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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Carbamic acid, N,N-dimethyl-, 1-ethenyl-1,5-dimethyl-4-hexen-1-yl ester

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (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 Ageing, 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, Water, Heritage and the Arts.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

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

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Givaudan Australia Pty Limited (ABN 87 000 470 280)
Unit 36, 5 Inglewood Place
Baulkham Hills NSW 2153

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

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

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (2005)
USA (2006)
Switzerland (2005)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Pepperwood

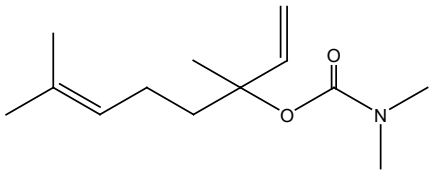
CAS NUMBER
67643-70-3

CHEMICAL NAME
Carbamic acid, N,N-dimethyl-, 1-ethenyl-1,5-dimethyl-4-hexen-1-yl ester

OTHER NAME(S)
GR-86-0999

MOLECULAR FORMULA
$C_{13}H_{23}NO_2$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
225.3 Da

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

3. COMPOSITION

DEGREE OF PURITY > 97%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)

Chemical Name 3,7-dimethyloct-6-en-3-yl dimethyl carbamate
CAS No. Not assigned *Weight %* 2.2

ADDITIVES/ADJUVANTS

Chemical Name Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, 1,1'-[2,2-bis[[3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-1-oxopropoxy]methyl]-1,3-propanediyl] ester
CAS No. 6683-19-8 *Weight %* 0.02

Chemical Name 1,2,3-Propanetricarboxylic acid, 2-hydroxy-
CAS No. 77-92-9 *Weight %* 0.1

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: liquid (almost colourless, pale yellow)

Property	Value	Data Source/Justification
Freezing Point	< -50°C	Measured
Boiling Point	264°C (pressure known)	Estimated using EPI Suite v4.0
Density	934 kg/m^3 at 20°C	Measured
Vapour Pressure	1.15 × 10^{-3} kPa at 20°C	Measured. The notified chemical is considered to be volatile in respect to environmental fate.
Water Solubility	0.067 g/L at 20°C	Measured. The notified chemical is considered to be moderately soluble in water.
Hydrolysis as a Function of pH	Not determined	The notified chemical contains a hydrolysable functional group (carbamate). The rate of hydrolysis at neutral pH is not expected to be rapid, but more rapid hydrolysis can be expected at the extremes of the environmental pH range (pH 4 and 9).
Partition Coefficient (n-octanol/water)	log K_{OW} = 4.3	Measured
Adsorption/Desorption	log K_{OC} = 2.73	Calculated. The notified chemical is expected to adsorb strongly to soil from water.
Dissociation Constant	Not determined	The notified chemical does not contain any dissociable functional groups.
Particle Size	Not determined	Liquid
Flash Point	128°C at 101.3 kPa	Measured
Flammability	Not expected to be highly flammable.	Based on measured flash point.
Autoignition Temperature	> 320°C	Measured
Explosive Properties	Not determined	A negative result is expected on structural grounds.

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 in water and air under normal conditions of temperature and pressure. The notifier states that rags impregnated with similar fragrance materials left unattended in a dustbin have caught fire. In light of these two facts, precautions should be taken to prevent combustion. The notifier states flushing rags impregnated with fragrance materials with water should prevent this risk.

Dangerous Goods classification
Based on the submitted physical-chemical data in the above table the notified chemical is not classified according to the Australian Dangerous Goods Code (NTC, 2007). However the data above do not address all Dangerous Goods endpoints. Therefore consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the chemical.

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 as a component (< 8.3%) of fragrance blends.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	0.2	0.4	0.6	0.8	1

PORT OF ENTRY
Sydney (by sea or air)
Perth (by air)

TRANSPORTATION AND PACKAGING
The fragrance blends containing up to 8.3% of the notified chemical are imported in glass, lacquer-lined containers. The proposed standard packaging sizes are: 1, 5, 10, 25, 100 and 190 kg. The blends will be transported by road in sealed containers to formulators. The finished product containing < 1.67% of the notified chemical will be transported to industrial customers or retail outlets.

