File No: LTD/1793

November 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1,3-Undecadien-5-yne

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.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Public Report is also 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

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/1793	Firmenich Limited	1,3-Undecadien-5-yne	Yes	≤ 1 tonne per annum	Fragrance ingredient

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard classification	*Hazard statement*
Flammable Liquids (Category 4)	H227 – Combustible liquid
Skin irritation (Category 2)	H315 – Causes skin irritation
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:

R38: Irritating to skin
R43: May cause sensitisation by skin contact

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.

Based on the available information, when used at ≤ 0.1% in cosmetic products, and ≤ 0.5% in household products, 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 reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Skin irritation (Category 2): H315 – Causes skin irritation
  - Skin sensitisation (Category 1): H317 – May cause an allergic skin reaction

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

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during reformulation processes:
  - Enclosed, automated processes, where possible
  - Ventilation system, including local exhaust ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical during reformulation processes:
  - Avoid contact with skin and eyes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Impervious gloves, eye protection and coveralls

  Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the (M)SDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Public Health

- The following measures should be taken to minimise public exposure to the notified chemical:
  - The notified chemical should only be used at ≤ 0.1% in cosmetic products and ≤ 0.5% in household products.
  - Products containing the notified chemical should be formulated to minimise the potential for autoxidation.

Disposal

- Where reuse or recycling are not available or appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Emergency procedures

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

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the concentration of the notified chemical exceeds or is intended to exceed 0.1% in cosmetic products and 0.5% in household products;
- information becomes available on the repeated dose toxicity potential of the notified chemical;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a fragrance ingredient, or is likely to change significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

(Material) Safety Data Sheet
The (M)SDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Firmenich Limited (ABN: 86 002 964 794)
73 Kenneth Road
BALGOWLAH, NSW 2093

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: other names, analytical data, degree of purity, impurities, additives/adjuvants and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: adsorption/desorption, dissociation constant, particle size, flammability limits, reactivity, explosive and oxidising properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
Low Volume Chemical (LVC) permit.

NOTIFICATION IN OTHER COUNTRIES
EU (1995), Philippines (2000), Switzerland (2007), USA (1996).

2. IDENTITY OF CHEMICAL

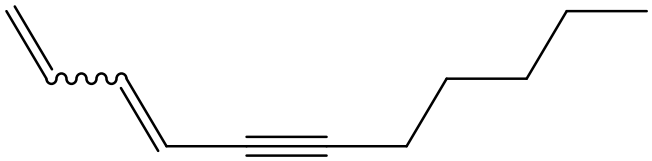
MARKETING NAME(S)
Violettyne

CAS NUMBER
166432-52-6

CHEMICAL NAME
1,3-Unecadien-5-yne

MOLECULAR FORMULA
$C_{11}H_{16}$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
148.24 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless liquid.

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -20 °C	Measured
Boiling Point	Decomposes from ~ 153 °C prior to boiling at 101.3 kPa	Measured
Density	816 kg/m^3 at 20 °C	Measured
Vapour Pressure	0.033 kPa at 20 °C	Measured
Water Solubility	1.0 x 10^{-5} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	t½ > 1 year at pH 2 & 5 t½ = 17.2 days at pH 7 t½ = 21.3 days at pH 8.5 t½ = 6.2 day at pH 12	Measured at 40 °C
Partition Coefficient (n-octanol/water)	log Pow > 6.2	Measured
Adsorption/Desorption	log K_{oc} > 5.38	Calculated (using KOCWIN v2.00; US EPA, 2009)
Dissociation Constant	Not determined	No dissociable functionality
Flash Point	83 ± 2 °C at 101.3 kPa	Measured
Autoignition Temperature	290 ± 5 °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 recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia The recommended hazard classification is presented in the following table.

Hazard classification	***Hazard statement***
Flammable Liquids (Category 4)	H227 – Combustible liquid

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 at 100% concentration, as well as a component of compounded fragrance formulations (at concentrations ≤ 5%) and various formulated end-use cosmetic and household products (at concentrations ≤ 0.5%).

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, by wharf or airport.

IDENTITY OF MANUFACTURER/RECIPIENTS
Firmenich Limited.

TRANSPORTATION AND PACKAGING
The notified chemical (at ≤ 100% concentration) will be imported into Australia in lacquered drums of sizes ranging from 5 kg up to 180 kg. The end-use products (≤ 0.5% notified chemical) will be packaged in typical consumer-sized containers suitable for retail sale.

