File No: LTD/1968

July 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

2-Pentanone, 3-methyl-5-((1R,3R)-2,2,3-trimethylcyclopentyl)-

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment and Energy.

This Public Report is available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1968	Takasago International (Singapore) Pte Ltd	2-Pentanone, 3-methyl-5-((1R,3R)-2,2,3-trimethylcyclopentyl)-	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 of 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 sensitisation (Category 1B)	H317 – May cause an allergic skin reaction

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

Hazard classification	*Hazard statement*
Acute (Category 1)	H400 – Very toxic to aquatic life
Chronic (Category 1)	H410 – Very toxic to aquatic life with long lasting effects

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

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

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the 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 sensitisation (Category 1B): 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:
  − Enclosed, automated processes, where possible
  − Adequate 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 reformulation:
  − Avoid contact with skin and eyes
  − Avoid inhalation

- 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
  − Respiratory protection, if inhalation exposure may occur

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

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

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

Disposal

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

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the concentration of the notified chemical exceeds or is intended to exceed 1% in cosmetic and 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.

Safety Data Sheet
The SDS of the notified chemical and products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT
Takasago International (Singapore) Pte Ltd (ABN: 29 099 666 832)
Level 5, 815 Pacific Highway
CHATSWOOD NSW 2067

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, use details and import volume.

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT
None

NOTIFICATION IN OTHER COUNTRIES
EU (2015)
Japan (2015)
China (2016)

2. IDENTITY OF CHEMICAL

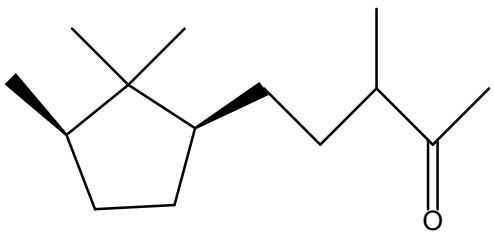
MARKETING NAME(S)
Blooming Musk

CAS NUMBER
Not assigned

CHEMICAL NAME
2-Pentanone, 3-methyl-5-((1R,3R)-2,2,3-trimethylcyclopentyl)-

MOLECULAR FORMULA
$C_{14}H_{26}O$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
210.36 Da

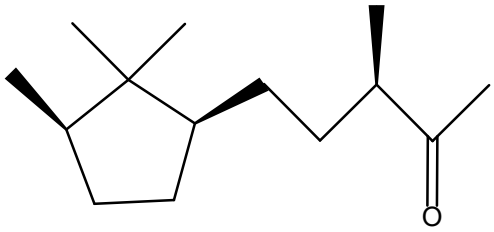
ANALYTICAL DATA
Reference NMR, IR, GC-MS and GC-FID spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 85%

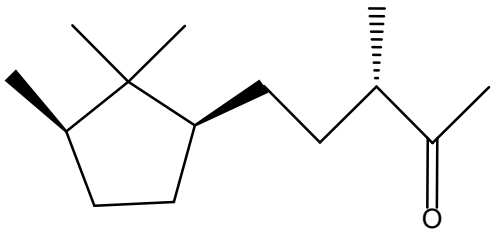
GC-FID spectra indicate that the notified chemical is mainly comprised of two diastereoisomers (A and B) in equimolar proportions.

Diastereoisomer A



Chemical Name: 2-Pentanone, 3(R)-Methyl-5-((1R,3R)-2,2,3-trimethylcyclopentyl)-
CAS number: Not assigned

Diastereoisomer B



Chemical Name: 2-Pentanone, 3(S)-Methyl-5-((1R,3R)-2,2,3-trimethylcyclopentyl)-
CAS number: Not assigned

IMPURITIES (> 1% BY WEIGHT)

Chemical Name	3-Methyl-5-((1S,3S)-2,2,3-trimethylcyclopentyl)-2-pentanone		
CAS No.	Not assigned	*Weight %*	< 10
Hazardous Properties	Not determined		
Chemical Name	3-Methyl-5-(2,2,3-trimethylcyclopentyl)-2-pentanone		
CAS No.	119464-63-0	*Weight %*	< 5
Hazardous Properties	Not determined		
Chemical Name	Unidentified		
CAS No.	-	*Weight %*	< 1
Hazardous Properties	Not determined		

4. PHYSICAL AND CHEMICAL PROPERTIES

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

Property	Value	Data Source/Justification
Freezing Point	< - 20 °C	Measured
Boiling Point	269 ± 1 °C at 101.3 kPa	Measured
Density	883 kg/m^3 at 20 °C	Measured
Vapour Pressure	2.2 × 10^{-3} kPa at 25 °C	Measured

Property	Value	Data Source/Justification
Water Solubility	9.17×10^{-3} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	$t_{1/2} > 1$ year at 25 °C pH 4, 7, 9	Measured
Partition Coefficient (n-octanol/water)	log Pow = 1.34×10^{5} at 30 °C	Measured
Surface tension	70.8 ± 1 mN/m at 21.3 °C (90% saturated solution)	Measured
Adsorption/Desorption	log K_{oc} = 3.96	Calculated using KOCWIN v2.00 (US EPA, 2009)
Dissociation Constant	Not determined	The notified chemical does not contain functionality that is expected to dissociate under environmental conditions
Flash Point	120 ± 2 °C (closed cup).	Measured
Flammability	Combustible liquid*	Based on flash point
Flammability in Contact With Water	Not highly flammable	Expert statement provided by the notifier.
Autoignition Temperature	340 ± 5 °C	Measured
Explosive Properties	No explosive properties	Expert statement provided by the notifier. The test substance does not contain chemical groups which are associated with explosive properties.
Oxidising Properties	No oxidising properties	Expert statement provided by the notifier. The test substance does not contain groups that act as an oxidising agent.