USE
The notified chemical will be used as an aroma chemical in perfumery, cosmetics, toiletries, household products, soaps, detergents and industrial perfumery. The concentration of the notified chemical in fragrance blend is up to 8.3%. The concentration of the notified chemical in end use consumer products will be < 1.67%.

OPERATION DESCRIPTION
Details on how the notified chemical is to be used are not available to the notifier. The following is a typical operation description for similar chemicals in fragrance blends.

The notified chemical will be imported as a component of a liquid fragrance blend at up to 8.3%.

Formulation
If imported as a component of a liquid fragrance blend, the blend will be blended with other ingredients at customer formulation sites, to make end use consumer products, such as alcoholic perfumes, cosmetics, toiletries, household products, detergents and soaps. While the formulation process will vary with the product type and formulation site, it is expected that most sites will have closed, automated mixing and dosing equipment. The packaged consumer products will be transported to retail outlets for sale to the public.

End use
There is potential for the formulated products to be used occupationally, for example by beauticians using cosmetic products (containing < 1.67%).

Cleaning products are generally applied with a cloth or sponge, by mop or brush or by spray followed by wiping. In some cases, the cleaning product will be diluted with water prior to application. The dilution factor, which is often on the label, depends on the type of surface to be cleaned, the soil loading, and the type and method of application.

Depending on the nature of the cosmetic product these could be applied 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

NUMBER AND CATEGORY OF WORKERS
Details of occupational exposure are not available to the notifier. The following occupational exposure table is given as an example of the likely exposure based on similar chemicals in fragrance blends.

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and Warehouse workers	5	None	Incidental Exposure only
Plant operators			
Mixer	5	4	2
Drum handling	5	4	2
Drum cleaning/washing	10	4	2
Maintenance	5	4	2
Quality control worker	2	0.5	2
Packager	10	4	2
End users (professionals)	> 1000	1-8	200

EXPOSURE DETAILS
Details on blending operations, worker exposure and life cycle of the notified chemical are not available to the notifier. The number and category of workers will vary depending on the nature of the business. However, it is anticipated that typical practices by cosmetic and consumer product manufacturers will include the use of adequate local ventilation, appropriate personal protective equipment (PPE), enclosed mixing vessel and filling areas as well as a high degree of process automation to protect workers.

At the formulation facilities, transport and warehouse workers will be exposed to the fragrance blend (up to 8.3% notified chemical) only in the event of a spill due to an accident or leaking drum. Workers will wear protective overalls, hard hats, chemical resistant gloves and safety glasses.

At formulation facilities (cosmetic and consumer product manufacturers), exposure to the fragrance blend (up to 8.3% notified chemical) or products containing the notified chemical at < 1.67% is possible during handling of the drums, cleaning and maintenance of the equipment. Skin, inhalation and eye contact (due to splashing) are likely to be the main routes of exposure. Exposure is likely to be minimised by good personal hygiene practices (eg. washing hands after any contact, before breaks and meals, etc) and use of industrial standard PPE.

End use
Exposure to no more than 1.67% notified chemical could occur during final application of the consumer products or during their addition to water if dilution is required. The main route of exposure is expected to be dermal, although ocular exposure to splashes is possible and inhalation of aerosols could occur where application is by spray. Although the level and route of exposure will vary depending on the method of application and work practices employed, exposure is considered to be low due to the low concentration of the notified chemical in end use products.

6.1.2. Public exposure
Public exposure from transport, storage, reformulation or disposal is considered to be negligible.

End use products containing the notified chemical at < 1.67% are designed to be sold to consumers. The general public will be repeatedly exposed to low levels of the notified chemical via a number of different consumer products.

6.2. Human health effects assessment

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

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation
Human, skin sensitisation – Repeat Insult Patch Test	no evidence of sensitisation at 30% concentration
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution
Given the low molecular weight of the notified chemical (225.3 Da), it is likely to be significantly absorbed following oral and dermal exposure and be widely distributed within the body. The notified chemical is highly lipophilic (logKow = 4.3), therefore there is potential to accumulate. However, based on the structure the notified chemical is likely to undergo significant metabolism.

