File No.: LTD/2078

July 2019

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

2,4-Decadienamide, *N*-(2-methylpropyl)-, (2*E*,4*E*)-

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/2078	Symrise Pty Ltd	2,4-Decadienamide, *N*-(2-methylpropyl)-, (2*E*,4*E*)-	Yes	≤ 1 tonne per annum	Component of oral care products

CONCLUSIONS AND REGULATORY OBLIGATIONS

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

Hazard Classification	*Hazard Statement*
Acute Toxicity, oral (Category 3)	H301 – Toxic if swallowed
Specific target organ toxicity, repeated exposure (Category 2)	H373 – May cause damage to organs through prolonged or repeated exposure
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 aquatic hazard (Short-term)	H400 – Very toxic to aquatic life

Human Health Risk Assessment
Provided that the recommended controls are being adhered to, 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 oral care products at a maximum concentration of 0.1%, 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, 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:
  - Acute Toxicity, oral (Category 3): H301 – Toxic if swallowed
  - Specific target organ toxicity, repeated exposure (Category 2): H373 – May cause damage to organs through prolonged or repeated exposure
  - 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.

Health Surveillance

- As the notified chemical is a skin sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation.

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 chemicals during reformulation processes:
  - Enclosed/automated processes where possible
  - Local exhaust ventilation

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

- 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:
  - Impervious gloves
  - Safety glasses
  - Protective clothing

  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.

Public Health

- The Delegate should consider the notified chemical for listing on the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).

Disposal

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

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment

Regulatory Obligations

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

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

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the concentration of the notified chemical exceeds or is intended to exceed 0.1% in oral care products;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of oral care products, 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 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(S)
Symrise Pty Ltd (ABN: 67 000 880 946)
168 South Creek Road
DEE WHY NSW 2099

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

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Schedule data requirements are varied for density and absorption/desorption.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
trans-Pellitorin
Pellitorin trans

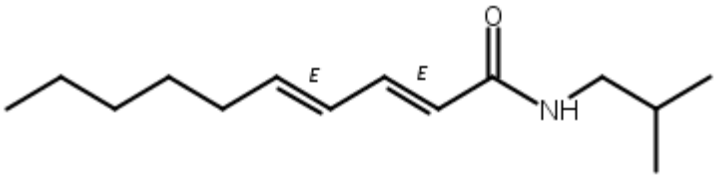
CAS NUMBER
18836-52-7

CHEMICAL NAME
2,4-Decadienamide, *N*-(2-methylpropyl)-, (2*E*,4*E*)-

OTHER NAME(S)
2,4-Decadienamide, N-(2-methylpropyl)-, (2E,4E)-
(2E,4E)-N- isobutyldeca-2,4-dienamide

MOLECULAR FORMULA
$C_{14}H_{25}NO$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
223.35 g/mol

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

3. COMPOSITION

DEGREE OF PURITY
Approximately 95 %
93.34 % pure in the GC

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

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

Chemical Name	2,4-Decadienamide, *N*-(2-methylpropyl)-, (2*Z*,4*E*)-		
CAS No.	unknown	*Weight %*	1.98
Chemical Name	2,4-Decadienamide, *N*-(2-methylpropyl)-, (2*E*,4*Z*)-		
CAS No.	Unknown	*Weight %*	1.69

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Light yellow to yellow solid

Property	***Value***	***Data Source/Justification***
Melting Point/Freezing Point	85 °C	Measured
Boiling Point	> 210 °C at 101.3 kPa	Measured, decomposition starts at 210 °C.
Density	882 ± 60 kg/m^3	Calculated
Vapour Pressure	9.6×10^{-8} kPa at 20 °C	Measured
Water Solubility	1.84 mg/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	The notified chemical contains no hydrolysable functional groups
Partition Coefficient (n-octanol/water)	log P_{ow} = 3.9	Measured
Adsorption/Desorption	log K_{oc} = 3.35 (MCI method) log K_{oc} = 3.06 (Kow method)	QSAR
Dissociation Constant	Not determined	The notified chemical contains no dissociable functional groups
Particle Size	Not determined	Introduced only as solution
Flash Point	85 °C*	SDS
Flammability	Not highly flammable	Measured
Autoignition Temperature	Not determined	
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties.
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties.

