File No: LTD/1788

November 2014

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Oxadiene

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/1788	Firmenich Pty Ltd	Oxadiene	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

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

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 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

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.

- Due to the combustible properties of the notified chemical, the notifier should consider their obligations under the Australian Dangerous Goods Code.

CONTROL MEASURES

Occupational Health and Safety

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

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

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

  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.

Disposal

- Where reuse or recycling are unavailable or impracticable, dispose of the 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 chemical exceeds or is intended to exceed 2% in air fresheners or 0.1% in cosmetic and other household products;

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 amount of chemical being introduced has increased, or is likely to increase, significantly;
  - the chemical has begun to be manufactured in Australia;

- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

(Material) Safety Data Sheet
The (M)SDS of the notified chemical 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: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, residual 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: dissociation constant and flammability limits

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA (2007), EU (2006), Switzerland (2008), China (2008), Philippines (2007)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Oxadiene

MOLECULAR WEIGHT
< 200 Da

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

3. COMPOSITION

DEGREE OF PURITY
> 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Colourless to slightly yellow liquid

Property	Value	Data Source/Justification
Freezing Point	< -20 °C	Measured
Boiling Point	187 °C at 98.8 kPa	Measured
Density	825 kg/m^3 at 20 °C	Measured
Vapour Pressure	0.111 kPa at 25 °C	Measured
Water Solubility	0.145 g/L at 20 °C	Measured
Hydrolysis as a Function of pH	$t_{½}$ = 150 h, 183 h, and 155 h at 20 °C, and pH 4, 7, and 9.	Measured
Partition Coefficient (n-octanol/water)	log Pow = 3.78	Measured
Surface Tension	69.7 mN/m at 20.2 ± 0.5 °C	Measured
Adsorption/Desorption	log K_{oc} = 2.78	Measured
Dissociation Constant	Not determined	The notified chemical does not contain

Property	Value	Data Source/Justification
		dissociable functionalities
Flash Point	67 °C at 101.3 kPa	Measured
Autoignition Temperature	228 °C	Measured
Explosive Properties	Predicted negative	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Predicted negative	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 either: (1) in the neat form for formulation into fragrance preparations and end-use products; (2) as a component of fragrance preparations (at concentrations ≤ 5%) to be blended into end-use products; and/or (3) as a component of end-use products (at concentrations ≤ 2%).

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 in the neat form or as a component of fragrance preparations will be imported into Australia in lacquered drums of sizes ranging from 5 kg up to 180 kg. The end-use products (≤ 2% 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 proposed usage concentrations of ≤ 2% for air fresheners and ≤ 0.1% for cosmetic and other household products.

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).

Reformulation
At the customer facilities, the notified chemical will be formulated into either a fragrance formula or end-use products. The reformulation procedure will likely vary depending on the nature of the product to be 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.

End-use
Household products containing the notified chemical (≤ 2% 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.

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 workers	unknown	unknown
Mixer	4	2
Drum Handling	4	2
Drum Cleaning	4	2
Quality Control	0.5	1
Packaging	4	2
End users (professionals)	unspecified	unspecified

EXPOSURE DETAILS
Transport and storage
Transport and storage workers may come into contact with the neat notified chemical, or as a component of the imported fragrance preparations (≤ 5% concentration) or end-use products (≤ 2% 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 ≤ 0.1% 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 cosmetic and household products (at ≤ 0.1% concentration) and air fresheners (at ≤ 2% concentration). The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

A combined internal dose of 0.2914 mg/kg bw/day was estimated using data on typical use patterns of cosmetic and household cleaning product categories in which the notified chemical may be used (SCCS, 2010; Cadby *et al.*, 2002; SDA, 2005; specific use details of the notified chemical are considered as exempt information). This estimation assumed a worst case scenario and is for a person who is a simultaneous user of a selection of cosmetic and household products that may contain the notified chemical.

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – local lymph node assay	inadequate evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days	NOAEL = 150 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non-mutagenic
Genotoxicity – in vitro chromosome aberration	non-clastogenic

Toxicokinetics
No information on the toxicokinetics of the notified chemical was provided. Based on the partition coefficient (log P_{ow} = 3.78) and the low molecular weight (< 200 Da) of the notified chemical, passive diffusion across the gastrointestinal tract (GI) and absorption across the skin may occur. The potential for systemic GI absorption is supported by the observation of treatment related effects in the 28 day repeated dose study in rats. The notified chemical may also be absorbed via the respiratory tract.