Acute toxicity
The notified chemical is of low acute toxicity *via* the oral route. No acute dermal or inhalation studies are provided.

Irritation
Based on the studies provided, the notified chemical is considered to be moderately irritating to the skin and slightly irritating to the eye. The skin irritation scores and persistence of effects do not warrant classification of the notified chemical as a skin irritant.

Sensitisation
The notified chemical is not considered to have the potential to cause skin sensitisation based on the Mouse Local Lymph Node Assay.

In a human repeat insult patch test conducted using a 30% solution of the notified chemical, there were no reactions indicative of irritation or sensitisation observed in any of the 97 subjects.

Repeated dose toxicity
No repeat dose toxicity studies are provided.

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

Health hazard classification
Based on the data provided the notified chemical is not classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

However, the notifier has classified the chemical as 'Irritating to skin (R38)'.

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
The notified chemical is not a skin sensitiser. It is irritating to the skin and slightly irritating to the eye.

The risk to transport and storage workers is expected to be low due to the negligible exposure expected.

The risk of skin and eye irritation effects in workers handling the notified chemical is expected to be low due to the PPE expected to be worn during formulation activities.

Skin irritation is not expected in workers using the end use products (cleaners, beauticians) due to the low concentrations of the notified chemical (< 1.67 %) in the end use products.

Overall, the risk to the health of workers from use of the notified chemical is not considered unacceptable given the expected use of PPE when handling the imported fragrance blend and low concentrations (< 1.67%) in end use products.

6.3.2. Public health
The public may come into contact with the notified chemical (at < 1.67%) through the use of a range of cosmetic and consumer products. No skin irritation risk is expected due to the low concentration of the notified chemical in end use products.

No repeat dose toxicity studies are provided for the notified chemical or any close analogues. Considering the 1 tonne/year maximum import volume, < 1.67% concentration used in end use products for consumers, and there are no NOAELs available from repeat dose toxicity studies, quantitative repeat dose risk assessment was not conducted.

Overall, the risk to public health from use of products containing the notified chemical at < 1.67% is not considered unacceptable.

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 blends for local reformulation into a variety of consumer products (cosmetics, household products, perfume). Losses during the blending processes at various sites throughout Australia are expected to be limited to traces of spills, formulation equipment cleaning and residues in empty packaging. Less than 0.5 % of the total annual import volume of notified chemical is expected to remain as residues in import containers. The empty containers will eventually be recycled or disposed of to landfill. At the end of the reformulation run the formulating equipment and packing equipment is washed and it is anticipated that the washings will be included in the next batch.

RELEASE OF CHEMICAL FROM USE

Most of the notified chemical will be incorporated into consumer products for dispersed use throughout Australia. Based on the use pattern as a fragrance additive in a variety of consumer products, the majority of the imported quantity of notified chemical is expected to be released to sewer in domestic situations.

RELEASE OF CHEMICAL FROM DISPOSAL

The residues in the final product containers are estimated to be approximately 1% and will most likely be sent to landfill with the empty containers.

7.1.2 Environmental fate

The notified chemical is a volatile compound and a fraction of the imported quantity of this chemical will partition to air which is a functional requirement for fragment products. Calculations with AOPWIN (US EPA 2009) indicate a short atmospheric half-life of 0.088 days (1.061 hours) for the notified chemical based on reactions with hydroxyl radicals. The reaction with ozone is also rapid ($t_{½}$ = 0.637 hours). The notified chemical is therefore not expected to persist in the air compartment.

The major proportion of the imported quantity of notified chemical will enter the sewer system as a result of the use of this chemical as an odorant in domestic consumer products such as cosmetics and detergents. The notified chemical is not readily biodegradable, although testing indicates that the chemical undergoes significant biodegradation in the presence of microorganisms from a sewage treatment plant. The notified chemical is therefore expected to undergo some biodegradation in sewage treatment plants. In addition, the notified chemical is hydrolysable and can be expected to undergo abiotic degradation. The combination of biotic and abiotic degradation processes is expected to significantly reduce the concentration of the notified chemical entering the aquatic environment in the effluent of sewage treatment plants. A significant proportion of the notified chemical is also expected to associate with sediment sludge based on the relatively high calculated adsorption/desorption constant (log K_{OC} = 2.73 – 3.2). This fraction of the notified chemical will be disposed of to soil or landfill where it will degrade to water and oxides of carbon and nitrogen. The notified chemical is not expected to be mobile in soil.