The notified chemical will be transported from the port of entry by road to the notifier's warehouse facilities for storage in its original packaging until transportation to the customer site. Alternatively, the notified chemical and products containing it will be shipped directly from the port of entry to the customer site.

USE
The notified chemical will be used as a fragrance component in a variety of cosmetic and household products. The content in the final consumer products will vary, with the following proposed usage concentrations: cosmetics (≤ 0.1%) and household products (≤ 0.5%).

OPERATION DESCRIPTION
No manufacturing, processing, reformulating or repackaging of the notified chemical will occur at the notifier's facility. The imported products containing the notified chemical will be stored at this facility until they are transported to customer facilities (in original importation packaging).

At the customer facilities, the procedures for incorporating the imported fragrance preparations (containing ≤ 100% notified chemical) into end-use products will likely vary depending on the nature of the cosmetic and household products formulated, and may involve both automated and manual transfer steps. However, in general, it is expected that the reformulation processes will involve blending operations that will be highly automated and occur in a fully enclosed environment, followed by automated filling of the reformulated products into containers of various sizes.

Household products
Household products containing the notified chemical at ≤ 0.5% concentration may be used by consumers and professional workers. The products may be used in either closed systems with episodes of controlled exposure, for example automatic washing machines, or open processes and manually applied by rolling, brushing, spraying and dipping, using a cloth, sponge, mop or brush and followed by wiping. In some cases the household product will be diluted with water prior to application.

Cosmetic products
The finished cosmetic products containing the notified chemical at ≤ 0.1% concentration will be used by consumers and professionals (such as beauticians and hairdressers). Depending on the nature of the product, application of products could be by hand, sprayed or through the use of an applicator.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and warehouse workers	unknown	unknown
Mixer	4	2
Drum Handling	4	2
Drum Cleaning	4	2
Maintenance	4	2
Quality Control worker	0.5	1
Packager	4	2
End users (professionals)	unspecified	unspecified

EXPOSURE DETAILS
Transport and storage

Transport and storage workers may come into contact with the notified chemical, at 100% concentration or as a component of the imported fragrance preparations (≤ 5% concentration) or end-use products (≤ 0.5% concentration), only in the event of accidental rupture of containers.

At the notifier facility, the primary work activity undertaken by transport and warehouse workers will include the handling, loading and off-loading of drums containing the notified chemical at ≤ 100% concentration. Exposures of these workers will be limited to situations of an accidental discharge, spill or leaking drum, requiring clean up. If such an event occurs, a worker may be exposed through dermal or ocular contact. The notifier states that such exposures will be minimised through the use of personal protective equipment (PPE) including protective clothing, chemical resistant gloves and eye protection.

Formulation of end products
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical (at ≤ 100% concentration) may occur during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. The notifier 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, impervious gloves and respiratory protection (if appropriate).

Beauty care and cleaning professionals
Exposure to the notified chemical in end-use products may occur in professions where the services provided involve the application of cosmetic products (at ≤ 0.1% concentration) to clients (e.g. hair dressers, workers in beauty salons) or the use of household products (at ≤ 0.5% concentration) 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 products containing the notified chemical.

6.1.2. Public Exposure

There will be widespread and repeated exposure of the public to the notified chemical through the use of the household products and the leave-on and rinse-off cosmetics (≤ 0.5% concentration in individual products). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

6.2. Human Health Effects Assessment

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

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

**Test substance: 10% notified chemical (in solution with BHT)*

Toxicokinetics, metabolism and distribution.
No toxicokinetic data were provided on the notified chemical. Based on the water solubility (1.0×10^{-5} g/L at 20 °C), partition coefficient (log $P_{ow} \geq 6.2$) and the low molecular weight (< 500 Da) of the notified chemical, passive diffusion across the gastrointestinal (GI) tract and dermal absorption are expected to occur (although the extent of absorption may be limited). The notified chemical may also be absorbed across the respiratory tract.

Acute toxicity.
The notified chemical was found to have low acute toxicity by the oral route in a study conducted in rats.

No acute dermal or inhalation toxicity data were provided for the notified chemical.

Irritation.
In an acute dermal irritation study in rabbits, a single 4-hour, semi-occluded application of the notified chemical resulted in very slight to well-defined erythema and/or very slight to slight oedema at all treated sites, with effects evident at all sites at the end of the observation period (14 days after patch removal). Skin thickening was also seen the treatment sites in 2/3 animals at the completion of the study.