Acute toxicity
The notified chemical was of low acute oral (LD50 >2000 mg/kg bw) and dermal (LD50 >2000 mg/kg bw) toxicity in rats. No acute inhalation toxicity data were provided for the notified chemical.

Irritation
The notified chemical was a skin irritant to rabbits. Well-defined erythema and slight oedema were observed in all three rabbits on day 3. Slight desquamation was observed in all three rabbits at the end of 14-day observation period.

The notified chemical was a slight eye irritant to rabbits.

Skin sensitisation
There was no evidence of skin sensitisation in a local lymph node assay (LLNA) in mice at up to 40% concentration. However, the study was inadequate to determine the skin sensitisation potential of the notified chemical at higher concentrations.

Repeated dose toxicity
In a 28-day repeated dose gavage study, rats (5/sex/dose) were treated at 0, 15, 150 or 1000 mg/kg bw/day. Treatment related findings of increased liver weights and hepatocellular hypertrophy were considered to be adaptive but provide evidence of systemic absorption by the oral route. The NOAEL was established as 150 mg/kg bw/day in this study, based on increased kidney weights and decreased heart weights in females treated at 1000 mg/kg bw/day.

Mutagenicity/Genotoxicity
The notified chemical was not mutagenic in a bacterial reverse mutation study. The notified chemical was not clastogenic to human peripheral blood lymphocytes in an in vitro chromosome aberration study.

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

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

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Transport and storage
Transport and storage workers are only expected to become exposed to the notified chemical (at ≤ 100% concentration) in 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. Should these workers become exposed, skin and eye irritation are possible, and skin sensitisation cannot be ruled out.

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. Therefore, provided adequate control measures are in place to minimise worker exposure, including PPE, the risk to transport and storage workers from use of the notified chemical (at ≤ 100% concentration) is not considered to be unreasonable.

Reformulation
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. At the proposed usage concentration, skin irritation, slight eye irritation and systemic toxicity may occur. The risk of skin sensitisation at this concentration cannot be ruled out. Caution should therefore be exercised when handling the notified chemical during reformulation processes.

The use of mechanical ventilation and/or enclosed systems, and the use of PPE such as protective clothing, eye protection, impervious gloves and respiratory protection (if appropriate) are expected 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 reformulation workers from use of the notified chemical (at ≤ 100% concentration) is not considered to be unreasonable.

End-use
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. 1% concentration) in the cleaning industry.

Such professionals may use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. For hairdressing salons, good ventilation would be recommended if hair spray is routinely used in a confined space. If PPE is used, the exposure of such workers is expected to be of a similar or lesser extent than

that experienced by consumers using the various cosmetic and household products containing the notified chemical (for details of the public health risk assessment, see Section 6.3.2.). Based on the information available, the risk to workers associated with use of the notified chemical in cosmetic and household products (at ≤ 0.1% concentration) is not considered to be unreasonable.

6.3.2. Public Health

Members of the public may be repeatedly exposed to the notified chemical during the use of leave-on and rinse-off cosmetics (at ≤ 0. 1% concentration), household products (at ≤ 0. 1% concentration) and air fresheners (at ≤ 2% concentration).

Systemic effects

The potential systemic exposure to the public from the use of the notified chemical in cosmetic and household products was estimated to be 0.2914 mg/kg bw/day (see Section 6.1.2). Using a NOAEL of 150 mg/kg bw/day derived from a 28-day repeated dose toxicity study on the notified chemical, the margin of exposure (MOE) was estimated to be 515. A MOE value ≥ 100 is generally considered to be acceptable for taking into account intra- and inter-species differences. The risk to the public of systemic toxicity from use of the notified chemical (at ≤ 2% concentration) is therefore not considered to be unreasonable.

Skin sensitisation

Proposed methods for the quantitative risk assessment of dermal sensitisation have been the subject of significant discussion (see for example, Api *et al.*, 2008 and RIVM, 2010). Using a fine fragrance (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). When tested in an LLNA study, the notified chemical was not a skin sensitiser when tested up to 40% concentration. Assuming a sensitisation cut-off concentration of 40%, consideration of the study details and application of appropriate safety factors, allowed for the derivation of an Acceptable Exposure Level (AEL) of 27.5 µg/cm^2. In this instance, the factors employed included an interspecies factor (3), intra-species factor (10), a matrix factor (3.16), and a use and time factor (3.16), giving an overall safety factor of > 300 (300 used for calculations).