The notified chemical is hydrophobic and has some potential to bioconcentrate in aquatic organisms based on the relatively high estimated octanol-water partition coefficient (log K_{OW} = 4.3). This is supported by calculation with BCFBAF v 3.0 which indicates log BCF = 2.504 based on a regression method (US EPA 2009). However, the concentrations of the notified chemical entering the aquatic environment are expected to be very low (< 1 µg/L) and will be significantly reduced by biotic and abiotic degradation of the notified chemical in the environment. The notified chemical is therefore not expected to present a significant risk of bioconcentration under typical exposure conditions.

For the details of the environmental fate studies refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

A PEC has been calculated assuming a worst case in which 100% of the annual imported quantity of notified chemical will be released to sewer nationwide and that no removal of the notified chemical will occur at sewage treatment plants.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	0%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.65	µg/L
PEC - Ocean:	0.06	µg/L

7.2. Environmental effects assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 = 5.6 mg/L	Toxic to aquatic invertebrates

The notified chemical is acutely toxic to aquatic invertebrates. Under the globally Harmonised System for the Classification and Labelling of Chemicals (GHS), the notified chemical is classified as toxic to aquatic life based on the acute toxicity to *daphnia*. The notified chemical is also classified as chronically toxic to aquatic life based on the high log K_{OW} (> 4) (estimated).

7.2.1 Predicted No-Effect Concentration

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50	5.6	mg/L
Assessment Factor	1000	
PNEC:	5.6	µg/L

A PNEC has been calculated using the endpoint for *Daphnia*. An assessment factor of 1000 was used since there is an acute toxicity endpoint for only one aquatic trophic level.

7.3. Environmental risk assessment

Risk Assessment	***PEC µg/L***	***PNEC µg/L***	***Q***
Q - River:	0.65	56	0.12
Q - Ocean:	0.06	56	0.01

The calculation shows that the Risk Quotient (PEC/PNEC) for the worst case scenario is < 1. The low PEC/PNEC value indicates that the notified chemical is not expected to pose a risk to the aquatic environment based on its maximum annual import volume.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the data provided the notified chemical is not classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

The classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2009) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Environment	Acute Category 2	Toxic to aquatic life
	Chronic Category 2	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 unacceptable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unacceptable 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 expected to pose a risk to the environment.

Recommendations

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced in fragrance blends:
  - Avoid contact with skin and eyes

- Employers should ensure that the following personal protective equipment is used by workers in formulation plants to minimise occupational exposure to the notified chemical in fragrance blends:
  - Protective gloves
  - Coveralls

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

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

- If products and mixtures containing the notified chemical/polymer are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

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

Regulatory Obligations

Secondary Notification

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

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

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from an aroma chemical used at < 1.67% in perfumery, cosmetics, toiletries, household products, soaps, detergents and industrial perfumery, or is likely to change significantly;
- the amount of chemical being introduced has increased from 1 tonne per year, 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.

No additional secondary notification conditions are stipulated.

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

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Freezing Point < -50°C

Method OECD TG 102 Melting Point/Melting Range.
Test Facility Givaudan Sussie SA (2004a)

Boiling Point 264°C (pressure known)

Method OECD TG 104 Vapour Pressure.
Remarks The vapour pressure curve as a function of temperature could not be determined with the notified chemical according to OECD method 104 (dynamic method) and thus could not be used to extrapolate the normal boiling temperature. The boiling point was estimated using EPI Suite v4.0.
Test Facility Givaudan Sussie SA (2005a)

Density 934 ± 1 kg/m^3 at 20°C

Method OECD TG 109 Density of Liquids and Solids.
Remarks Oscillating densitometer method was used.
Test Facility Givaudan Sussie SA (2004b)