* Product containing a < 20% concentration of the notified chemical.

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

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

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

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. The notified chemical will be imported as a component of oral care flavour blends (at a maximum concentration of 0.5%) or in personal care products at a maximum concentration of 0.1%.

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
Throughout Australia

TRANSPORTATION AND PACKAGING
The oral care flavour blends containing the notified chemical will be imported in closed 25 kg (30 L) plastic canisters into Australia for reformulation. Finished oral care consumer products containing the notified chemical at ≤ 0.1% concentration will be packaged in containers suitable for retail sale.

USE
The notified chemical will be used as a flavouring ingredient in oral care products. The proposed maximum use concentration of the notified chemical in various consumer products such as toothpaste and mouthwash will be ≤ 0.1%.

OPERATION DESCRIPTION

Reformulation
Reformulation of the imported oral care products containing the notified chemical at 0.5% concentration may vary depending of the type of product and may involve both automated and manual transfer steps. Typically, reformulation processes may incorporate blending operations that are highly automated and occur in a fully enclosed/contained environment, followed by automated filling of the reformulated end-use products into containers of various sizes.

End-use
Finished oral care products containing the notified chemical at ≤ 0.1% concentration will be used by consumers and professionals such as dentists.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and warehouse workers	None	Incidental
Reformulation	4	2
Quality control	0.5	2
Professional end users (dentists, etc.)	1-8	200

EXPOSURE DETAILS
Transport and storage
Transport, storage and warehouse workers may come into contact with the notified chemical at up to 0.5% concentration in in oral care products, only in the event of accidental rupture of containers.

Reformulation
During reformulation, dermal, ocular and perhaps inhalation exposure of workers to the notified chemical at < 0.5% 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 personal protective equipment (PPE) such as protective clothing, eye protection and suitable gloves.

End-use
Exposure to the notified chemical in end-use products at ≤ 0.1% concentration may occur in professions where the services provided involve the application of oral care products to clients (e.g. dentists). The principal route of exposure will be dermal. Such professionals are expected to use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place.

6.1.2. Public Exposure

Public exposure to the notified chemical is expected to be widespread and frequent through daily use of oral care products containing the notified chemical at ≤ 0.1% concentration. The principal route of exposure will be oral while dermal and ocular exposure is also possible.

Data on typical use patterns of toothpaste and mouth rinse products in which the notified chemical is proposed to be used are shown in the following tables. For the purposes of the exposure assessment, Australian use patterns for toothpaste and mouth rinse are assumed to be similar to those in Europe (SCCS, 2012). An adult bodyweight of 64 kg has been used for calculation purposes (enHealth, 2012). In addition, 100% systemic exposure has been assumed based on buccal and/or gastrointestinal absorption. Using these data, the total systemic exposure is estimated to be 0.036 mg/kg bw/day of the notified chemical.

The contribution to dermal exposure from the proposed product categories is considered negligible due to the low concentrations of the notified chemical in these products and has therefore not been included in the exposure calculations.

Exposure

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (mg/kg bw/day)
Toothpaste	2,750	0.1	0.05	**0.0021**
Mouth rinse	21,620	0.1	0.1	**0.034**

C = concentration (%); RF = retention factor; assumed brushing twice daily and using mouth rinse 4 times/day

Daily systemic exposure = (Amount × C (%) × RF × oral absorption)/body weight (64 kg)

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***
Acute oral toxicity – rat	LD50 50-300 mg/kg bw; toxic
Skin irritation – *in vitro* Human Skin Model Test – Epiderm-	non-corrosive
Skin irritation – rabbit	slightly irritating
Skin sensitisation – HRIPT	no evidence of sensitisation
Skin sensitisation – mouse local lymph node assay	evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, Metabolism and Distribution
No toxicokinetics data were submitted for the notified chemical. Based on the molecular weight of the notified chemical (< 500 g/mol), there is potential for the chemical to cross biological membranes (ECHA, 2017). However, absorption is expected to be limited based on the relatively low water solubility (1.84 mg/L at 20 °C) and partition coefficient (log Pow = 3.9) of the notified chemical.