* Based on Australian Standard AS1940 definitions

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

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

The notified chemical has a flash point of 120 °C. Based on Australian Standard AS1940 definitions for combustible liquids, a liquid that has a flash point of 150 °C or less is a Class C1 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. It will be imported into Australia as a component of fragrance mixtures at ≤ 10% concentration.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 1	< 1	< 1	< 1	< 1

PACKAGING
Fragrance mixtures containing the notified chemical at ≤ 10% concentration will be introduced in 200 L drums and will be transported by road to the notifier's warehouse or formulation sites. The final consumer products will be transported by road to the retailers' sites.

USE
The notified chemical will be used as a fragrance ingredient in cosmetic and household products at ≤ 1% concentration.

OPERATION DESCRIPTION
Reformulation of fragrance mixtures containing the notified chemical at ≤ 10% concentration into finished consumer goods may vary depending of the type of product produced and may involve both automated and manual transfer steps. Typically, reformulation processes may incorporate blending operations that are highly automated and occur in a fully enclosed/contained environment, followed by automated filling of the reformulated end-use products into containers of various sizes.

End-use products containing the notified chemical (at ≤ 1% concentration) will be used by consumers and professionals such as hairdressers, beauticians and cleaners. Depending on the nature of the product, these could be applied in a number of ways, such as by hand, using an applicator or sprayed.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage (10-20 workers)	1-2	50
Mixers (10-20 workers)	≤ 8	240
QC samplers (1-2 workers)	0.5	240
Cleaners/maintenance (5-10 workers)	≤ 8	240
End users (professionals) > 1,000	1-8	200

EXPOSURE DETAILS
Transport and storage
Transport, storage and warehouse workers may come into contact with the notified chemical at ≤ 10% concentration (in fragrance mixtures) or at ≤ 1% concentration (in final formulated products), only in the event of accidental rupture of containers.

Formulation of end products
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical at ≤ 10% concentration may occur during handling of drums, during weighing and transfer stages, blending, quality control analysis and cleaning and maintenance of equipment. The notifier states that exposure is expected to be minimised through the use of mechanical ventilation and/or enclosed systems, and through the use of PPE such as protective clothing, eye protection and suitable gloves.

End use professionals
Exposure to the notified chemical at ≤ 1% concentration in end-use products may occur in professions where the services provided involve the application of cosmetic products to clients or the use of household products in the cleaning industry. The principal route of exposure will be dermal, while ocular and inhalation exposure is also possible. Such professionals may use some PPE to minimise repeated exposure and good hygiene practices are expected to be in place. If PPE is used, exposure of such workers is expected to be of a similar or less 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 (at ≤ 1% concentration) through the use of the cosmetic and household products. The main route of exposure will be dermal, while ocular and inhalation exposure is also possible, particularly if products are applied by spray.

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	slightly irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian chromosome aberration test	non genotoxic
Genotoxicity – *in vitro* mammalian cell micronucleus test	non genotoxic

Toxicokinetics

Given the low molecular weight (210.36 Da) of the notified chemical, there is potential for the chemical to be readily absorbed across biological membranes. However dermal absorption is expected to be limited by the high lipophilicity (log Pow = 5.13) and low water solubility (9.17×10^{-3} g/L at 20 °C) of the notified chemical limiting penetration of the hydrophilic epidermis.

Acute toxicity

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

Irritation and sensitisation

Based on studies conducted in rabbits, the notified chemical is slightly irritating to skin and eyes.

In the skin irritation study well-defined erythema and very slight to slight oedema were noted in one animal after exposure to the notified chemical for up to 72 hours. Moderate desquamation was noted in one animal 7 days after exposure. All signs of irritation were resolved at the 14-day observation. The notified chemical is slightly irritating to skin; however the findings observed did not warrant hazard classification under the GHS.

In the eye irritation study, moderate iridial inflammation and conjunctival discharge was noted after exposure to the notified chemical. These effects disappeared by the 24-hour time-point. Moderate reddening of the conjunctiva was noted after treatment. This effect was reduced to slight conjunctival redness by 48 hours and had resolved by the 72 hour time point. Slight to very slight chemosis occurred up to 24 hours after exposure to the notified chemical and disappeared at 48 hours. Based on the effects observed, the notified chemical is considered to be slightly irritating to the eyes. However, the scores of the effect observed did not warrant a classification under the GHS.

In a mouse LLNA, the notified chemical showed evidence of skin sensitisation with an EC3 of 100%.

Repeated dose toxicity

No information was provided on the repeated dose toxicity of the notified chemical.