Vapour Pressure 1.15 ± 0.10 × 10^{-3} kPa at 20°C

Method OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks The static method was used with a capacitance manometer. A total of 42 measurements were conducted at temperatures of 25.80, 31.5 and 36.62°C. The vapour pressure at 20°C was extrapolated from the measured data. The notified chemical is classified as volatile.
Test Facility NOTOX B.V. (2005a)

Water Solubility 0.067 g/L in water at 20°C

Method OECD TG 105 Water Solubility.
Remarks A modified Flask method was used. After a preliminary flask test, the definite test was conducted using a saturation equilibrium method to allow separation of the dissolved from the undissolved chemical in water: about 1.0 g of the notified chemical was separately added to the surface of 400 mL of double-distilled water or reconstituted water, with caution to avoid the formation of small droplets. Aqueous phase samples were withdrawn for HPLC analysis after up to 43 days of contact time.

The notified chemical contains a hydrolysable functional group but only the equilibrium concentration of the notified chemical was considered. Additional peaks were observed in the chromatogram of the saturated solution after 43 days of contact time, which may indicate the presence of hydrolysis products.

The solubility was determined to be 67 mg/L at 20°C for water and 60 mg/L at 20°C for reconstituted water. On this basis, the notified chemical is classified as moderately soluble.
Test Facility Givaudan Sussie SA (2005b)

Partition Coefficient (n-octanol/water) log K_{OW} = 4.3

Method OECD TG 117 Partition Coefficient (n-octanol/water).
EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks HPLC Method was used. The column temperature was set at 35°C. Thiourea was used for the determination of the dead tome (t_0 = 1.72 min). A total of seven reference substances with log K_{OW}s in the range 0.9 – 5.7 were used to determine the calibration curve.
Test Facility Givaudan Sussie SA (2005c)

Adsorption/Desorption log K_{oc} = 2.73

Method	Calculated by means of a quantitative structure-activity relationship (QSAR) from EUSES.
Remarks	The QSAR used was: log K_{OC} = 0.37 × log P_{OW} + 1.14. The log K_{OC} calculated using KOCWIN v 2.0 is 3.2 (US EPA 2009).
Test Facility	Givaudan Sussie SA (2010a)

Flash Point 128ºC at 101.3 kPa

Method	DIN 51758
Remarks	The Pensky-Martens method was used.
Test Facility	Givaudan Sussie SA (2004c)

Autoignition Temperature > 320 ± 10ºC

Method	DIN 51794
Remarks	SUR NERLIN oven with 250 mL glass ignition vessel was used. No ignition observed (steam and smoke only).
Test Facility	Givaudan (2010b)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
EC Directive 92/69/EEC B.1tris Acute Oral Toxicity – Acute Toxic Class Method.

Species/Strain	Rat/HanBrl: Wist (SPF)
Vehicle	Polyethylene glycol 300
Remarks - Method	No deviations from the protocol.

RESULTS

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

LD50	> 2000 mg/kg bw
Signs of Toxicity	No clinical signs were observed during the course of the study.
Effects in Organs	No macroscopic findings were recorded at necropsy.
Remarks - Results	The body weight of the animals was within the range commonly recorded for this strain and age.

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

TEST FACILITY: RCC Ltd (2004a)

B.2. Irritation – skin

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation).

Species/Strain	Rabbit/New Zealand White
Number of Animals	1 M, 2 F
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks - Method	No deviations from the protocol.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	2	1.7	1.7	2	14 days	1
Oedema	1	1	1	2	< 7 days	0

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

Remarks - Results	No clinical signs of systemic toxicity were observed in the animals during the study and no mortality occurred. Very slight to well-defined erythema were noted in all animals from the 1-hour to the 72-hour reading and very slight erythema persisted up to 10-day examination in one animal and up to the 14-day examination in another animal.

Very slight swelling (oedema) was noted in two animals at the 1-hour examination and very slight to slight swelling (oedema) was observed in all animals at the 24-hour examination. Very slight swelling persisted up to the 48-hour examination in one animal and up to the 72-hour examination in two animals.
Scaling was present in one animal at the 72-hour reading, in all animals at the 7-day reading and persisted up to 10-day examination in one animal and up to the 14-day examination in another animal.
No staining produced by the test substance of the treated skin was observed.
Neither alterations of the treated skin were observed nor were corrosive effects evident on the skin.
The body weights of all rabbits were considered to be within the normal range of variability.