Acute Toxicity
The notified chemical was found to have acute toxicity (harmful) in rats via the oral route. No acute dermal or inhalation toxicity information was provided.

Irritation and Sensitisation
According to the results of an *in vitro* assay, the notified chemical was not corrosive to skin. In a skin irritation assay in the rabbit the notified chemical was determined to be slightly irritating.

The notified chemical was found to be a skin sensitiser at 25% concentration in a modified mouse local lymph node (LLNA) skin sensitisation test. In a HRIPT test at 0.5% with 54 subjects, the notified chemical showed no indication of being sensitising, however, the low concentration and low number of test subjects used in the HRIPT mean that the probability of identifying a weak sensitiser in this study is low (McNamee *et al.*, 2008).

Repeated dose toxicity
The European Food Safety Authority evaluated a 90-day repeated dose toxicity study where the notified chemical was administered in the diet to rats, with the NOAEL determined to be 10 mg/kg bw/day based on histological changes in the submandibular salivary glands at 40 and 100 mg/kg bw/day. There were no mortalities up to 100 mg/kg bw/day. As the EFSA report stated: "Microscopically, hypertrophy of the acinar cells in the submandibular salivary gland was observed in males at 40 mg/kg bw/day (4/10) and 100 mg/kg bw/day (10/10) and in females only at 100 mg/kg bw/day (9/10) at 100 mg/kg bw/day. Hypertrophy was characterised microscopically by diffuse enlargement of acinar cells with slightly basophilic, stippled cytoplasm. The severity was predominantly slight in males at 40 mg/kg bw/day and moderate at 100 mg/kg bw/day, indicating a dose-dependent effect. Since the changes in the submandibular salivary glands were not observed in the naïve and vehicle control groups in male and female, this effect was attributed to the test substance" (EFSA, 2015).

Mutagenicity/Genotoxicity
The notified chemical was non-mutagenic in a bacterial reverse mutation assay.

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

Hazard Classification	*Hazard Statement*
Acute Toxicity, oral (Category 3)	H301 – Toxic if swallowed
Specific target organ toxicity, repeated exposure (Category 2)	H373 – May cause damage to organs through prolonged or repeated exposure
Skin sensitisation (Category 1B)	H317 – May cause an allergic skin reaction.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified chemical is acutely toxic following oral administration, and a skin sensitiser at 25% concentration.

Workers may experience dermal and accidental ocular and perhaps inhalation exposure to the notified chemical (at ≤ 0.5% concentration) during formulation processes. The use of enclosed, automated processes and PPE (impervious gloves, goggles, coveralls and respiratory protection where possible) should minimise the potential for exposure. Therefore, provided that adequate control measures are in place to minimise worker exposure, including the use of automated processes and PPE, the risk to workers from use of the notified polymer is not considered to be unreasonable.

End-use
Workers involved in professions where the services provided involve the use of oral care products, for example dentists, may be exposed dermally to the notified chemical. Such professionals are expected to use PPE to minimise repeated exposure, and good hygiene practices are expected to be in place. If PPE is used, the exposure of such workers is expected to be very low and the notified chemical is not considered to pose an unreasonable risk to the health of workers.

6.3.2. Public Health
Members of the public will experience widespread and frequent exposure to the notified chemical at < 0.1% concentration through daily use of oral care products. The main route of exposure is expected to be oral, while ocular and dermal exposures are also possible.

At the proposed use concentration (at < 0.1%) in oral care products such as in tooth pastes and mouthwash, the risk of sensitisation is expected to be low although it cannot be ruled out entirely.

The potential systemic exposure from the use of the notified chemical in oral care products was estimated to be 0.036 mg/kg bw/day. Using a NOAEL of 10 mg/kg bw/day established from the 90-day repeat dose toxicity study on the notified chemical, the margin of exposure (MoE) was estimated to be 278. A MoE value greater than or equal to 100 is considered acceptable to account for intra- and inter-species differences, and to account for long-term exposure. Additionally the European Food Safety Authority concluded that the notified chemical posed "no safety concern at the estimated level of intake based on the MSDI approach" where the EU Maximised Survey-derived Daily Intake (MSDI) was estimated to be 11 µg/capita/day (EFSA, 2015).