In a rabbit eye irritation study, minimal to moderate conjunctival irritation was noted in all treated eyes from 1 hour after treatment, with the eyes generally appearing normal within 7 days following instillation (or within 14 days for 1 animal, which was unable to fully open its eye at the 7 day observation). The effects observed in this study did not warrant classification of the chemical as an eye irritant.

Sensitisation.
Two separate guinea pig Maximisation tests (both using the Magnusson-Kligman method), were conducted to determine the skin sensitisation potential of the notified chemical in guinea pigs.

In the first study, the notified chemical (at 80% induction concentration; 40% challenge concentration) was found to be a sensitiser with responses noted in 17/20 and 13/20 animals at 24 and 48 hours after patch removal, respectively. At rechallenge, responses were noted in the test animals at ≥ 2% concentration.

The test substance used in the second study was 10% notified chemical in solution with BHT (CAS no. 128-37-0). Under the conditions of this study (100% induction concentration; 100% challenge concentration), there was no evidence of reactions indicative of skin sensitisation to the notified chemical.

Based on the available information, the notified chemical is considered to be a skin sensitiser. The notifier has indicated that the notified chemical is prone to autoxidation giving rise to allergenic oxidation products and that BHT was present in the test substance of the second (negative) sensitisation study to prevent autoxidation of the notified chemical. However, it is noted that this study was conducted at a lower concentration (induction: 0.5% intradermal; 10% topical) of notified chemical than the first (induction: 25% intradermal; 80% topical). In addition, while the notified chemical itself does not contain any structural alerts for skin sensitisation, the potential for the formation of skin sensitising components following skin metabolism cannot be ruled out.

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

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

Phototoxicity.
In a human phototoxicity patch test completed on 21 subjects, there was no evidence of phototoxicity to the notified chemical (10% in solution with BHT).

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

Hazard classification	***Hazard statement***
Skin irritation (Category 2)	H315 – Causes skin irritation
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction

Based on the available information, the notified chemical is recommended for hazard classification according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrase(s):
R38: Irritating to skin
R43: May cause sensitisation by skin contact

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Reformulation
Exposure of workers to the notified chemical (at ≤ 100% concentration) may occur during blending operations. The notified chemical has the potential to cause skin irritation and is considered to be a skin sensitiser. In addition, harmful effects following repeated exposure and/or inhalation exposure to the notified chemical cannot be ruled out. Therefore, caution should be exercised when handling the notified chemical during reformulation processes.

Therefore, provided that control measures are in place to minimise worker exposure, including the use of automated processes and PPE, the risk to the health of workers from use of the notified chemical is not considered to be unreasonable.

End-use
Cleaners and beauty care professionals will handle the notified chemical at ≤ 0.5% concentration, similar to public use. Therefore, the risk to workers who regularly use products containing the notified chemical is expected to be of a similar or lesser extent than that experienced by members of the public who use such products on a regular basis. For details of the public health risk assessment see Section 6.3.2.

6.3.2. Public Health

Sensitisation
The main identified risk associated with use of the notified chemical at the proposed concentration of ≤ 0.1% in cosmetic products and ≤ 0.5% in household products, is its potential to cause sensitisation by skin contact. Methods for the quantitative risk assessment of dermal sensitisation have been proposed and been the subject of significant discussion (see for example, Api *et al.*, 2008 and RIVM, 2010). Using a fine fragrances (containing 0.1% notified chemical) as an example product that may contain the notified chemical, as a worst case scenario, the Consumer Exposure Level (CEL) is estimated to be 3.75 μg/cm^2 (Cadby *et al.*, 2002). Although data are available only from studies conducted in guinea pigs, which are not suited to potency estimation, interpretation in terms of potency is possible (WHO, 2012 and ECHA, 2012). Using the available information, from a conservative perspective, an equivalent LLNA EC3 may be estimated for the purposes of conducting a quantitative risk assessment. Therefore, using an assumed EC3 value of 2% (and assuming standard test conditions), an Acceptable Exposure Level (AEL) of 1.36 μg/cm^2 was derived.

As the CEL > AEL (fine fragrances category), the risk to the public of the induction of sensitisation that is associated with the use of the notified chemical in fine fragrances at ≤ 0.1% concentration would generally be considered to be unreasonable. However, in this instance, it is noted that the mechanism of sensitisation is only expected to occur following activation of the chemical, and there is potential to minimise the formation of autoxidation products through the use of stabilisers during formulation of the end-use products. Therefore, the risk to the public of the induction of sensitisation that is associated with the use of the notified chemical in fine fragrances (a worst case example of a cosmetic product) at ≤ 0.1% concentration is not considered to be unreasonable. Based on the significantly lower expected exposure level from other cosmetic (containing ≤ 0.1% notified chemical) and household products (containing ≤ 0.5% notified chemical), by inference, the risk of induction of sensitisation associated with the use of these products is also not considered to be unreasonable.

Irritation
The notified chemical is considered to be a skin irritant and was slightly irritating to eyes. Skin and eye irritation effects are not expected from use of the notified chemical at the proposed concentrations in cosmetic and household products.

Repeated-dose toxicity
The repeated dose toxicity effects of the notified chemical have not been determined. However, exposure is expected to be limited by the low concentrations of the notified chemical in end use products.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 0.1% in cosmetic products and ≤ 0.5% in household products, is not considered to be unreasonable. In the absence of data on the repeated dose toxicity potential of the notified chemical, use of the notified chemical is supported only under limited exposure conditions, which are reflected in the low concentration of the notified chemical in end-use products.

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 at 100% concentration or as a component of fragrance preparations for local reformulation into a variety of cosmetic and household products. Release during reformulation in Australia is expected to arise from spills (0.1%), formulation equipment cleaning (no release estimate as cleaning water will be recycled) and residues in import containers (0.1%). Accidental spills during transport or reformulation are expected to be collected with inert material and disposed of to landfill. Import containers will either be recycled or disposed of through an approved waste management facility. Therefore, up to 0.2% or up to 2 kg of the import volume is estimated to be released to landfill as a result of reformulation in Australia.

RELEASE OF CHEMICAL FROM USE

The notified chemical is expected to be released to sewers in domestic situations across Australia as a result of its use in cosmetic and household products, which will either be washed off the hair and skin of consumers, or disposed of following cleaning activities.

RELEASE OF CHEMICAL FROM DISPOSAL

It is estimated that a maximum of 3% of the consumer products containing the notified chemical will remain in end-use containers. These will be disposed of through domestic garbage disposal and will enter landfill or be recycled.

7.1.2. Environmental Fate

Following its use in Australia, the majority of the notified chemical is expected to enter the sewer system before potential release to surface waters on a nationwide basis. The notified chemical is not readily biodegradable based on the provided test report. For the details of the environmental fate studies please refer to Appendix C. It is expected to have bioaccumulative potential based on the reported log P_{OW} of > 6.2. This is not considered to be a concern since the notified chemical showed a biodegradability of 20% in 28 days.

The half-life of the notified chemical in air is calculated to be < 1 hour based on reactions with hydroxyl radicals (AOPWIN v1.92; US EPA, 2011). Therefore, in the event of release to atmosphere, the notified chemical is not expected to persist in the atmospheric compartment.

Most of the notified chemical will be released to the sewer after use and directed to sewage treatment plants (STPs) nationwide. A small amount of the notified chemical may be sent to landfill as collected spills or container residues. In STPs, the majority of the notified chemical is expected to be removed from the water column via adsorption to sludge sediment given the hydrophobic structure and the estimated log K_{OC} of > 5.38, and eventually be sent to landfill. In landfill or water, the notified chemical is expected to undergo biotic or abiotic degradation processes, forming water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated assuming a worst case scenario of 100% release of the notified chemical into sewer systems nationwide and no removal from 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)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML

Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.61	µg/L
PEC - Ocean:	0.06	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 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 0.61 µg/L may potentially result in a soil concentration of approximately 4.04 µg/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 20.2 µg/kg and 40.4 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. By using ECOSAR (US EPA, 2012), the following acute toxicity data have been predicted for the notified chemical.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 0.48 mg/L	Very toxic to fish
Daphnia Toxicity	48 h EC50 = 0.35 mg/L	Very toxic to daphnia
Algal Toxicity	72 h EC50 = 0.72 mg/L	Very toxic to alga

The notified chemical is considered to be very toxic based on the above predicted endpoints. These data are for risk assessment purposes only. Modelled data are not used for the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009). Therefore, the notified chemical has not been formally classified under GHS.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) was calculated using the predicted endpoint for daphnia which is considered to be the most sensitive species. A safety factor of 100 was used as acute toxicity values from three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (daphnia)	0.35	mg/L
Assessment Factor	100	
PNEC:	3.5	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River:	0.61	3.5	0.17
Q - Ocean:	0.06	3.5	0.017