CONCLUSION The notified chemical is irritating to the skin. However, the irritation scores and persistence of effects do not warrant classification according to the Approved Criteria (NOHSC, 2004).

TEST FACILITY RCC Ltd (2004b)

B.3. Irritation – eye

TEST SUBSTANCE Notified Chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 2004/73/EC B.5 Acute Toxicity (Eye Irritation).

Species/Strain Rabbit/New Zealand White
Number of Animals 1 M, 2 F
Observation Period 72 hours
Remarks - Method No deviations from the protocol.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.7	0.3	0.3	2 (1 hour)	< 72 hours	0
Conjunctiva: chemosis	0	0	0	1 (1 hour)	< 24 hours	0
Conjunctiva: discharge	0	0	0	Slight (1 hour)	< 24 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results
No clinical signs of systemic toxicity were observed in the animals during the study and no mortality occurred.
No abnormal findings were observed in the cornea or iris of any animal at any of the measurement intervals.
Moderate reddening of the conjunctivae was noted in all animals 1 hour after treatment. Slight reddening of the conjunctivae was noted in all animals at the 14-hour reading and persisted in one animal up to the 48-hour examination.
Slight swelling (chemosis) of the conjunctivae was observed in one animal 1 hour after treatment.
Moderate reddening of the sclerae was present in all animals at the 1-hour examination. Two animals still showed slight reddening of the sclerae at the 24-hour reading.
Slight ocular discharge was noted in all animals at the 1-hour reading.
No abnormal findings were observed in the treated eye of any animal 72

hours after treatment.
No staining of the treated eyes produced by the test substance was observed.
No corrosion of the cornea was observed at any of the reading times.

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY RCC Ltd (2005a)

B.4. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE Notified Chemical

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay)
Species/Strain Mouse/CBA/CaOlaHsd
Vehicle Acetone/olive oil (4/1, v/v)
Remarks - Method No deviations from the protocol.

RESULTS

Concentration (% w/v)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	563	-
25	876	1.6
50	1144	2.0
100	871	1.5
Positive Control (alpha-hexyl cinnamaldehyde)		
0	192	-
5*	513	2.7*
10*	655	3.4*
25	2382	12.4

*This value was used in calculation of EC3.

Remarks - Results No death occurred during the study period.

No clinical signs of local toxicity at the ears of the animals and no systemic findings were observed during the study period.

No dose-response relationship was observed.

The body weight of the animals, recorded prior to the first application and prior to necropsy, was within the range commonly recorded for animals of the strain and age.

The EC3 value for the positive control was calculated by the study author as 7.1% (w/v).

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

TEST FACILITY RCC Ltd (2005b)