As the AEL > CEL, 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 and household products (containing ≤ 0. 1% notified chemical), by inference, the risk of induction of sensitisation associated with the use of these products is also not considered to be unreasonable. It is acknowledged that consumers may be exposed to multiple products containing the notified chemical, and a quantitative assessment based on the aggregate exposure has not been conducted.

Local effects

The notified chemical is a skin irritant and a slight eye irritant. Irritation is not expected at the proposed usage concentrations when used in the proposed manner. The risk to the public of skin and eye irritation from use of the notified chemical (at ≤ 2% concentration) is therefore not considered to be unreasonable.

Therefore, based on the information available, the risk to the public associated with use of the notified chemical at ≤ 0.1% in cosmetic and household products and ≤ 2% in air freshener products is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia at 100% concentration or as a fragrance component of compounded formulations and various formulated end-use cosmetic and household products. Environmental release of the notified chemical during transportation and storage is expected to be minimal and will be limited to accidental spills or leaks of drums.

It is expected that the reformulation processes will involve blending operations that will be highly automated. It is expected to occur in a fully enclosed environment, followed by automated filling of the reformulated products

into containers of various sizes. A total of 0.2% of waste is expected to be generated from blending or formulation activities as a result of spills and residues.

RELEASE OF CHEMICAL FROM USE

The notified chemical is expected to enter the aquatic compartment during use of the various products into which it will be incorporated. Cosmetic products will be washed off the hair and skin and will be released to sewers. Cleaning products will also be diluted in water and will be released to sewers. It is estimated that a maximum of 3% of the consumer products will remain in the consumer containers once the consumer product is used up. These containers are expected to be sent to landfill or to be recycled.

RELEASE OF CHEMICAL FROM DISPOSAL

Containers containing residual notified chemical are expected to be released to landfill or to be recycled.

7.1.2. Environmental Fate

The notified chemical is readily biodegradable based on the provided study report. For the details of the environmental fate study please refer to Appendix C. The notified chemical has a medium log K_{OW} of 3.78, and the bioaccumulative potential in aquatic organisms is not considered to be a concern.

The vapour pressure of the notified chemical of 111 Pa at 25°C provided by the notifier indicates a high volatility. Based on a calculated (AOPWIN v 1.92; US EPA, 2011) half-life of 0.884 hours through atmosphere oxidation, it is not expected to be persistent in the air.

Most of the notified chemical is expected to be released into sewer systems after use of the associated products. A small amount of the notified chemical may be released to landfill as container residues or spills or thermally decomposed during containers' recycling, forming water and oxides of carbon. In landfill, the notified chemical is not expected to leach given the high adsorption/desorption constant. In sewage treatment plants (STPs), a small proportion of the notified chemical may be removed by adsorption to sludge sediment given the low logK_{OC} of 2.78, and be disposed of to landfill or during soil application for remediation or agriculture. The majority of the notified chemical is expected to be released into public waters. In water or soil/landfill, 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 100% release of the notified chemical into sewer systems nationwide. Based on the SimpleTreat model (EC, 2003), 70% of the notified chemical is expected to be removed from water surface by evaporation (52%) and sludge adsorption (18%).

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	70%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.18	µg/L
PEC - Ocean:	0.02	µg/L

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 1.09 mg/kg (dry wt). Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1500 kg/m^3 and a soil-mixing zone of 10 cm, the concentration of the notified chemical may approximate 7 µg/kg in applied soil. This assumes that degradation of the notified chemical occurs in the soil within 1 year from application. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated biosolids application, the concentration of notified chemical in the applied soil in 5 and 10 years may approximate 0.035 mg/kg and 0.07 mg/kg, respectively.