The risk quotient (RQ = PEC/PNEC) 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 based on its annual import quantity. Therefore, on the basis of the PEC/PNEC ratio and the assessed use pattern, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point < -20 °C

Method OECD TG 102 Melting Point/Melting Range.
Remarks Determined by placing a test tube containing the test substance in a dry ice/acetone bath until the temperature of the substance reached ~-20 ºC. The test substance did not show any indication of freezing.
Test Facility Safepharm (1995a)

Boiling Point Decomposes from approximately 153 °C at 101.3 kPa

Method OECD TG 103 Boiling Point.
Remarks The test substance decomposed (from ~153 °C) prior to boiling, when tested according to the Siwoloboff method. At the reduced pressure of 1.3 kPa, the boiling temperature was determined to be > 89 °C, using the distillation method.
Test Facility Safepharm (1995a)

Density 816 kg/m^3 at 20.0 ± 0.5 °C

Method OECD TG 109 Density of Liquids and Solids.
Remarks Determined using the oscillating density meter method
Test Facility Firmenich SA (2014a)

Vapour Pressure 0.033 kPa at 20 °C

Method OECD TG 104 Vapour Pressure.
Remarks Determined using a standard dynamic approach.
Test Facility Firmenich SA (1999)

Water Solubility 1 x 10^{-5} g/L at 20 °C

Method OECD TG 105 Water Solubility.
EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks Flask Method
Test Facility Safepharm (1995a)

Hydrolysis as a Function of pH $t_{½}$ = > 1 year at pH 2 & 5, 17.2 days at pH 7, 21.3 days at pH 8.5 and 6.2 days at pH 12. The test was conducted at 40 °C.

Method OECD TG 111 Hydrolysis as a Function of pH.

The notified chemical was added in the pH buffers (at pH 2, 5, 7, 8.5 and 12) to reach concentrations in the range of 200 - 300 ppm. The mixtures were then kept in an oven at 40°C. Small aliquots of the test solutions were extracted using an organic solvent containing a hydrocarbon standard on a regular basis throughout the test. The extracts were analysed by gas chromatography.

pH	*T (°C)*	*$t_{½}$ (days)*
2	40	> 365
5	40	> 365
7	40	17.2
8.5	40	21.3
12	40	6.2

Remarks The determined half-life at different pH indicates that the notified chemical is less stable under basic conditions.
Test Facility Firmenich SA (2014b)

Partition Coefficient (n-octanol/water) log Pow > 6.2

Method	OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks	HPLC Method
Test Facility	Safepharm (1995a)

Flash Point 83 ± 2 °C at 101.3 kPa

Method	Commission Directive 92/69/EEC A.9 Flash Point.
Remarks	Determined using a closed cup equilibrium method.
Test Facility	Safepharm (1995b)

Autoignition Temperature 290 ± 5 °C

Method	Similar to EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	Determination of the minimum temperature of the inner surface of an enclosure that will result in ignition of the liquid injected into the enclosure. Determined using an AIT instrument.
Test Facility	Firmenich SA (2007)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity - Fixed Dose Method.
Species/Strain	Rat/ Sprague-Dawley (Crl: CD (SD) BR)
Vehicle	Aqueous carboxymethyl cellulose (0.5%)
Remarks - Method	GLP Compliance. A 7 day preliminary range-finding test was conducted at 500 and 2,000 mg/kg bw (using 1 female animal per dose level) to determine the appropriate dose level for the main study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity	There were no treatment related signs of systemic toxicity noted in any of the animals over the study period. A scab was noted on the head of a female animal from day 8 to day 13, but this observation was deemed to be not treatment related by the study authors.
Effects in Organs	Cloudy foci were apparent in areas of the spleen of 4 males and 1female animal, with the size of the affected area varied (up to 4 x 2 mm). The spleen itself was enlarged in 1 of these affected males. An additional female animal was noted to have a shrunken spleen. On histopathological examination of the affected spleens, 1 male showed slight capsular fibrosis. No histological changes corresponding to the macroscopic findings were detected in the other animals. This abnormal finding was hence considered by the study authors to be of no significance. A female animal showed a uterus distended with fluid, however this observation was deemed by the study authors to be of no toxicological significance.
Remarks - Results	All animals survived until the scheduled termination and showed gains in bodyweight over the study period (body weight loss only noted in a single female animal on day 2, with weight gain observed thereafter).
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Toxicol Laboratories (1994a)

B.2. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 F
Vehicle	None – used as supplied.
Observation Period	14 days.
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations. GLP Compliance.