Mutagenicity/Genotoxicity

The notified chemical tested negative in a bacterial reverse mutation assay, in an *in vitro* chromosomal aberration test and in an *in vitro* mammalian cell micronucleus test.

Health hazard classification

Based on the available information, the notified chemical is recommended for hazard classification according to the *Globally Harmonised System of 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 sensitisation (Category 1B)	H317 – May cause an allergic skin reaction

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Based on the available information the critical health effect of the notified chemical is skin sensitisation with the chemical also being a slight skin and eye irritant. The toxicity of the notified chemical following repeated exposure is unknown.

Reformulation

During reformulation workers may be at risk of sensitisation when handling the notified chemical at ≤ 10% concentration. It is anticipated by the notifier that engineering controls such as enclosed and automated processes and local ventilation will be implemented where possible, and appropriate PPE will be used to limit workers exposure.

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

End-use

End use professionals such as be beauticians, hairdressers and cleaners may be exposed to the notified chemical at ≤ 1% concentration. Dermal, and to a lesser extent, ocular and inhalation exposure may occur. PPE may be employed by these professionals to minimise repeated exposure and good hygiene practices are expected to be in place. If PPE is used, the risk to such workers is expected to be of a similar or lesser extent than that for consumers using products containing the notified chemical at ≤ 1% concentration.

6.3.2. Public Health

Members of the public may be repeatedly exposed to the notified chemical during the use of a variety of cosmetic and household products at ≤ 1% concentration. The main route of exposure is expected to be dermal with some potential for accidental ocular or oral exposure.

Irritation

The notified chemical is slightly irritating to skin and eyes. Given the low proposed use concentration (i.e. ≤ 1%), irritation effects are not expected.

Skin sensitisation

Proposed methods for the quantitative risk assessment of the dermal sensitisation have been the subject of significant discussion (i.e., Api *et al.,* 2008 and RIVM, 2010). Using fine fragrance as an example product that may contain the notified chemical (at a maximum of 1% concentration), as a worst case scenario, the Consumer Exposure Level (CEL) for the notified chemical is estimated to be 37.5 μg/cm^2/day (Cadby *et al.,* 2002). When tested in an LLNA study, the notified chemical was a skin sensitiser with an EC3 value of 100%. Consideration of the study details and application of appropriate safety factors allowed the derivation of an Acceptable Exposure Level (AEL) of 2498.89 μg/cm^2/day. In this instance, the factors employed included an interspecies factor (3), intraspecies factor (10), a matrix factor (3.16), use/time factor (3.16) and database factor (1), giving an overall safety factor of > 300 (300 used for calculation).

As the CEL is estimated to be less than the AEL, the risk to the public of induction of sensitisation that is associated with the use of fine fragrances (a worst case example of a leave-on cosmetic product) is not considered to be unreasonable. Based on the lower expected exposure level from other cosmetic and household products, by inference, the risk of induction of sensitisation associated with the use of these products is also not considered to be unreasonable. However, it is acknowledged that consumers may be exposed to multiple products containing the notified chemical, and a quantitative assessment based on aggregate exposure has not been conducted.

Repeat 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 concentration of the notified chemical (≤ 1%) in end use products.

Therefore, based on the information available, the risk to the public associated with the use of the notified chemical at ≤ 1% concentration in cosmetic and household 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 as a component of fragrance mixtures, for reformulation into finished cosmetic formulations and household products. There is unlikely to be any significant release to the environment from transport and storage, except in the case of accidental spills and leaks. In the event of spills, the product containing the notified chemical is expected to be collected with adsorbents, and disposed of to landfill in accordance with local government regulations.

The reformulation process will involve blending operations that will be highly automated, and is expected to occur within a fully enclosed environment. Therefore, significant release of the notified chemical from this process to the environment is not expected. Wastes containing the notified chemical generated during reformulation include equipment wash water, residues in empty import containers and spilt materials. This will be collected and released to sewers in a worst case scenario, or disposed of to landfill in accordance with local government regulations. Empty import containers are expected to be recycled or disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

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

RELEASE OF CHEMICAL FROM DISPOSAL

Residues of the notified chemical may remain in containers once the consumer products are used up. Wastes and residues of the notified chemical in empty containers are likely to either share the fate of the container and be disposed of to landfill, or be released to the sewer system when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

Following its use in cosmetic formulations and household products in Australia, the majority of the notified chemical is expected to enter the sewer system, before potential release to surface waters nationwide. Based on the result of the biodegradability study, the notified chemical is not considered readily biodegradable (6% in 28 days). For details of the environmental fate studies, please refer to Appendix C.

Although the measured partition coefficient of the notified chemical is high (log P_{OW} = 5.13), it is not expected to be bioaccumulative based on the results of a bioaccumulation study (BCF = 72 – 150). Based on its low water solubility and estimated high adsorption coefficient (log K_{OC} = 3.96), the notified chemical is expected to bind to sludge and sediment. As such, during sewage treatment plant (STP) processes the notified chemical is expected to be at least partially removed in sewage sludge. Therefore it is unlikely to be released to supernatant waters at ecotoxicologically significant concentrations. In surface waters, soil and sediment, the notified chemical is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has been calculated to assume a worst case scenario, with 100% release of the notified chemical into sewer systems nationwide and no removal within sewage treatment plants (STPs).