Based on the available information, the risk to the public associated with the use of the notified chemical in oral care products at up to 0.1% concentration 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 is not manufactured in Australia and will only be imported as a component of oral care flavour blends for reformulation into oral health care products. In general, the reformulation processes are expected to involve blending operations that will normally be automated and occur in an enclosed system. Release of the notified chemical to the environment in the event of accidental spills or leaks during reformulation, storage and transport is expected to be disposed of to landfill in accordance with local government regulations. Empty containers containing the notified chemical will be rinsed and then be recycled or disposed of through an approved waste management facility.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be primarily washed into the sewers during use of the various end-use oral care products.

RELEASE OF CHEMICAL FROM DISPOSAL

Wastes and residues of the notified chemical in empty end-use containers are likely to either share the fate of the container and be disposed of to landfill, or be released to sewer when containers are rinsed before recycling through an approved waste management facility

7.1.2. Environmental Fate

Following its use in oral hygiene products, the majority of the notified chemical will enter the sewers and be treated at sewage treatment plants (STPs) before the potential release to surface waters nationwide.

A ready biodegradation test determined that the notified chemical is readily biodegradable (75.45% after 28 days). For further details on the biodegradability study, refer to Appendix C.

The notified chemical is expected to be effectively removed at STPs due to its ready biodegradability. Approximately 11 % of the notified chemical is expected to be released to surface waters. A proportion of the notified chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill. The notified chemical residues in landfill and soils are expected to have low mobility based on its modelled soil adsorption coefficient (log K_{oc} = 3.06). The notified chemical is not expected to be bioaccumulative based on its measured partition coefficient (log P_{ow} = 3.9) and the modelled bioconcentration factor (BCF) of 174 L/kg wet-wt. In the aquatic and soil compartments, the notified chemical is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

The Predicted Environmental Concentration (PEC) has been calculated based on a 100 % release rate into the sewer system over 365 days per year. It is assumed that there is a 89 % removal during the sewage treatment processes based on the physical and chemical properties. The resulting PEC in sewage is displayed in the table below.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100.000%	
Annual quantity of chemical released to sewer	1,000.000	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)	24.386	million
Removal within STP	89%	**Mitigation**
Daily effluent production:	4,877	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.0618	µg/L
PEC - Ocean:	0.00618	µg/L

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 0.899 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 6µg/kg in applied soil.

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. The endpoints for fish toxicity and algal toxicity are calculated using QSAR modelling software modelling (US EPA 2012).

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	EC50 = 0.534 mg/L	Expected to be toxic to fish
Daphnia Toxicity	EC50 = 0.456 mg/L	Toxic to daphnia
Algal Toxicity	EC50 = 0.142 mg/L	Expected to be very toxic to algae

The notified chemical is acutely toxic to daphnia and, based on ECOSAR modelling, is expected to be acutely toxic to fish and very acutely toxic to algae.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) was calculated using the most sensitive endpoint for ecotoxicity (Algae E_rC50 = 0.142 mg/L) with an assessment factor of 1,000 as only one measured endpoint was available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
E_rC50 (Algae)	0.142	mg/L
Assessment Factor	1,000	
Mitigation Factor	1	
PNEC:	0.142	µg/L

7.3. Environmental Risk Assessment

Risk Assessment	*PEC µg/L*	*PNEC µg/L*	*Q*
Q - River:	0.0618	0.142	0.435
Q - Ocean:	0.00618	0.142	0.044

The risk quotient (Q = PEC/PNEC) has been calculated based on the assumption of release of 100 % of the notified chemical into the sewers. Since the Q value determined was less than 1 for both river and ocean compartments the notified chemical is unlikely to reach ecotoxicologically significant concentrations based on the proposed annual importation and use patterns. Therefore, on the basis of the predicted PEC/PNEC ratio the notified chemical is not expected to pose an unreasonable risk to the aquatic environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point 85 °C

Method	OECD TG 102 Melting Point/Melting Range
Remarks	Determined using differential scanning calorimetry
Test Facility	Siemens (2005)