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	0.33	1	2	2	> 14 days	1
Oedema	0.33	1	1.33	2	> 14 days	2

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

Remarks - Results

Only 1 animal showed very slight erythema and oedema at the 1 hour observations. However, in general, the signs of irritation appeared to increase in prevalence and severity over the course of the study period, with effects evident in all animals at the completion of the study.

All animals showed very slight to well defined erythema and very slight oedema at the 24 hour observations. A single animal had no signs of irritation at the following 48 and 72 hour observations, but irritation was then observed 7 and 14 days after patch removal. The remaining 2 animals showed very slight to well defined erythema and/or very slight to slight oedema from the 24 hour observations until the completion of the study.

At the completion of the study, oedema was present at all treated sites and erythema was present at the treated sites of 2 animals. Skin thickening was also present at 2 treated sites at the end of the study.

CONCLUSION

The notified chemical is irritating to the skin.

TEST FACILITY

Toxicol Laboratories (1994b)

B.3. Irritation – eye

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 405 Acute Eye Irritation/Corrosion.

Species/Strain: Rabbit/New Zealand White

Number of Animals: 3 F

Observation Period: 14 days

Remarks - Method: No significant protocol deviations.
GLP Compliance.

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	1.33	1.33	1.33	2	< 7 days	0
Conjunctiva: chemosis	1.33	1.33	1.33	2	< 7 days	0
Conjunctiva: discharge	0	0	0	2	< 24 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results

Minimal to moderate conjunctival irritation was noted in all treated eyes 1 hour after treatment and in 2/3 animals at the 24, 48 and 72 hour observations.

No corneal opacity or iridial inflammation was observed at any of the measuring intervals.

All signs of irritation had dissipated by the observation 7 days after instillation, however, 1 animal could not fully open their eye at this point and so this animal was observed for an additional week (with the eye noted to be fully open at the completion of the study period).

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Toxicol Laboratories (1994c)

B.4. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation - Magnusson and Kligman guinea pig maximisation test.

Species/Strain Guinea pig/Dunkin Hartley

PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 25%
topical: 40%

MAIN STUDY

Number of Animals Test Group: 20 Control Group: 10

INDUCTION PHASE Induction Concentration:
intradermal: 25% v/v in light liquid paraffin
topical: 80% v/v in acetone

Signs of Irritation Following the intradermal administration, the test and control animals were noted to have exhibited a similar degree of irritation at the injection sites. Following topical induction, the test animals were noted to have shown an increased level of irritancy in comparison to the control animals.

CHALLENGE PHASE

1st challenge topical: 40% v/v in acetone

2nd challenge topical: 1%, 2%, 5% and 10% v/v in acteone

Remarks - Method Prior to rechallenge, the animals were split into groups, each consisting of 10 test and 5 control animals. The first group was rechallenged at 10% and 5% and the second group was rechallenged at 2% and 1%.

A positive control study using Mercaptobenzothiazole (MBT) had previously been conducted in the test laboratory.

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	40%	17/20	13/20		
	10%			8/10	4/10
	5%			4/10	0/10
	2%			3/10	3/10
	1%			0/10	0/10
	0%	0/20	0/20		
Control Group	40%	0/10	0/10		
	10%			1/5	0/5
	5%			0/5	0/5
	2%			0/5	0/5
	1%			0/5	0/5
	0%	0/10	0/10		

Remarks - Results The test item was shown to be a skin sensitiser based on the results after challenge treatment at 40% concentration. Additionally, at rechallenge positive responses were noted in the test animals at ≥ 2% concentration.

CONCLUSION	There was evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Toxicol Laboratories (1994d)

B.5. Skin sensitisation

TEST SUBSTANCE	10% Notified chemical (solution in the presence of BHT)
METHOD	Similar to OECD TG 406 Skin Sensitisation - Magnusson and Kligman guinea pig maximisation test.
Species/Strain	Guinea pig/ Hartley derived
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 5% v/v in ethanol topical: undiluted
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: 5% v/v in ethanol topical: undiluted
Signs of Irritation	Prior to the topical induction phase, the animals were pre-treated with 10% sodium lauryl sulfate (SLS) to create a local irritation, as the test item was not considered irritating based on the preliminary screening.
CHALLENGE PHASE	
1st challenge	topical: undiluted
Remarks - Method	The vehicle control was ethanol. A positive control study using phenylacetaldehyde was also conducted using 10 animals.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*	
		24 h	*48 h*
Test Group	100%	0/20	0/20
	0%	0/20	0/20
Control Group	100%	0/10	0/10
	0%	0/10	0/10
Positive Control Group	10%	10/10	10/10
	0%	0/10	0/10

Remarks - Results	No observations were noted in the test or control animals following challenge with the test substance. In the positive control group, skin reactions were noted for 10/10 animals at both the 24 and 48 hour observations. The results of the positive and negative control tests confirmed the validity of the study.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test.
TEST FACILITY	Leberco-Celsis Testing (1997)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	Similar to OECD TG 471 Bacterial Reverse Mutation Test.

	Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA1538, TA98, TA100
Metabolic Activation System	S9 fraction from phenobarbitone/β-naphthoflavone-induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 8 – 5,000 µg/plate b) Without metabolic activation: 0.064 – 40 µg/plate
Vehicle	Acetone
Remarks - Method	No significant protocol deviations. GLP Compliance. A preliminary toxicity test (1.6 - 5,000 µg/plate) was performed to determine the toxicity of the test material (using TA98 strain) in both the presence and absence of metabolic activation. A reduction of the growth of the bacterial background lawn was only noted in the absence of metabolic activation (at ≥ 40 µg/plate). Positive control tests were conducted in parallel to the main test using 9-aminoacridine (TA1537), 2-nitrofluorene (TA98, TA1538) and sodium azide (TA100), in the absence of S9 and .2-Aminoanthracene (all strains) in the presence of S9 mix

RESULTS

Remarks - Results	The first test, in the absence of metabolic activation, was only conducted at ≤ 8 µg/plate, but was increased to ≤ 40 µg/plate in the second test, as the authors noted that the expected reduction in bacterial lawn at the top dose was not seen. There were no statistically significant increases in the number of revertant colonies, with or without metabolic activation under the conditions of the test. The positive controls produced satisfactory responses, thus confirming the validity of the test system.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Toxicol Laboratories (1995)

B.7. Phototoxicity – human volunteers

TEST SUBSTANCE	10% notified chemical (solution in the presence of BHT)
METHOD	Phototoxicity patch test response in human subjects
Study Design	The test substance was evaluated in parallel with 4 other substances Preparatory procedure: The test subjects had 6 equal sized skin areas irradiated for varying exposure times (increased at each site by a factor of 1.25). Irradiation was conducted with full spectrum UVL (UVB plus UVA) and evaluation was undertaken 16 to 26 hours later to determine the Minimal Erythemal Dose (MED), indicated by the site exhibiting the least amount of perceptible erythema. Test sites: Three equal sized areas of virgin skin on the subject's backs were selected, with 2 sites treated with the test substance. One of the treated sites was then irradiated using a filtered light source, with the other treated site serving as a non-irradiated control. The third (untreated) site served as the irradiated control. Light source: A Xenon Arc Solar Simulator (150 W) was used to emit in

	the UVA (320 – 400 nm) and UVB (290 – 320 nm) range. A UVB-absorbing filter was then used to eliminate erythemogenic wavelengths below 320 nanometers, to allow delivery of only UVA irradiation. Treatment: 0.2 mL of the test substance was applied to a 2 cm × 2 cm Webril pad on an adhesive dressing to form an occluded patch that was applied to subjects. The patches were removed after 24 hours and the appropriate sites were irradiated with 24 J/cm^2 of UVA (320 – 400 nm) irradiation. Test and control sites were examined at 24 and 48 hours after the irradiation (48 and 72 hours after the application).
Study Group	20 F, 2 M; age range 20 to 75 years
Vehicle	None
Remarks - Method	A panel of 22 healthy human subjects (devoid of any physical or dermatological conditions) was amassed. Of these, 21 (19 female and 2 male) test subjects completed the study (1 female subject was discontinued by the study authors prior to the 24 hour observation following irradiation, as the subject was deemed to have an inadequate MED).
RESULTS	
Remarks - Results	Minimal or doubtful erythema was noted at the treated sites of 1 subject at the patch removal observation. At the 24 hour reading following irradiation, 6 subjects showed mild, but definite erythema at both irradiated sites, with an additional 2 subjects showing mild, but definite erythema or minimal or doubtful erythema at the irradiated control site. Only one subject was noted to have a minimal or doubtful response at the irradiated sites 48 hours following irradiation. Several subjects were observed to develop hyperpigmentation of the treated and/or control irradiated sites, at the 24 and 48 hour readings. No other clinical reactions were noted. Six subjects did not show any reactions during the course of the study.
CONCLUSION	Under the conditions employed in this study, there was no evidence of phototoxicity to the test substance.
TEST FACILITY	TKL (2004)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE: Notified chemical

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

Inoculum	Activated sewage sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Chemical Oxygen Demand (COD)
Remarks - Method	No significant protocol deviations. GLP Compliance.