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4523	ML

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

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.61 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 20.19 µg/kg and 40.39 µg/kg, respectively.

7.2. Environmental Effects Assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LC50 = 1.49 mg/L	Toxic to fish
Daphnia Toxicity	48 h EC50 = 0.24 mg/L	Very toxic to invertebrates
Algal Toxicity	96 E_rC50 = 2.2 mg/L	Toxic to algae

Based on the above ecotoxicological endpoints for the notified chemical, it is expected to be very toxic to invertebrates and toxic to fish and algae. Therefore, under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009), the notified chemical is formally classified as "Acute Category 1; Very toxic to aquatic life". Based on the acute toxicity and lack of ready biodegradability of the notified chemical, it is classified as 'Chronic Category 1: Very toxic to aquatic life with long lasting effects' under the GHS.

7.2.1. Predicted No-Effect Concentration

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

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Daphnia)	0.24	mg/L
Assessment Factor	100.00	
Mitigation Factor	1.00	
PNEC:	2.4	µg/L

7.3. Environmental Risk Assessment

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

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.61	2.4	0.252
Q - Ocean	0.06	2.4	0.025

The risk quotient for discharge of treated effluents containing the notified chemical to the aquatic environment indicates that the notified chemical is unlikely to reach ecotoxicologically significant concentrations in surface waters, based on its maximum annual importation quantity and use pattern. Although the notified chemical is not considered readily biodegradable, it is determined to have a low potential for bioaccumulation. On the basis of the PEC/PNEC ratio, maximum annual importation volume and assessed use pattern in cosmetic formulations and household products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Freezing Point < -20 °C

Method OECD TG 102 Melting Point/Melting Range, 27 July 1995
EC Council Regulation No 440/2008 A.1 Melting/Freezing Temperature, 30 May 2008
Remarks Test item became slightly viscous during cooling.
Test Facility Harlan (2015a)

Boiling Point 269 ± 1 °C at 101.3 kPa

Method OECD TG 103 Boiling Point, 27 July 1995
EC Council Regulation No 440/2008 A.2 Boiling Temperature, 30 May 2008
Remarks Differential scanning calorimetry method used
Test Facility Harlan (2015a)

Density 883 kg/m^3 at 20 °C

Method OECD TG 109 Density of Liquids and Solids, 2 October 2012
EC Council Regulation No 440/2008 A.3 Relative Density, 30 May 2008
Remarks Pycnometer method used
Test Facility Harlan (2015a)

Vapour Pressure 2.2×10^{-3} kPa at 25 °C

Method EC Council Regulation No 440/2008 A.4 Vapour Pressure, 30 May 2008
Remarks Vapour pressure balance method used
Test Facility Harlan (2014a)

Water Solubility 9.17×10^{-3} g/L at 25 °C

Method OECD TG 105 Water Solubility.
EC Council Regulation No 440/2008 A.6 Water Solubility.
Remarks Flask Method
Test Facility Harlan (2015a)

Hydrolysis as a Function of pH $t_{1/2}$ > 1 year at 25 °C at pH 4, 7, 9

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

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

Remarks The test substance was stable towards hydrolysis.
Test Facility Harlan (2015a)

Partition Coefficient (n-octanol/water) log Pow = 1.34×10^5 at 30 °C

Method OECD TG 117 Partition Coefficient (n-octanol/water).
EC Council Regulation No 440/2008 A.8 Partition Coefficient.
Remarks HPLC Method. The test was performed at neutral pH with the test substance in a non-ionised form. The small peaks eluting before and after the main peak in the sample chromatograms were considered to be due to impurities.
Test Facility Harlan (2015a)

Surface Tension 70.8 ± 1.0 mN/m at 21.3 °C

Method	OECD TG 115 Surface Tension of Aqueous Solutions, 27 July 1995 EC Council Regulation No 440/2008 A.5 Surface Tension, 30 May 2008
Remarks	– Ring method was used. Ring circumference was 4 cm instead of 6 cm (as specified in the guidelines). The study authors noted that the reduced ring dimensions did not affect the integrity of the test. – Concentration: 90% (saturated)
Test Facility	Harlan (2015a)

Flash Point 120 ± 2 °C at 101.3 kPa

Method	EC Council Regulation No 440/2008 A.9 Flash Point, 30 May 2008
Remarks	Closed cup flash point tester method (Anon., 1983; Anon., 1989) used
Test Facility	Harlan (2014b)

Flammability in Contact with Water Not highly flammable

Method	EC Council Regulation No 440/2008 A.12 Flammability (Contact with Water)
Remarks	Expert statement provided by the notifier stated that the notified chemical was considered "not highly flammable" in contact with water due to the absence of groups in the molecular structure of the test substance that might lead to ignition in contact with water and/or to the evolution of a flammable gas.
Test Facility	WIL (2014)

Autoignition Temperature 340 ± 5 °C

Method	EC Council Regulation No 440/2008 A.15 Auto-Ignition Temperature (Liquids and Gases), 30 May 2008.
Remarks	Carbolite flask heater method (Anon., 1987) used.
Test Facility	Harlan (2014b)

Explosive Properties No explosive properties

Method	EC Council Regulation No 440/2008 A.14 Explosive Properties, 31 May 2008
Remarks	The test substance does not contain chemical groups which are associated with explosive properties (statement provided by the study authors).
Test Facility	WIL (2014)

Oxidizing Properties No oxidising properties

Method	EC Council Regulation No 440/2008 A.21 Oxidizing Properties (Liquids), 31 May 2008.
Remarks	The test substance does not contain groups that act as an oxidising agent (statement provided by the study authors).
Test Facility	WIL (2014)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 420 Acute Oral Toxicity - Fixed Dose Method (2001).
EC Directive 44/2008 B.1 bis Acute Toxicity (Oral).