Boiling Point Decomposes at 210 °C at 101.3 kPa

Method	OECD TG 103 Boiling Point
Remarks	Determined using differential scanning calorimetry
Test Facility	Siemens (2005)

Vapour Pressure 9.6×10^{-8} kPa at 20 °C
2.1×10^{-7} kPa at 25 °C

Method	OECD TG 104 Vapour Pressure
Remarks	Effusion method
Test Facility	Siemens (2005)

Water Solubility 1.84 mg/L at 20 °C
2.13 mg/L at 30 °C

Method	OECD TG 105 Water Solubility
Remarks	Determined using the Column Elution Method
Test Facility	NOACK (2006a)

Partition Coefficient (n-octanol/water) **Partition Coefficient (n-octanol/water)**

Method	OECD TG 117 Partition Coefficient (n-octanol/water)
Remarks	HPLC Method
Test Facility	NOACK (2005)

Flammability Not highly flammable

Method	EC Council Regulation No 440/2008 A.10 Flammability (Solids)
Remarks	The test item melted when approached by the ignition flame.
Test Facility	Bayer (2004)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute Oral Toxicity – Rat, Fixed Dose

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity – Fixed Dose Method
Species/Strain	Rat/Female SPF Wistar Shoe:WIST
Vehicle	Olive oil
Remarks – Method	No significant protocol deviations

RESULTS

Sighting Study

Dose (mg/kg bw)	*Evident Toxicity*	*Mortality*
2000	Yes	1/1
300	Yes	1/1
50	Yes	0/1

Signs of Toxicity	The rat treated at 2000 mg/kg bw showed piloerection, hunched posture, tremours and a clear expression of pain. The rat treated at 300 mg/kg bw showed hunched posture, piloerection, apathy, tremours and expression of pain. Both rats treated at 2000 and 300 mg/kg bw were humanely killed 2 hours and 4 hours respectively after the administration of the test item. The post mortem observation revealed that both of the animals dosed at 2000 or 300 mg/kg bw were conspicuous by a 'total cramped posture' which the study authors stated could not be attributed to post mortem rigidity. The rat treated at 50 mg/kg bw showed hunched posture (up to day 3), piloerection (up to day 4), and apathy (up to day 3). From day 5 until the end of the observation period on day 14 no adverse effects were observed. Loss of weight has been observed in all rats between day 7 and day14.
Effects in Organs	Necropsy of the animals showed no pathological abnormalities in the organs.

Main Study

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	4 F	50	0/4

Discriminating Dose	50 mg/kg bw
Signs of Toxicity	All animals in the main study showed hunched posture, and piloerection at all observations up to and including one day after administration of the test substance. From day 2 onwards no adverse effects were observed.
Effects in Organs	Necropsy of the animals showed no pathological abnormalities.
Remarks – Results	No rats died at 50 mg/kg bw indicating an LD50 > 50.
CONCLUSION	The notified chemical is toxic via the oral route.
TEST FACILITY	Frey Tox (2003a)

B.2. Skin Irritation – *In Vitro* Human Skin Model Test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 431 *In vitro* Skin Corrosion – Human Skin Model Test
Vehicle	Distilled water

Remarks – Method	No significant protocol deviations Negative Control (NC): distilled water Positive Control (PC): 8N KOH An additional blank control consisting of 25 mg of the test item, 25 µl distilled water and 300 µl MTT solutions was incubated at 37 °C for approx. 3 hours in order to exclude a chemical interaction between test item and MTT solution. After approximately 3-hours incubation of the blank control a yellowish solution with violet crumbles was observed indicating formazan synthesis and reducing properties of the test item.

RESULTS

Test Material	*Mean OD_{570} of Triplicate Tissues after*		*Relative Mean Viability (%) after*	
	3 minutes	*1 hour*	*3 minutes*	*1 hour*
Negative control	2.028	1.647	100	100
Test substance	1.875	1.576	92	96
Positive control	0.422	0.180	21	11

Remarks – Results	In comparison to the negative control (NC) the test item gave a cell viability of 92% and 96% after a 3 minute and 1 hr. application, respectively.
CONCLUSION	The notified chemical was considered non-corrosive to the skin.
TEST FACILITY	Frey Tox (2003b)