B.5. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified Chemical (30%)
METHOD	Human Repeated Insult Patch Test (In-house method)
Study Design	Induction Procedure: A sufficient amount of the test substance (approximately 0.2 mL) was placed onto a modified Parker-Davis Readi-Bandage occlusive patch and applied to the upper arm of each subject. This procedure was performed and repeated every Monday, Wednesday, and Friday until 9 applications of the test substance had been made. The subjects were instructed to remove the patch 24 hours after application. Twenty-four hour rest periods followed Tuesday and Thursday removals and 48-hour rest periods followed each Saturday removal. Subjects returned to the testing Facility and the site was scored just prior to the next patch application. If a subject developed a positive reaction of a level 2 erythema or greater during the induction phase or if, at the discretion of the study director, the skin reaction warranted a change in site, the patch was applied to a previously unpatched, adjacent site for the next application. If a level 2 reaction or greater occurred at the new site, no further applications were made. However, any reactive subjects were subsequently challenge patch tested. Rest Period: 14 days Challenge Procedure: After a rest period of approximately 2 weeks (no applications of the test substance), the challenge patch was applied to a previously unpatched test site. The site was scored 24 and 72 hours after application. All subjects were instructed to report any delayed skin reactivity that occurred after the final challenge patch reading. When warranted, selected test subjects were called back to the clinic for additional examinations and scoring to determine possible increases in challenge patch reactivity.
Study Group	20 males and 90 females ranging in age from 18 to 74 years - exclusive panel
Vehicle	Not known
Remarks - Method	No significant protocol deviations.
RESULTS	
Remarks - Results	Ninety-seven (97/110) subjects satisfactorily completed the test procedure using 30% notified chemical. Thirteen (13/110) subjects discontinued for personal reasons unrelated to the conduct of the study. Discontinued panellist data are shown up to the point of discontinuation, but are not used in the conclusion of the final report. There was no skin reactivity observed at any time during the course of the study.
CONCLUSION	A repeated insult patch test was conducted using the notified chemical diluted to 30% under occlusive dressing. The notified chemical was non-irritating and non-sensitising under the conditions of the test.
TEST FACILITY	Essex Testing Clinic, Inc. (2006)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure (test 1)/Pre incubation procedure (test 2)
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102
Metabolic Activation System	S9 was prepared from phenobarbital/β-naphthoflavone (p.o.) induced rate liver.
Concentration Range in Main Test	Test 1 with and without metabolic activation: 0, 10, 33, 100, 333, 1000, 2500 and 5000 µg/plate Test 2 with and without metabolic activation: 0, 3, 10, 33, 100, 333, 1000, 2500 and 5000 µg/plate
Vehicle	DMSO
Remarks - Method	E. coli strains were not used. No significant protocol deviations.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	≥ 333			
Test 1		≥ 333	> 5000	negative
Test 2		≥ 333	> 5000	negative
Present	≥ 333			
Test 1		≥ 333	> 5000	negative
Test 2		≥ 333	> 5000	negative

Remarks - Results

The plate incubated with the test substance showed reduced background growth at higher concentrations with and without S9 mix in all strains used, except in strain TA 1535 in both experiments and in strain TA 98 (test 2 without S9 mix).
Toxic effects, evident as a reduction in the number of revertants, occurred in nearly all test groups (except for TA 1535) with and without metabolic activation.
No substantial increase in revertant colony numbers of any of the five tester strains was observed following treatment with the notified chemical at any concentration level, neither in the presence or absence of metabolic activation (S9 mix). There was also no tendency of higher mutation rates with increasing concentrations in the range below the generally acknowledged border of biological relevance.
Appropriate reference mutagens were used as positive controls. They showed a distinct increase in induced revertant colonies.
During the described mutagenicity test and under the experimental conditions reported, the test substance did not induce gene mutation by base pair changes or frameshifts in the genome of the strains used.
In test 1, the number of colonies did not quite reach the lower limit of the historical control data in strain TA 102 in the negative and solvent control with metabolic activation. Since this deviation is rather small, this effect is judged to be based upon statistical fluctuations and has no detrimental impact on the outcome of the study.

CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	RCC Ltd (2005c)

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 from a biological waste water treatment plant treating predominantly domestic sewage
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	The biological oxygen demand (BOD) was measured and expressed as percentage of theoretical oxygen demand (ThOD) for expression of the biodegradability
Remarks - Method	The test was conducted in duplicates at a nominal concentration of 100 mg/L. A blank control, a reference control (nominal 100 mg/L sodium benzoate) and a toxicity control (nominal 100 mg/L notified chemical and 100 mg/L sodium benzoate) were also set up in duplicates. For each of the vessels the initial pH was 7.43 and the temperature was maintained at 22˚C.

RESULTS

Notified Chemical		*Sodium Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	13	--	--
7	50	5	75
12	58	7	81
14	60	14	89
21	66	21	92
28	69	28	94

Remarks - Results	All the criteria for test validity were met. The notified chemical achieved 69% degradation after 28 days. However, it narrowly missed the 10-day window criterion for ready biodegradability. Therefore, it cannot be classified as readily biodegradable according to the OECD test guideline. However, it is considered to have potential for biodegradation.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	Givaudan Sussie SA (2005d)

C.1.2. Bioaccumulation

TEST SUBSTANCE	Notified chemical
CONCLUSION	A test for the bioaccumulation properties of the notified chemical was not conducted. The notified chemical has some potential to bioaccumulate in aquatic organisms based on its estimated log K_{OW} of 4.3 and low molecular weight of 225.3. However, bioaccumulation is expected to be limited by the low potential for aquatic exposure and degradation of the notified chemical by both biotic and abiotic processes in the environment.