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 0.18 µg/L may potentially result in a soil concentration of approximately 1.21µg/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 6.1 µg/kg and 12.1 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted. By using ECOSAR (US EPA, 2011), the following acute toxicity data have been predicted for the notified chemical.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 EC50 = 0.079 mg/L	Very toxic to fish
Daphnia Toxicity	48 h EC50 =1.768 mg/L	Toxic to *Daphnia*
Algal Toxicity	96 h EC50 = 2.73 mg/L	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 fish which is considered to be the most sensitive species. A conservative 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 (Fish)	0.08	mg/L
Assessment Factor	100	
PNEC:	0.79	µg/L

7.3. Environmental Risk Assessment

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

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	0.18	0.79	0.23
Q - Ocean:	0.02	0.79	0.02

The risk quotient (Q = PEC/PNEC) was calculated to be < 1 for discharge of effluent containing the notified chemical to the aquatic environment, indicating that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters based on its maximum annual use quantity.

Based on the calculated risk quotient 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

Freezing Point < - 20 °C

Method EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature.
Remarks The test substance did not melt when cooled to -20.0 °C
Test Facility Firmenich (2006)

Boiling Point 187 ± 2 °C at 98.8 kPa

Method EC Council Regulation No 440/2008 A.2 Boiling Temperature.
Remarks Siwoloboff method
Test Facility Firmenich (2006)

Density 825 kg/m^3 at 20 °C

Method EC Council Regulation No 440/2008 A.3 Relative Density.
Remarks Oscillating density meter method
Test Facility Firmenich (2006)

Vapour Pressure 0.111 kPa at 25 °C

Method EC Council Regulation No 440/2008 A.4 Vapour Pressure.
Remarks Determined using an isoteniscope system
Test Facility Safepharm (2007a)

Water Solubility 0.145 g/L at 20 °C

Method EC Council Regulation No 440/2008 A.6 Water Solubility
Remarks Flask Method. Mixtures of the notified chemical and water were added to three flasks and shaken at approximately 30°C for 8 hours. Following shaking, the flasks were left to stand at 20°C for 24 hours to allow the mixture to settle. A1iquots of the water solution (excluding undissolved material) were taken 24, 48 and 72 hours after the initial shaking, filtered through a 45 µm filter and analysed by HPLC. The pH of each solution was also measured to be 5.5. The water solubility was determined to be 0.145 g/L at 20 ± 0.5 °C.
Test Facility Firmenich (2006)

Hydrolysis as a Function of pH $t_{½}$ = 150 h, 183 h, and 155 h at 20 °C, and pH 4, 7, and 9, respectively

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

pH	*T (°C)*	*$t_{½}$ (hours)*
4	25	150
7	25	183
9	25	155

Remarks Sample solutions were maintained at pH 4, 7, 9, and at 50 ± 0.5°C for 90 hours, 60 ± 0.5°C for 42 hours, and 70 ± 0.5°C for 27 hours, respectively. A co-solvent tetrahydrofuran was used for preparation of the solutions. The test concentrations were determined using gas chromatography. By plotting the natural logarithm of the rate constants against the reciprocal of the temperature (K), the rate constant and half-lives at 25°C were obtained by extrapolation.
Test Facility Safepharm (2007b)

Partition Coefficient (n-octanol/water) log Pow = 3.78

Method EC Council Regulation No 440/2008 A.8 Partition Coefficient
Remarks HPLC Method. The column temperature was 30°C. The partition coefficient of the notified

chemical was determined to be P_{OW} = 6.02 × 103 or logP_{OW} = 3.78.
Test Facility Firmenich (2006)

Surface Tension 69.7 mN/m at 20.2 ± 0.5 °C

Method EC Council Regulation No 440/2008 A.5 Surface Tension.
Remarks Concentration:7.61 x 10^{-2} g/L
Test Facility Safepharm (2007b)

Adsorption/Desorption – screening test log K_{OC} = 2.78

Method Method of C19 of Commission Directive 2001/59/EC (which constitutes Annex V of Council Directive 67/548/EEC)
Remarks HPLC method. The log K_{OC} was determined to be 2.78 for the notified chemical.
Test Facility Safepharm (2007b)

Flash Point 67 ± 2 °C at 101.3 kPa

Method EC Council Regulation No 440/2008 A.9 Flash Point.
Remarks Closed cup method
Test Facility Firmenich (2006)

Autoignition Temperature 228 ± 5 °C

Method EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases).
Test Facility SafePharm (2007a)

Explosive Properties Predicted Negative

Method EC Council Regulation No 440/2008 A.14 Explosive Properties.
Remarks Predicted negative based on chemical structure and oxygen balance.
Test Facility Safepharm (2007a)

Oxidizing Properties Predicted Negative

Method EC Council Regulation No 440/2008 A.21 Oxidizing Properties (Liquids).
Remarks Predicted negative based on chemical structure.
Test Facility Safepharm (2007a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE Notified chemical

METHOD OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method
Species/Strain Rat/Sprague-Dawley
Vehicle None
Remarks - Method No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 F	2000	0/3
2	3 F	2000	0/3

LD50 > 2000 mg/kg bw
Signs of Toxicity Hunched posture, ataxia, piloerection and decreased respiratory rate were observed up to one day post dosing.
Effects in Organs No abnormalities observed.