B.3. Skin Irritation – Rabbit

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion EEC commission 2001/59/EC Acute Toxicity (Skin Irritation)
Species/Strain	Rabbit/ Female albino Chbb:HM(SPF)
Number of Animals	Three
Vehicle	Olive oil
Observation Period	7 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	1.0	2.0	2.0	2	72 hours	0
Oedema	0.0	0.0	0.0	0	72 hours	0

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

Remarks – Results	Under the experimental conditions described in this study report the mean score for erythema was 1.7 and for oedema 0.0
CONCLUSION	The notified chemical is slightly irritating to the skin.
TEST FACILITY	Frey Tox (2003c)

B.4. Skin Sensitisation – Human Volunteers

TEST SUBSTANCE	Notified chemical at 0.5%

METHOD	Repeated insult patch test with challenge
Study Design	Induction procedure: Patches (3.63 cm^2 size) were applied three times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. Patches containing approximately 0.2 mL of the test substance were used occlusively and applied the left side of the back. Patches were removed by the applicants after 24 hours. Rest periods consisted of 24 hours following each Tuesday and Thursday removal, and 48 hours following each Saturday removal. Challenge procedure: A patch (3.63 cm^2 size) was used occlusive and 0.2 mL of the test substance was applied to a virgin test site adjacent to the original induction patch site. Patches were removed after 24 hours and the site scored by the test facility technician after 24 hours and 72 hours post application.
Study Group	57 Female and Male (54 subjects completed the test. Three subjects discontinued due to personal reasons. No subject discontinued due to test material reaction), age range 16 - 79 years
Vehicle	The solvent for dilution was DEP:EtOH (3:1).
Remarks – Method	Occluded.
RESULTS	
Remarks – Results	During the Induction and the Challenge Phases, no skin reactions were exhibited.
CONCLUSION	The test substance at 0.5% concentration was non-sensitising under the conditions of the test.
TEST FACILITY	Consumer Product Testing Co. (2005)

B.5. Skin Sensitisation – LLNA

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay. Integrated Model for the Differentiation of Skin Reactions (IMDS)
Species/Strain	Mouse/ Female SPF albino Shoe:NMRI
Vehicle	Acetone and olive oil 4:1-mixture (v/v)
Preliminary study	No
Positive control	Not conducted in parallel with the test substance but had been conducted previously in the test laboratory using α-hexylcinnamaldehyde.
Remarks – Method	No significant protocol deviations The alternate Integrated Model for the Differentiation of Skin Reactions (IMDS) was used to determine if the test substance was a sensitiser.

RESULTS

Concentration	*Proliferative response[1]*		*Irritant response − Ear swelling ($x10^{-2}$ mm)[2]*			*Irritant response – Ear Weight*	
(% w/v)	*Lymph node weight index*	*Cell count index*	*Mean (Day3-0)*	*Ear thickness mean (Day 3)*	*Day 3 Index*	*Ear weight Mean (g)[3]*	*Ear weight index[4]*
0	1.00	1.00	0.0	20.6	1.00	0.0116	1.00
10	1.00	0.96	0.6	20.5	1.00	0.0119	1.03
25	1.21	1.40	1.3	21.4	1.04	0.0132	1.14
50	1.00	1.07	4.7	24	1.17	0.0133	1.15

1 Test/control index calculated from measurements from animals treated with the test substance compared to animals treated with the vehicle control.
2 Ear swelling was determined by measuring the thickness of both auricles of the animals before first treatment and before sacrifice.
3 Ear weights were determined by measuring the weight of a 7 mm diameter piece of the ear of the sacrificed animals on Day 3.
4 Ear weight index was calculated from measurements from animals treated with the test substance compared to animals treated with the vehicle control.

Concentration (% w/w)	*Number and Sex of Animals*	*Proliferative Response (ear swelling mean×10-2 mm)*	*Stimulation Index (Differentiation Index)*
Test Substance			
0 (vehicle control)	5 F	604 (0)	1.00 (0)
10	5 F	578 (-0.1)	0.96 (NA)
25	5 F	847 (0.8)	1.4 (4.21)
50	5 F	646 (3.4)	1.07 (0.88)

Remarks – Results

A normal body weight gain was observed on all animal groups. Only the test groups with the two highest test concentrations showed a concentration-related ear swelling compared with the negative control. The positive threshold value was exceeded only in the 50% test concentration.