The test substance (100 mg) was dispersed in culture medium and the volume was adjusted to 1 litre to give a stock solution of 100 mg/L. An aliquot (90 mL) of this stock solution was dispersed in 6 litres of inoculated medium to give the test concentration of 1.5 mg/L.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
3	5	3	28
9	14	9	43
16	19	16	72
28	20	28	81

Remarks - Results: All validity criteria were satisfied and no significant deviations to protocol were reported.

Examination of the degradation curve for the toxicity control showed that the toxicity control attained ~ 30% degradation by day 14 of the study, thereby confirming that the notified chemical was not toxic to the sewage treatment micro-organisms used in the study. After 28 days the toxicity control attained 46% degradation.

The notified chemical attained 20% degradation after 28 days. Therefore, the notified chemical cannot be considered as readily biodegradable under the conditions of OECD Guideline 301D.

CONCLUSION: The notified chemical is not readily biodegradable.

TEST FACILITY: Safepharm (1995b)

BIBLIOGRAPHY

ECHA (2012) Guidance on information requirements and chemical safety assessment (Chapter R.8: Characterisation of dose [concentration] – response for human health, Version 2.1, November, 2012) Helsinki, Finland, European Chemicals Agency.

Firmenich (2014) Stability Test of Perfumery Raw Materials (Study/project number not provided, April, 2014). Geneva, Switzerland, Firmenich Laboratory of Analysis and Measurements (Unpublished report submitted by the notifier).

Leberco (1997) Notified chemical: Guinea Pig Dermal Sensitisation – Magnussen, Kligman Maximisation Test (Study No. 976316, June, 1997). New Jersey, USA, Leberco Celsis Testing (Unpublished report submitted by the notifier).

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia.

Safepharm (1995a) Notified chemical: Determination of Water Solubility and Partition Coefficient (Project No. 161/003, June, 1995). Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (1995b) Notified chemical: Assessment of Ready Biodegradability: Closed Bottle Test (Project No. 161/34, April, 1995). Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/managing-risks-of-hazardous-chemicals-in-the-workplace.

TKL (2004) Notified chemical: Human Phototoxicity Study (Study No. PB610304, April, 2004). New Jersey, USA, TKL Research INC. (Unpublished report submitted by the notifier).

Toxicol (1994a) Notified chemical: Acute Oral Toxicity in the Rat (Study No. A/O/40633, September, 1994). Herefordshire, UK, Toxicol Laboratories Limited (Unpublished report submitted by the notifier).

Toxicol (1994b) Notified chemical: Acute Dermal Irritation in the Rabbit (Study No. A/S/40634, September, 1994). Herefordshire, UK, Toxicol Laboratories Limited (Unpublished report submitted by the notifier).

Toxicol (1994c) Notified chemical: Acute Eye Irritation in the Rabbit (Study No. A/E/40635, September, 1994). Herefordshire, UK, Toxicol Laboratories Limited (Unpublished report submitted by the notifier).

Toxicol (1994d) Notified chemical: Skin Sensitisation in the Guinea Pig (Study No. A/K/40428, June, 1994). Herefordshire, UK, Toxicol Laboratories Limited (Unpublished report submitted by the notifier).

Toxicol (1995a) Notified chemical: Bacterial Reverse Mutation Test: Five *Salmonella Typhimurium* Strains (Study No. M/AMES/40636, January, 1995). Herefordshire, UK, Toxicol Laboratories Limited (Unpublished report submitted by the notifier).

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 (2009) Estimations Programs Interface Suite™ for Microsoft® Windows, v 4.00. United States Environmental Protection Agency. Washington, DC, USA. Accessed on 30 September 2014.

US EPA (2012) Ecological Structure Activity Relationship toxicological Structural activity v1.11.United States Environmental Protection Agency. Washington, DC, USA. Accessed on 30 September 2014.

WHO (2012) Guidance for Immunotoxicity Risk Assessment for Chemicals (Harmonization Project Document No. 10, 2012). Geneva, Switzerland, World Health Organization.