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test - Flow-Through
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Acetone
Water Hardness	Not reported
Analytical Monitoring	The actual test concentrations were measured at 4- and 1-hour before start and at the end of the test using HPLC.
Remarks - Method	Following a range-finding test, 20 *Daphina* (in four replicates, 5 in each container) were exposed to an acetone (100 µL/L) control and the notified chemical at target concentrations of 1.0, 1.8, 3.2, 5.6 and 10 mg/L at 21.4 – 21.7˚C and pH 7.7 – 8.0 under flow-through test conditions. Acetone was used for preparation of stock solutions. A reference test was also conducted using potassium dichromate at blank control, 0.10, 0.18, 0.32, 0.56, 1.0 and 1.8 mg/L in four replicates using 20 animals for each concentration (48 h EC50 = 0.63 mg/L).

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*[1]		*24 h*	*48 h*
Solvent-control	0	20	0	0
1.0	1.1[2]	20	0	0
1.8	1.9[3]	20	0	1(1)
3.2	3.2[2]	20	0	1
5.6	5.7[2]	20	2	7
10	10.5[3]	20	6 (16)[4]	20 (3)[4]

[1] Mean value of the duplicate measurements at 4- and 1-hour before start and the end of the test.
[2] Concentrations at one-hour before start were not determined.
[3] Outlying start concentrations not included in determination of the mean exposure concentrations.
[4] Numbers of daphnia in parentheses indicate numbers observed trapped at the surface of the test solutions. These organisms were reimmersed into respective test solutions before recording of mobility.

EC50	5.6 mg/L (95% confidence limits 4.9 – 6.6 mg/L) at 48 hours
NOEC	3.2 mg/L at 48 hours
Remarks - Results	All the test validity criteria were met. No immobilisation was observed at 1.0 mg/L and 5% (not biologically significant) immobilisation of *Daphnia* was observed at levels of notified chemical of 1.8 and 3.2 mg/L. The NOEC was therefore determined to be 3.2 mg/L. The 48 h EC50 was calculated to be 5.6 mg/L (95% confidence limits 4.9 – 6.6 mg/L) using the maximum likelihood estimation method. The notified chemical is considered to be acutely toxic to *Daphnia magna*.
CONCLUSION	The notified chemical is acutely toxic to aquatic invertebrates.
TEST FACILITY	NOTOX B.V. (2005b)

BIBLIOGRAPHY

Essex Testing Clinic, Inc. (2006) Notified Chemical: Clinical Safety Evaluation Repeated Insult Patch Test, Final Report, April 2006 for Givaudan, Teaneck, NJ 07666, USA. Essex Testing Clinic, Inc., Verona, NJ 07044, USA (unpublished report provided by the notifier).

Givaudan Sussie SA (2004a) Determination of the Freezing Point of GR-86-0999, Final Report, December 2004, Study No. 04-E092. Givaudan Suisse SA, Ecotoxicological Laboratory, CH-1214 Vernier/Geneva, Switzerland (unpublished report provided by the notifier).

Givaudan Sussie SA (2004b) Determination of the Density of GR-86-0999, Final Report, December 2004, Study No. 04-E090. Givaudan Suisse SA, Ecotoxicological Laboratory, CH-1214 Vernier/Geneva, Switzerland (unpublished report provided by the notifier).

Givaudan Sussie SA (2004c) Flash Point of GR-86-0999, Final Report, December 2004, Study No. 04-E096. Givaudan Suisse SA, Ecotoxicological Laboratory, CH-1214 Vernier/Geneva, Switzerland (unpublished report provided by the notifier).

Givaudan Sussie SA (2005a) Vapour Pressure Curve of GR-86-0999 and Determination of the Boiling Point, Final Report, March 2005, Study No. 04-E094. Givaudan Suisse SA, Ecotoxicological Laboratory, CH-1214 Vernier/Geneva, Switzerland (unpublished report provided by the notifier).

Givaudan Sussie SA (2005b) Water Solubility of GR-86-0999, