure Liquid Chromatography (HPLC)
Remarks – Method	Due to low solubility of the test substance in water, a super saturated dispersion of the test substance with a loading rate of 100 mg was stirred for one hour and filtered through 0.45µm membrane. The filtrate was used a test medium.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*			
Nominal	*Actual*		*24 h*	*48 h*	*72 h*	*96 h*
Control	Control	10	0	0	0	0
1.25	0.88	10	0	0	0	0
2.0	1.39	10	0	0	0	0
3.15	1.75	10	1	3	4	7
5.0	2.56	10	10	10	10	10
7.9	3.84	10	10	10	10	10

LC50 1.73 mg/L at 96 hours (95% confidence limit of 1.61-1.87 mg/L). The data analysis was conducted using the Trimmed Spearman-Karber (Version 5) for calculating toxicity values and 95% confidence limit.

Remarks – Results All validity criteria for the test were satisfied. The test solutions were renewed every 24 hours during the test period. The actual concentration of the test substance was measured every 24 hour. The 96 h LC50 for fish were determined to be 1.73 mg/L, based on the measured concentrations.

CONCLUSION The notified chemical is toxic to fish.

TEST FACILITY SAES (2010)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical (96.9% purity)

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test – Semi-static.

Species *Daphnia magna*

Exposure Period 48 hours

Auxiliary Solvent Acetone

Water Hardness 140 - 268 mg $CaCO_3$/L

Analytical Monitoring Gas Chromatography (GC)

Remarks - Method The test substance was dissolved in acetone due to its low solubility in water. This was followed by diluting the solution in test medium. The definitive test was conducted at the concentration of 0.093, 1.49, 2.38, 6.1, 9.77, 15.6 and 25 mg/L of the test substance. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Concentration mg/L	*Number of D. magna*	*Cumulative Immobilised*	
Measured		*24 h*	*48 h*
Control	20	0	0
Solvent Control	20	0	0
0.93	20	0	0
1.49	20	0	0
2.38	20	0	0
3.81	20	0	0
6.1	20	3	4
9.77	20	5	10
15.6	20	9	16
25	20	19	20

EC50 3.91 mg/L at 48 hours (Calculated by Probit analysis)

Remarks - Results All validity criteria for the test were satisfied. The test solutions were renewed every 24 hours during the test period. The initial content of the test substance was 80.6 - 102 % of nominal at all concentrations. The

concentration of the test substance decreased over the entire period of the test, most likely to be related to the volatility of the test substance from water. Therefore, the results are based on measured concentrations. The actual concentrations of the test substance were measured every 24 hours during the 48 h test period. The 48 h EC50 was determined to be 3.91 mg/L, based on the average measured concentration.

CONCLUSION The notified chemical is considered to be toxic to aquatic invertebrates

TEST FACILITY GAB (2003d)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical (96.9% purity)

METHOD OECD TG 201 Freshwater Alga and Cyanobacteria, Growth Inhibition Test.

Species	*Desmodesmus subspicatus* (green alga)
Exposure Period	72 hours
Concentration Range	Actual: 1.25, 2.5, 5, 10 ,20 ,40 and 80 mg/L
Auxiliary Solvent	Acetone
Water Hardness	Not reported
Analytical Monitoring	GC
Remarks - Method	The test substance was dissolved in acetone due to its low solubility in water. This was followed by diluting the solution in test medium. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Biomass		*Growth*	
EC50	*NOEC*	*EC50*	*NOEC*
mg/L at 48 h	*mg/L*	*mg/L at 48 h*	*mg/L*
> 6.61	4.83	> 6.61	4.83

Remarks - Results

The growth factor of cell numbers, measured in the control between 0 h and 72 h was found to be 176.30. The test, therefore, fulfils this validity criterion.
The concentration of the test substance decreased over the entire period of the test, most likely to be related to the volatility of the test substance from water. The average measured concentration variance was 33% compared to the nominal concentration. Therefore, the results are based on average measured concentrations. The actual average measured concentrations of the test substance were measured every 24 hours during the test period.
The 72 h EC50 and NOEC for algae were determined to be > 6.61 mg/L and 4.83 mg/L, respectively, based on the average measured concentrations.

CONCLUSION The notified chemical is not considered to be harmful to algae up to the limit of its solubility in water.

TEST FACILITY GAB (2003e)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical (96.9% purity)
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sewage sludge
Exposure Period	3 hours
Concentration Range	Nominal: 1.02 and 100 mg/L Actual: Not determined
Remarks – Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported. The test substance was dissolved in acetone due to its low solubility in water. This was followed by diluting the solution in test medium. 3,5-Dichlorophenol was used as the reference control. The respiration rate was determined by measurement of Biochemical Oxygen Demand during the test after 30 minutes and 3 hours of exposure.
RESULTS	
EC50	> 100 mg/L at 3 hours
NOEC	Not determined
Remarks – Results	The EC50 value for reference control was in the range between 5 and 30 mg/L alter 30 min and 3 hours. The test, therefore, fulfils the validity criterion. The 3 h EC50 was determined to be > 100 mg/L, based on the nominal concentration.
CONCLUSION	The notified chemical is not inhibitory to microbial respiration up to the limit of its solubility in water.
TEST FACILITY	GAB (2002b)

BIBLIOGRAPHY

ACI (2010) Consumer Product Ingredient Safety, Exposure and risk screening methods for consumer product ingredients, 2nd Edition, American Cleaning Institute, Washington DC.

Cadby, P.A., Troy, W.R., Vey, M.G. (2002); Consumer exposure to fragrance: Providing estimates for safety evaluation, Regulatory Toxicology and Pharmacology 36 (2002) 246-252.

Earnest, C.W., Jr. (2009) A Two-Zone Model to Predict Inhalation Exposure to Toxic Chemicals in Cleaning Products, MSCEng thesis, The University of Texas at Austin

enHealth (2012) Australian Exposure Factor Guide, companion document to: Environmental Health Risk Assessment: Guidelines for assessing human health risks from environmental hazards, EnHealth, Commonwealth of Australia.

GAB (2001) Ready Biodegradability (Project No. 20001348/01-AACB, January, 2001). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

GAB (2002a) Adsorption Coefficient (Project No: 20011436/01-PCAD, August 2002). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

GAB (2002b) Activated Sludge Respiration Inhibition Test (Project No. 20011436/01AAHT, May, 2002). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

GAB (2003a) Water Solubility (Project No. 20011436/01-PCSB, March, 2003). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

GAB (2003b) Hydrolysis (Project No. 20011436/01-PCHY, February, 2003). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

GAB (2003c) Partition Coefficient (Project No. 20011436/01-PCPC, March, 2003). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

GAB (2003d) Daphnia Acute Immobilization Test (Project No. 20011436/01AADm, February, 2003). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

GAB (2003e) Algae Growth Inhibition Test (Project No. 20011436/01AADs, February, 2003). Niefern-Öschelbronn, Germany, GAB Biotechnologie GmbH (Unpublished report submitted by the notifier).

Loretz, L., Api, A.M., Barraj, L., Burdick, J. Davis, D.A., Dressler, W., Gilberti, E., Jarrett, G., Mann, S., Pan, Y.H.L., Re, T., Renskers, K., Scrafford, C., Vater, S. (2006) Exposure data for personal care products : Hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant, Food and Chemcial Toxicology 44 (2006) 2008-2018.

LPT (2002a) Acute Toxicity Study of F-1135 in Sprague-Dawley Rats by Dermal Administration (Report No. 15222/01, May, 2002). Hamburg, Germany, Laboratory of Pharmacology and Toxicology KG (Unpublished report submitted by the notifier).

LPT (2002b) Mutagenicity Study of F-1135 in the *Salmonella typhimurium* Reverse Mutation Assay (*In Vitro*) (Project No. 15225/01, May, 2002). Hamburg, Germany, Laboratory of Pharmacology and Toxicology KG (Unpublished report submitted by the notifier).