Species/Strain	Wistar Rat/RccHan™
Vehicle	Arachis oil BP (for 300 mg/kg bw dose only)
Remarks - Method	No significant protocol deviations.

RESULTS

Sighting Study

Dose mg/kg bw	*Administered*	*Evident Toxicity*	*Mortality*
2000	1F	None	0/1
300	1F	None	0/1

Signs of Toxicity	No signs of systemic toxicity were detected during the observation period.
Effects in Organs	No abnormalities detected at post-mortem.

Main Study

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	4F	2000	0/4

LD50	> 2000 mg/kg bw
Signs of Toxicity	No signs of systemic toxicity were detected during the observation period.
Effects in Organs	No abnormalities detected at post-mortem.
Remarks - Results	No mortality occurred. All animals made expected body weight gains during the observation period.

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

TEST FACILITY: (Harlan 2014c)

B.2. Acute toxicity – dermal

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 402 Acute Dermal Toxicity (24 February 1987)

Species/Strain	Rat/Sprague-Dawley (Crl:CD(SD)), SPF.
Vehicle	None
Type of dressing	Occlusive
Remarks - Method	No significant protocol deviations. The dose used in this study was established in a previous study (Biotoxtech Study No. J14214), where no mortality occurred following the dermal administration of 2000 mg/kg bw to one male and one female rat.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5F/5M	0	0/10
2	5F/5M	2000	0/10

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	None observed during the study.
Signs of Toxicity - Systemic	None observed during the study.
Effects in Organs	No abnormalities detected at post-mortem.

Remarks - Results	No impairments in body weight development were observed during the study.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Biotoxtech (2014a)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion (24 April 2002). EC Council Regulation No 440/2008 B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White (Hsdlf:NZW)
Number of Animals	2
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			
Erythema/Eschar	0	2	2	< 7days	0
Oedema	0	1	2	< 7 days	0

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

Remarks - Results	One hour after treatment with the test substance, well-defined erythema and slight oedema was noted in one animal. At the 24, 48 and 72 hour readings, the well-defined erythema persisted and the oedema was noted as very slight. These effects were resolved by the 7-day time point. Moderate desquamation however, was noted in this animal at this time point. No signs of irritation were noted in the other animal throughout the study. All signs of irritation were resolved at the 14-day time point. Body weight gains of all animals were as expected. No signs of systemic toxicity were noted in the animals during the study. No mortality occurred.
CONCLUSION	The notified chemical is slightly irritating to the skin.
TEST FACILITY	Harlan (2014d)

B.4. Irritation – eye

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion (2 October 2012). EC Council Regulation No 440/2008 B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White (Hsdlf:NZW)
Number of Animals	2
Observation Period	72 hours
Remarks - Method	No significant protocol deviations. Test item was used as supplied.

RESULTS

Lesion	*Mean Score* Animal No.*		*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2			
Conjunctiva: redness	0.67	1.00	2.00	< 72 h	0.00
Conjunctiva: chemosis	0.33	0.33	2.00	< 48 h	0.00
Conjunctiva: discharge	1.00	0.00	1.00	< 24 h	0.00
Corneal opacity	0.00	0.00	-	-	0.00
Iridial inflammation	0.00	0.00	1.00	< 24 h	0.00

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

Remarks - Results

One hour after treatment, one animal displayed moderate iridial inflammation and both animals displayed conjunctival discharge. These effects were resolved by the 24-hour time-point.

Moderate reddening of the conjunctiva was noted in both animals 1 hour after treatment. At the 24 hour time-point, this effect remained in one animal and regressed to slight conjunctival redness in the other animal. Slight conjunctival redness remained in both animals at 48 hours after treatment and had disappeared by the 72 hour time point. Slight chemosis was noted in one animal and very slight chemosis noted in the other at 1 hour after treatment. By the 24 hour time-point both animals displayed very slight chemosis, which resolved at 48 hours.

No abnormal findings in the cornea were observed in any animal during the course of the study. No impairments in body weight development were observed during the study. No signs of systemic toxicity were noted in the animals during the study. No mortality occurred.

CONCLUSION

The notified chemical is slightly irritating to the eye.

TEST FACILITY

Harlan (2014e)

B.5. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 429 Skin Sensitisation: Local Lymph Node Assay (22 July 2010).

Species/Strain: Mouse/[CBA/J(SPF)]
Vehicle: Acetone/olive oil mixture (4:1) for all doses, excluding 100% solution.
Preliminary study: Yes.
Positive control: α-Hexylcinnamaldehyde

Remarks - Method

No deviation from the guideline was noted. A pre-screening test (Experiment No. E931, Study No. 432-028) using the test substance at 25, 50 and 100% concentration was conducted to determine dose concentrations for the main study. Based on the preliminary test results, 100% concentration was chosen as the high dose for the main study as it was expected not to induce any systemic toxic effects, 25% or more increase in ear thickness, moderate to severe erythema on the application site or more than 5% body weight loss.