No deaths or signs of systemic toxicity were noted in the test or control animals during the test.

The determination of lymph node weights and lymph node cell counts showed a positive proliferation increase at the test group treated with the 25 % test item, whereas the results of the two other test groups were comparable to the negative control group.

CONCLUSION

There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical as SI was > 1 at 25% concentration.

TEST FACILITY

Frey Tox (2003d)

B.6. Genotoxicity – Bacteria

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 471 Bacterial Reverse Mutation Test
Plate incorporation procedure

Species/Strain: *Salmonella typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System: S9 fraction of liver homogenate from male rats treated with Aroclor 1254
Concentration Range in Main Test: a) With metabolic activation: 5-5000 µg/plate; b) Without metabolic activation: 5-1500 µg/plate
Vehicle: Dimethyl sulfoxide (DMSO)
Remarks – Method: No significant protocol deviations.
Negative control was dimethyl sulfoxide (DMSO)
Positive controls for experiments without S9 were:
Sodium azide (NaN_3), 2-nitrofluorene (2-NF), Mitomycin C (MMS), and 9-aminoacridine (9-AA)
Positive controls for experiments with S9 were:
2-aminoanthracene (2-AA)

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				

Test 1	≥ 500		≥ 1500	Negative
Test 2		TA1535 ≥ 150 µg/plate	≥ 1500	Negative
Present				
Test 1	> 5000 µg/plate		≥ 1500	Negative
Test 2		≥ 5000 µg/plate	≥ 1500	Negative

Remarks – Results

In the concentration range investigated, the test substance did not induce any increase in the mutation frequency of the tester strains in the presence or absence of metabolic activation.

Precipitation of the test compound on the plates was observed at 1500 µg per plate.

The positive and negative controls produced satisfactory responses, thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.

CONCLUSION

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

TEST FACILITY

King Harnasch (2003)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready Biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	None
Remarks – Method	As per OECD guidelines, no deviations were noted.

RESULTS

Test Substance		*Sodium Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
4	58.35	4	61.20
9	73.15	9	76.00
10	ND	10	ND
22	73.45	22	76.30
25	75.00	25	76.90
28	75.45	28	77.20

Remarks – Results	Due to a computer error results from days 10 through 21 were not recorded. However it could be determined that the test substance reached the pass level of 60 % within the 10-day window and therefore it is considered to be readily biodegradable. A microbial toxicity control was also conducted which indicated no toxicity to the bacteria. All of the validity criteria were met; the difference in replicate values was less than 20 % at the end of the study, the reference substance reached 76 % degradation at day 9 and the O_2 uptake of the inoculum blank was 6.5 mg/L at day 28.
CONCLUSION	The test substance is readily biodegradable.
TEST FACILITY	Fraunhofer (2005)

C.2. Ecotoxicological Investigations

C.2.1. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test – Static
Species	*Daphnia magna*
Exposure Period	48 hours
Dispersant	Ultraturrax
Water Hardness	246 mg $CaCO_3$/L
Analytical Monitoring	LC-MS/MS
Remarks – Method	As per OECD guidelines, no significant deviations were noted.

RESULTS

Geometric mean of measured concentrations (mg/L)*	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
Control	20	0	0

0.075	20	0	0
0.134	20	0	1
0.292	20	1	4
0.527	20	0	12
1.13	20	12	20

*Measured at 0 h and 48 h

EC50	0.456 mg/L at 48 hours
LOEC	0.292 mg/L at 48 hours
Remarks – Results	Potassium dichromate was used as the reference substance which returned an EC50 value of 2.1 mg/L which is within the acceptable limits, however this value was not able to be verified as the raw data was not included in the study report. All validity criteria were met. The dissolved O_2 concentration was > 7.6 mg/L, pH did not deviate by more than ± 1 and temperature was maintained at 20 ± 1 °C. The EC50 was calculated by sigmoidal dose-response regression.
CONCLUSION	The test substance is toxic to aquatic invertebrates.
TEST FACILITY	NOACK (2006b)

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