LPT (2003a) 28-Day Subchronic Toxicity Study of F-1135 in Sprague-Dawley Rats by Repeated Oral Administration (Project No. 15224/01, March, 2003). Hamburg, Germany, Laboratory of Pharmacology and Toxicology KG (Unpublished report submitted by the notifier).

LPT (2003b) *In Vitro* Assessment of the Clastogenic Activity of F-1135 in Cultured Human Peripheral Lymphocytes (Project No. 15226/01, March, 2003). Hamburg, Germany, Laboratory of Pharmacology and Toxicology KG (Unpublished report submitted by the notifier).

Rothe, H., Fautz, R., Gerber, E., Neumann, L., Rettinger, K., Schuh, W., Gronewold, C (2006) Special aspects of cosmetic spray evaluations: Principles on inhalation risk assessment, Toxicology Letters 205 (2011) 97-104.

SAES (2010) Fish Acute Toxicity Test (Project No: S-042-2010, December, 2010). Shanghai, PRC, Shanghai Academy of Environm. Sciences (Unpublished report submitted by the notifier).

SafePharm (2000) F-1135: Acute Oral Toxicity in the Rat-Acute Toxic Class Method (Project No. 1355/020, December, 2000). Derby, UK, SafePharm Laboratories Limited (Unpublished report submitted by the notifier).

SafePharm (2001a) P-4399: Acute Dermal Irritation in the Rabbit (Project No. 1355/026, April, 2001). Derby, UK, SafePharm Laboratories Limited (Unpublished report submitted by the notifier).

SafePharm (2001b) F-1355 (Peroxide free, stablished with 0.1% BHT): Acute Eye Irritation in the Rabbit (Project No. 1353/048, November, 2001). Derby, UK, SafePharm Laboratories Limited (Unpublished report submitted by the notifier).

SafePharm (2001c) P-4399: Skin Sensitisation in the Guinea Pig – Magnusson and Kligman Maximisation Method (Project No. 1353/027, April, 2001). Derby, UK, SafePharm Laboratories Limited (Unpublished report submitted by the notifier).

SafePharm (2001d) F-1135 (Peroxide free, stablished with 0.1% BHT): Skin Sensitisation in the Guinea Pig – Magnusson and Kligman Maximisation Method (Project No. 1353/038, October, 2001). Derby, UK, SafePharm Laboratories Limited (Unpublished report submitted by the notifier).

SCCS (2010) Notes of Guidance for testing of Cosmetic Ingredients and Their Safety Evaluation (7th revision). European Commission - Scientific Committee on Consumer Safety.

SCCS (2012) The SCCS' Notes of Guidance for the Testing of Cosmetic Substances and their Safety Evaluation (8th revision) European Commission – Scientific Committee on Consumer Safety

Siemens (2002a) Melting Point/Melting Range/Boiling Point/Boiling Range Vapour Pressure (Project No. 20011534.01, March, 2002). Frankfurt, Germany, Siemens Axiva GmbH & Co. KG (Unpublished report submitted by the notifier).

Siemens (2002b) Relative Density (Project No. 20011534.02, February, 2002). Frankfurt, Germany, Siemens Axiva GmbH & Co. KG (Unpublished report submitted by the notifier).

Siemens (2002c) Flash Point (Project No. 20011534.04, February, 2002). Frankfurt, Germany, Siemens Axiva GmbH & Co. KG (Unpublished report submitted by the notifier).

Siemens (2002d) Autoflammability (Determination of the Temperature of Self-Ignition of Volatile Liquids and of Gases) (Project No. 20011534.05, February, 2002). Frankfurt, Germany, Siemens Axiva GmbH & Co. KG (Unpublished report submitted by the notifier).

Steiling, W., Bascompta, M., Carthew, P., Catalano, G., Corea, N., D'Haese, A., Jackson, P., Kromidas, L., Meurice, P., Rothe, H., Singal, M..; Principle considerations for the risk assessment of sprayed consumer products, Toxicology Letters 227 (2014) 41-49.

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

US EPA (2011) Estimations Programs Interface Suite™ for Microsoft® Windows, v 4.00. United States Environmental Protection Agency. Washington, DC, USA.