RESULTS

Concentration (% w/w)	*Number and sex of animals*	*Proliferative response (DPM/animal)*	*Stimulation Index (Test/Control Ratio)*
Test Substance			
0 (vehicle control)	4F	1145.8	-
25%	4F	2420.9	2.1
50%	4F	2982.5	2.6
100%	4F	3420.1	3.0
Positive Control			
25%	4F	5475.6	4.8

EC3	100%
Remarks - Results	No mortalities and no signs of systemic toxicity were noted in the test or control animals during the study. The results showed that the test substance at 100% concentration elicited a stimulation index of 3. As such, an EC3 value could be derived. The EC3 value of the test substance is 100% and therefore categorised as a Category 1B skin sensitiser (EC3 > 2%).
CONCLUSION	There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	BSRC (2013)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test (21 July 1997). Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 fraction from phenobarbital/5, 6-benzoflavone induced rat liver.
Concentration Range in Main Test	a) With metabolic activation: 9.77 - 5000 µg/plate b) Without metabolic activation: 0.610 – 19.5 µg/plate
Vehicle	Dimethylsulfoxide (DMSO)
Remarks - Method	There were no deviations from the study plan. The dose range for the main test was determined from the pre-experiment test.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 19.5	≥ 9.77	> 19.5	Negative
Test 2	-	≥ 9.77	> 19.5	Negative
Present				
Test 1	≥ 313.0	≥ 156	> 5000	Negative
Test 2	-	≥ 156	> 5000	Negative

Remarks - Results	No substantial increase in revertant colony numbers of any of the five tester strains was observed following treatment with the test substance at any dose level, in the presence or absence of metabolic activation. Positive controls performed as expected, confirming the validity of the test system.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions

of the test.

TEST FACILITY CMIC (2013)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test (21 July, 1997).

Species/Strain	Chinese hamster
Cell Type/Cell Line	Lung (CHL/IU)
Metabolic Activation System	S9 fraction from phenobarbital/5, 6-benzoflavone induced rat liver.
Vehicle	Acetone
Remarks - Method	In the second test, a different substance was mistakenly used (instead of the test substance) in the continuous treatment without metabolic activation. Once discovered, slide observation from this part of the study was stopped immediately. As such, the incorrect contents of the second test were not included by the authors of this study in the final report and therefore were not considered by these authors to have affected the results of the study. A preliminary cell growth inhibition study was conducted by the authors of this study to determine the high dose of the main study.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	9*, 18*, 36*, 72	6 h	24 h
Test 2**	9.77*, 19.5*, 39.1*, 78.1, 156	24 h	24 h
Present			
Test 1	156, 313, 625, 1250, 2500	6 h	24 h
Test 3	38.8*, 77.5*, 155*, 310	6 h	24 h
Test 4	38.8*, 77.5*, 155*, 310	6 h	24 h

*Cultures selected for metaphase analysis.
**Data from selected cultures in this test not included in final report. See Method remarks for more details.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 78.1	≥ 72	> 36	Negative
Test 2	≥ 78.1	≥ 78.1	> 156	Negative
Present				
Test 1	≥ 2500	≥ 313	-	-
Test 3		≥ 310	> 155	Negative
Test 4		≥ 310	> 155	Negative

Remarks - Results In Test 1 with metabolic activation, a sufficient number of metaphase cells could not be observed in 4 out of the 5 doses administered. Therefore, no cultures from this test were selected for metaphase analysis. Two additional studies (Test 3 and 4) at lower doses were therefore conducted.

In all main tests, no statistically significant increases in the frequency of cells with structural or numerical chromosome aberrations were observed in the presence or absence of metabolic activation.

	The positive controls performed as expected, confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to Chinese hamster lung cells treated *in vitro* under the conditions of the test.
TEST FACILITY	Biotoxtech (2014b)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 487 Mammalian Cell Micronucleus Test (22 July 2010).
Species/Strain	Chinese hamster
Cell Type/Cell Line	Lung cells (CHL/IU)
Metabolic Activation System	S9 fraction from phenobarbital/5, 6-benzoflavone induced rat liver.
Vehicle	DMSO
Remarks - Method	There were no deviations from the study plan. The dose range for the main test was determined from a preliminary dose-ranging study.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	41.8*, 52.6*, 66.3*, 83.5, 105	6 h	24 h
Test 2	44.2, 52.6*, 62.5*, 74.4*, 88.4, 105	24 h	24 h
Test 3	44.2, 52.6, 62.5, 74.4, 88.4, 105	48 h	48 h
Test 4	52.6, 57.4, 62.5*, 68.2*, 74.4*	48 h	48 h
Present			
Test 1	52.6*, 105*, 210*	6 h	24 h

*Cultures selected for micronucleus analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 105	≥ 66.3	> 105	Negative
Test 2	≥ 105	≥ 74.4	> 105	Negative
Test 3*	≥ 105	-	> 105	-
Test 4**	-	> 74.4	> 74.4	Negative
Present				
Test 1	> 210	> 210	> 210	Negative

* Main test not conducted
**No preliminary test conducted

Remarks - Results	No increase in either micronucleated or multinucleated cells was observed in any of the tests using short-term treatment processes with or without metabolic activation or using continuous treatment processes. Positive and negative controls performed as expected, confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic to Chinese hamster lung cells treated *in vitro* under the conditions of the test.
TEST FACILITY	UBE (2014).

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical (99.2% purity)
METHOD	OECD TG 301 C Ready Biodegradability: Modified MITI Test (I).
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Oxygen consumption measuring apparatus and gas chromatography
Remarks - Method	The test was conducted according to the test guideline without significant deviation from the protocol.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
7	0	7	76
14	0	14	92
21	0	21	93
28	6	28	94

Remarks - Results	The difference of the BOD biodegradation between replicates is 30%, which does not meet the validity criterion of < 20%. However, the same conclusion can be derived based on the test results, irrelevant of the difference between replicates.
CONCLUSION	The notified chemical is not considered to be readily biodegradable.
TEST FACILITY	CERI (2014)

C.1.2. Bioaccumulation

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 305 Bioaccumulation in Fish: Aqueous and Dietary Exposure. Japanese Chemical Substance Control Law: Method for Testing the Degree of Accumulation of Chemical Substances in Fish Body.
Species	*Cyprinus carpio* (Common carp)
Exposure Period	Exposure: 28 days Depuration: None
Auxiliary Solvent	None
Concentration Range	Nominal: 0.5 µg/L Actual: 0.428 µg/L
Analytical Monitoring	Gas chromatography mass spectrometry
Remarks - Method	The test was conducted under semi static conditions (test water was renewed every 8-16 hours). The BCF of the test item was observed to be independent of the test concentration in the preliminary test. Thus, the BCF study was performed on one test concentration. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.
RESULTS	
Bioconcentration Factor	BCF = 72 - 150
CT50	Not determined
Remarks - Results	All validity criteria for the test were satisfied. During the exposure period of 28 days, the mortalities in both control and treated fish were 0% at the

end of the test. No abnormality in behaviour or appearance was observed during the uptake test period. The depuration phase was not reported in the test report.

CONCLUSION The notified chemical is not considered to be bioaccumulative.

TEST FACILITY CERI (2015)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE Notified chemical (98.5% purity)

METHOD OECD TG 203 Fish, Acute Toxicity Test - static.

Species	*Oryzias latipes*
Exposure Period	96 hours
Auxiliary Solvent	Acetone
Water Hardness	Not reported
Analytical Monitoring	Gas chromatography
Remarks – Method	The test substance is not readily soluble in water. Therefore, the stock solution was prepared by dissolving the test substance in acetone. This stock solution was then diluted with water to prepare the test solutions. The test was conducted according to the test guideline above with no significant deviation from the protocol.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality (%)*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	-	10	0	0	0	0	0
Solvent control	-	10	0	0	0	0	0
10	0.54	10	0	0	0	0	0
18	0.98	10	0	0	0	0	0
32	1.83	10	0	70	80	80	80
56	2.89	10	0	100	100	100	100
100	5.51	10	0	100	100	100	100

LC50	1.49 mg/L at 96 hours.
Remarks – Results	Less than 10% morality was observed in the control groups. The dissolved oxygen concentration in the test and control groups was greater than 60%. Therefore, the test results are considered valid given all the above validity criteria are met.

CONCLUSION The notified chemical is toxic to fish.

TEST FACILITY Biotoxtech (2014c)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical (98.5% purity).

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

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	148 mg $CaCO_3$/L
Analytical Monitoring	Chemical analysis

Remarks - Method	The test substance is not readily soluble in water. The test solutions were prepared by stirring an excess of test item in test water for 24 hours. Any undissolved test item was removed by filtration to produce a saturated solution. This saturated solution was then further diluted to prepare the test solutions. The test was conducted according to the test guideline above with no significant deviation from the protocol.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised (%)*	
Nominal	*Actual*		*24 h*	*48 h*
Control	-	20	0	0
1.0	-	20	0	0
3.2	0.13	20	0	0
10	0.39	20	25	90
32	0.62	20	100	100
100	1.47	20	100	100

EC50	0.24 mg/L at 48 hours (95% confidence limits: 0.22 – 0.27 mg/L)
NOEC	0.13 mg/L at 48 hours
Remarks - Results	Less than 10% of the test daphnids in control are observed showing immobilisation or other signs of disease or stress. The dissolved oxygen concentration at the end of the test is greater than 3 mg/L. Therefore, the test results are considered valid given all the above validity criteria are met.
CONCLUSION	The notified chemical is very toxic to aquatic invertebrates.
TEST FACILITY	Harlan (2015b).

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical (98.5%)
METHOD	US EPA Ecological Effects Test Guideline OCSPP 850.5400 “Algal Toxicity”.
Species	*Pseudokirchneriella subcapitata*
Exposure Period	96 hours
Concentration Range	Nominal: control, 100 mg/L Actual: control 2.2 mg/L
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	Chemical analysis
Remarks - Method	The test substance is not readily soluble in water. The test solutions were prepared by stirring an excess of test item in test water for 24 hours. Undissolved test item was removed by filtration to produce a saturated solution. An aliquot of each this saturated solution was incubated with algae suspension. The test was conducted according to the test guideline above with no significant deviation from the protocol.