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

TEST FACILITY Safepharm (2006a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE Notified chemical

METHOD OECD TG 402 Acute Dermal Toxicity – Limit Test
Species/Strain Rat/Sprague-Dawley
Vehicle None
Type of dressing Semi-occlusive
Remarks - Method No significant protocol deviations.

RESULTS

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

LD50 > 2000 mg/kg bw
Signs of Toxicity - Local No signs of dermal irritation were observed.
Signs of Toxicity - Systemic None observed.
Effects in Organs None observed.

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

TEST FACILITY Safepharm (2007c)

B.3. Irritation – skin

TEST SUBSTANCE Notified chemical

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion
Species/Strain Rabbit/New Zealand White
Number of Animals 3 males

Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive
Remarks - Method	No significant 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	2.0	2.0	2.0	2	< 14 days	0
Oedema	2.0	2.0	2.0	2	< 7 days	0

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

Remarks - Results

Well-defined erythema (grade 2) and slight oedema (grade 2) were observed in all animals up to an including the 72-hour observation point, with very slight erythema (grade 1) observed in one animal at 7 days. Severe desquamation was noted in another animal at 7 days, which prevented evaluation of erythema and oedema. Slight desquamation was observed in all animals at the day 14 observation. Blanching of the skin, light brown discolouration of the epidermis, and loss of skin elasticity were also noted up to the 72 hour observation.

CONCLUSION

The notified chemical is irritating to the skin.

TEST FACILITY

Safepharm (2006b)

B.4. Irritation – eye

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 405 Acute Eye Irritation/Corrosion

Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Observation Period	72 hours
Remarks - Method	No significant protocol deviations.

A rabbit enucleated eye test (REET) was conducted prior to the main test. The corneas of three enucleated eyes from New Zealand White Rabbits were treated with 0.1 mL notified chemical and maintained at 32°C. A control group of two enucleated eyes was treated with 0.9% sodium chloride. The eyes were assessed for corneal thickness (swelling), corneal opacity, alteration of the corneal epithelium and fluorescein uptake, for an observation period of 4 hours.

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	0.3	0.7	0.7	2	< 72 h	0
Conjunctiva: chemosis	0	0	0	1	< 24 h	0
Conjunctiva: discharge	0	0	0	2	< 24 h	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

The REET test indicated that the notified chemical was unlikely to be a

severe occular irritant, based on similar observations in the measured parameters in treated and control groups.

In the main study, slight (grade 1) to moderate (grade 2) conjunctival irritation was observed at one hour post dose. Slight conjunctival redness (grade 1) was observed in two animals up to and including 48 hours and up to 24 hours in the other animal. All eyes were normal after 72 hours.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY Safepharm (2006c)

B.5. Skin sensitisation – mouse local lymph node assay

TEST SUBSTANCE Notified chemical

METHOD Similar to OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
Species/Strain Mouse/ CBA/J (female)
Vehicle Acetone:olive oil (4:1)
Remarks - Method The main study was conducted using 5 mice/group at 1, 5, 10, 20 or 40%. A vehicle control group was conducted using 8 mice/group. The study authors reported that the sponsor requested the tested dosing regime.

RESULTS

Concentration (%)	*Proliferative response (DPM)*	*Stimulation Index (Test/Control Ratio)*
Test substance		
0 (vehicle control)	38.9	-
1	39.0	1.0
5	28.0	0.7
10	19.7	0.5
20	60.0	1.5
40	83.6	2.1
Positive control (isoeugenol)		
5	274.0	7.0
Positive control (HCA)		
15	34.2	0.9
60	172.7	4.4

Remarks - Results No signs of systemic toxicity or irritation were observed.