RESULTS

Biomass		*Growth*	
E_bC50 *mg/L at 96 h*	*NOE_bC* *mg/L*	*E_rC50* *mg/L at 96 h*	*NOE_rC* *mg/L*
> 2.2	2.2	> 2.2	2.2

Remarks - Results

All validity criteria for the test are satisfied. The cell concentration of the control increased by a factor of 234 after 96 hours. This is in line with the guideline criterion that enhancement must be at least by a factor of 100. The coefficient of variation for average specific growth rate for the contrail was 1% in 96 hours. This satisfied the validation criterion that the coefficient of variation must not exceed 15%. The coefficient of variation of the mean control yield was 3%, meeting the validation criterion of less than 15%.

CONCLUSION

The notified chemical is toxic to algae.

TEST FACILITY

Harlan (2015c).

BIBLIOGRAPHY

Anon (1983) Paints, Varnishes Petroleum and Related Products – Determination of Flash Point – Rapid Equilibrium Method, *International Standard ISO 3679-2004 (E),* Second Edition – *2004-04-01,* P1-18.

Anon (1987), Electrical Apparatus for Explosive Gas Atmospheres. Part 4: Method of Test for Ignition Temperature. *IEC Publications 79-4,* P1-19.

Anon (1989) Flash Point of Liquids by Setaflash Closed-Cup Apparatus, *ATSM D-3278-89,* P1-7.

Biotoxtech (2014a) Acute Dermal Dose Toxicity Study of [notified chemical] in Sprague-Dawley Rats (Study No. J14214, August, 2014). Chungcheongbuk-do, Korea, Biotoxtech Co., Ltd. (Unpublished report submitted by the notifier).

Biotoxtech (2014b) *In Vitro* Chromosome Aberration Test of [notified chemical] using Mammalian Cultured Cell (Study No. J14215, October, 2014). Chungcheongbuk-do, Korea, Biotoxtech Co., Ltd. (Unpublished report submitted by the notifier).

Biotoxtech (2014c) Acute Toxicity Test of [Notified Chemical] in fish (Study No. J14217, November 2014), Cheongju-si, Korea, Biotoxtech Co., Ltd. (Unpublished report submitted by the notifier).

BSRC (2013) Mouse Local Lymph Node Assay of [notified chemical] (Exp. No. E932 (432-029), October, 2013). Shizuoka, Japan, Public Interest Incorporated Foundation Biosafety Research Center (Unpublished report submitted by the notifier).

CERI (2014) Biodegradation study of [notified chemical] (Study No. 16056, March, 2014). Kurume-shi, Japan, Chemicals Evaluation and Research Institute, CERI Kurume. (Unpublished report submitted by the notifier).

CERI (2015) Bioconcentration study of [notified chemical] in common carp (Study No. 46086, July, 2015) Kurume-shi, Japan, Chemicals Evaluation and Research Institute, CERI Kurume. (Unpublished report submitted by the notifier).

CMIC (2013) Bacterial Reverse Mutation Test of [notified chemical] (Study No. 13K3918G, July, 2013). Yamanashi, Japan, CMIC Bioresearch Center Co., Ltd. (Unpublished report submitted by the notifier).

Harlan (2014a) [Notified chemical]: Determination of Vapour Pressure (Study No. 41401310, November, 2014). Derbyshire, England, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2014b) [Notified chemical]: Determination of Flash Point and Auto-Ignition Temperature (Liquids and Gases) (Study No. 41401311, December, 2014). Derbyshire, England, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2014c) [Notified chemical]: Acute Oral Toxicity in the Rat – Fixed Dose Method (Study No. 41401312, November, 2014). Derbyshire, England, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2014d) [Notified chemical]: Acute Dermal Irritation in the Rabbit (Study No. 41401313, November, 2014). Derbyshire, England, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2014e) [Notified chemical]: Acute Eye Irritation in the Rabbit (Study No. 41401314, November, 2014). Derbyshire, England, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2015a) [Notified chemical]: Determination of General Physico-Chemical Properties (Study No. 41401309, April, 2015). Derbyshire, England, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2015b) [Notified chemical]: Daphnia sp., 48-hour Acute Immobilization Test (Study No. 41401315, January, 2015). Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2015c) [Notified chemical]: Algal Growth Inhibition Test (Study No. 41401316, January, 2015). Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, https://www.safeworkaustralia.gov.au/doc/model-code-practice-managing-risks-hazardous-chemicals-workplace.

UBE (2014) *In Vitro* Mammalian Cell Micronucleus Test (Study No. USA-R-14145, August, 2014). Yamaguchi, Japan, UBE Scientific Analysis Laboratory, Inc. (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 2 June 2017.

WIL (2014) Determination of Physico-Chemical Properties of [notified Chemical] (Study No. 507321, November, 2014). DD 's-Hertogenbosch, The Netherlands, WIL Research Europe B.V. (Unpublished report submitted by notifier).