The stimulation index values for the test substance groups were < 3, indicating the absence of a skin sensitisation response at the tested concentrations. However, testing guideline recommends the highest concentration to maximise exposure while avoiding systemic toxicity and/or excessive local skin irritation. Undiluted test substance (100%) should have been considered for this test. The results of this study are therefore inadequate to characterise the skin sensitisation potential of the notified chemical at concentrations above 40%.

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

CONCLUSION There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY BRT (2006)

B.6. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents
Species/Strain	Rat/Sprague-Dawley
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week
Vehicle	Arachis oil BP
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 M + 5 F	0	0/10
low dose	5 M + 5 F	15	0/10
mid dose	5 M + 5 F	150	0/10
high dose	5 M + 5 F	1000	0/10

Clinical Observations

There were no treatment related clinical signs of toxicity. Increased salivation was observed sporadically throughout the study, either shortly after dosing or up to 5 hours post dose. The salivation occurred at all doses but was most commonly observed in animals treated at 1000 mg/kg bw/day where it was also accompanied by staining of external body surfaces (eyes, fur, mouth and snout). These effects are likely due to an unpalatable or irritant nature of the test material that is being administered by gavage, not test substance related systemic toxicity.

Slight salivation was observed in two males treated at 1000 mg/kg bw/day during a weekly behavioural assessment conducted on day 24. There were statistically significant decreases in mean forelimb grip strength in all groups of treated males during one of the three functional performance tests, with no clear dose response. Based on their transient nature and lack of a clear dose response, these effects are considered to be of low toxicological concern. There were no treatment related changes in sensory reactivity assessments.

There was a non-statistically decrease in terminal body weight in males treated at 1000 mg/kg bw/day, with a statistically significant reduction in body weight gain in this group over the first (↓19%) and third (↓16%) weeks of the study. There was a non-statistically significant (two-tailed t-test, P=0.12) decrease in overall body weight gain in males treated at 1000 mg/kg bw/day (↓16%). In the absence of a clear effect on overall body weight gain in this group, these findings are not considered to represent an adverse finding under the conditions of the study. Body weights were unaffected in females.

The mean weekly and overall food efficiency (body weight/food consumption) was increased in males treated at 1000 mg/kg bw/day, with no change seen in females. There was a tendency for increased water consumption in females treated at 1000 mg/kg bw/day.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

There were statistically significant decreases in mean cell haemoglobin concentration (MCHC) in females treated at 150 (↓1%) and 1000 mg/kg bw/day (↓1%) and in males treated at 1000 mg/kg bw/day (↓3%). These changes were small and within the normal range for this strain of rats. In females treated at 1000 mg/kg bw/day, there were statistically significant decreases in platelets (↓29%) and neutrophils (↓39%). The relevance of these findings is unclear.

There was a statistically significant increase in cholesterol levels in females treated at 1000 mg/kg bw/day (↑53%), whilst in males treated at 1000 mg/kg bw/day there was a statistically significant decrease in cholesterol (↓15%) and bilirubin (↓51%).

There were statistically significant reductions of inorganic phosphate in all male treated groups, whilst females treated at 1000 mg/kg bw/day exhibiting a statistically significant increase. These changes of inorganic phosphate levels were reported as being within expected normal ranges for both males and females, with the

exception of a single male animal in each of the 150 and 1000 mg/kg bw/day groups.

There were dose dependent statistically significant increased calcium concentration in all treated females, with a statistically significant increase in potassium levels and a statistically significant decrease in chloride levels in females treated at 1000 mg/kg bw/day. The relevance of these findings is unclear.

Effects in Organs

There were statistically significant increases in absolute and relative liver weights in males (↑10%/↑21% absolute/relative) and females (↑38%/↑28% absolute/relative) treated at 1000 mg/kg bw/day. Minimal to slight centrilobular hepatocellular hypertrophy was observed in males and females treated at 150 and 1000 mg/kg bw/day (see following Table).

There were statistically significant increases in absolute and relative kidney weights in females treated at 1000 mg/kg bw/day (↑26%/↑16% absolute/relative), additionally there were statistically significant decreases in absolute and relative heart weights in this group (↓6%/↓13% absolute/relative). There were no associated histopathological findings in the kidney or heart.

At gross necropsy, small epididymides and seminal vesicles were observed mostly in males treated at 150 and 1000 mg/kg bw/day but with a single incidence in males treated at 15 mg/kg bw/day. Small testes were observed in males treated at 150 and 1000 mg/kg bw/day. There were no statistically significant changes in epididymides or testes weights and there were no treatment related histopathological findings in these organs. These macroscopic observations are therefore considered to be incidental.

	Males (mg/kg bw/day)				*Females (mg/kg bw/day)*			
	0	*15*	*150*	*1000*	*0*	*15*	*150*	*1000*
Centrilobular hepatocellular hypertrophy	0/5	0/5	2/5 (1.0)	5/5 (1.6)	0/5	0/5	1/5 (1.0)	4/5 (1.0)

( ), Average severity of affected animals: 1=minimal, 2=slight, 3=moderate, 4=severe.

Remarks – Results

Treatment related findings of increased liver weights and hepatocellular hypertrophy were observed in males and females. These findings are commonly observed in toxicology studies, indicative of an adaptive response to a xenobiotic. In this study, there were no accompanying clinical chemistry findings indicative of liver toxicity, thus are of low toxicological concern and are likely adaptive in nature.

The findings of increased kidney weights and decreased heart weight are considered to be potentially adverse effects in the absence of a recovery period or studies of longer duration to definitely establish the relevance of these effects.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 150 mg/kg bw/day in this study, based on increased kidney weights and decreased heart weights in females treated at 1000 mg/kg bw/day.

TEST FACILITY Safepharm (2008)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test – Plate incorporation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA$^-$
Metabolic Activation System	Phenobarbitone/β-naphthoflavone induced rat liver (S9 homogenate)
Concentration Range in Main Test	a) With metabolic activation: 0, 15, 50, 150, 500, 1500, 5000 µg/plate b) Without metabolic activation: 0, 1.5, 5, 15, 50, 150, 500, 1500, 5000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	No significant protocol deviations.

Vehicle and positive controls were conducted in parallel with the test material in accordance with the testing guideline.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test**	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 5000	≥ 500	> 5000	negative
Test 2	-	≥ 500	> 5000	negative
Present				
Test 1	≥ 5000	≥ 1500	> 5000	negative
Test 2	-	≥ 500	> 5000	negative

*Partial absence of bacterial lawn

Remarks - Results

No statistically or biologically significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains up to and including the maximum dose, 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 mutagenic to bacteria under the conditions of the test.

TEST FACILITY

Safepharm (2006d)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 473 In vitro Mammalian Chromosome Aberration Test

Cell Type/Cell Line: Human peripheral lymphocytes

Metabolic Activation System: Phenobarbitone/β-naphthoflavone induced rat liver (S9 homogenate)

Vehicle: Dimethyl sulfoxide

Remarks - Method: No significant protocol deviations.

Vehicle and positive controls were conducted in parallel with the test substance.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 24.11*, 48.22*, 96.44*, 192.88, 289.32, 385.75, MMC 0.4*	4 h	24 h
Test 2	0*, 24.11, 48.22*, 96.44*, 128.60*, 160.73*, 192.88, MMC 0.2*	24 h	24 h
Present			
Test 1	0*, 24.11*, 48.22*, 96.44*, 192.88, 289.32, 385.75, CP 5*	4 h	24 h
Test 2	0*, 24.11, 48.22, 96.44*, 128.60*, 160.73*, 192.88*, CP 5*	4 h	24 h

* Cultures selected for metaphase analysis.
MMC, Mitomycin C. CP, Cyclophosphamide.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*		
	*Cytotoxicity**	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 96.44	none	negative
Test 2	≥ 160.73	none	negative
Present			

Test 1	> 96.44	none	negative
Test 2	> 192.88	none	negative

*Reduction in mitotic index of ≥50%.

Remarks - Results	Under all experimental conditions, there was no evidence of an increase in the proportion of cells with chromosomal aberrations. No statistically significant increases in polyploidy metaphases were observed. The positive and vehicle controls gave satisfactory responses confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to human peripheral blood lymphocytes cells treated in vitro under the conditions of the test.
TEST FACILITY	Safepharm (2007d)

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	Sewage treatment micro-organisms
Exposure Period	28 days
Auxiliary Solvent	Not applied
Analytical Monitoring	The dissolved oxygen depletion was measured for determination of the degree of degradation
Remarks - Method	The test was conducted following the above test guideline and good practice laboratory practice (GLP). A saturated solution of the notified chemical at 109 mg/L in culture medium was prepared followed by further dilution to a test level of 1.5 mg/L. A blank control, a reference control and a toxicity control test were performed.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
3	7	3	51
14	8	11	62
28	14	28	72

Remarks - Results	All the test validity criteria were met. The toxicity control attained 26% degradation after 14 days and 33% degradation after 28 days. Therefore the notified chemical was not toxic to the sewage treatment micro-organisms used in the study. The notified chemical is not considered to be readily biodegradable based on the test results.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	Safepharm (2006e)

BIBLIOGRAPHY

BRT (2006) [Notified Chemical]: Local Lymph Node Assay (LLNA) in Mice (Study No: BRT 20060106, March, 2006). North Carolina, USA, Burleson Research Technologies Inc. (Unpublished report provided by the notifier).

Cadby, P.A., Troy, W.R. and Vey, M.G.H. (2002) Consumer Exposure to Fragrance Ingredients: Providing Estimates for Safety Evaluation. Regulatory Toxicology and Pharmacology, 36: 246-252.

enHealth (2004) Environmental Health Risk Assessment, Guidelines for Assessing Human Health Risks from Environmental Hazards. Canberra, Department of Health and Ageing and enHealth Council, Commonwealth of Australia.

European Commission (2003) Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances and Directive 98/8/EC of the European Parliament and of the Council Concerning the Placing of Biocidal Products on the Market – Part I. Institute for Health and Consumer protection, European Chemicals Bureau, European Communities.

European Commission (2003). Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances and Directive 98/8/EC of the European Parliament and of the Council Concerning the Placing of Biocidal Products on the Market – Part II. Institute for Health and Consumer protection, European Chemicals Bureau, European Communities. Available at <http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/doc/tgd>.

Firmenich (2006) [Notified Chemical]: Determination of General Physico-Chemical Properties: Melting/Freezing Temperature, Boiling Temperature, Relative Density, Flash Point, Partition Coefficient and Water Solubility (Study No. E043-01.2006, February, 2006). Geneva, Switzerland, Firmenich SA (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 (2006a) [Notified Chemical]: Acute Oral Toxicity in the Rat – Acute Toxic Class Method (Project No. 0161/0505, July, 2006). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report provided by the notifier).

Safepharm (2006b) [Notified Chemical]: Acute Dermal Irritation in the Rabbit (Project No. 0161/0506, July, 2006). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report provided by the notifier).

Safepharm (2006c) [Notified Chemical]: Acute Eye Irritation in the Rabbit (Project No. 0161/0507, July, 2006). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report provided by the notifier).

Safepharm (2006d) [Notified Chemical]: Reverse Mutation Assay "Ames Test" using Salmonella Typhimurium and Escherichia Coli (Project No. 0161/0504, June, 2006). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report provided by the notifier).

Safepharm (2006e) [Notified Chemical]: Assessment of Ready Biodegradability; Closed Bottle Test (Project No. 0161/0508, June, 2006). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2007a) Oxadiene: Determination of Hazardous Physico-chemical Properties (Project No. 0161/0568, September, 2007). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2007b) Oxadiene: Determination of General Physico-chemical Properties (Project No. 0161/0573, December, 2007). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (2007c) Oxadiene: Acute Dermal Toxicity (Limit Test) in the Rat (Project No. 0161/0569, August, 2007). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report provided by the notifier).

Safepharm (2007d) Oxadiene: Chromosome Aberration Test in Human Lymphocytes In Vitro (Project No. 0161/0571, December, 2007). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report provided by the notifier).

Safepharm (2008) Oxadiene: Twenty-Eight Day Repeated Dose Oral (Gavage) Toxicity Study in the Rat (Project No. 0161/0570, February, 2008). Shardlow, Derbyshire, UK, Safepharm Laboratories Limited (Unpublished report provided 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.

SDA (2005) Exposure and Risk Screening Methods for Consumer Product Ingredients. Washington DC USA, The Soap and Detergent Association.

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.

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) Estimation Programs Interface (EPI) Suite™ for Microsoft® Windows, v 4.10. United States Environmental Protection Agency. Washington DC, USA Available at http://www.epa.gov/oppt/exposure/pubs/episuite.htm.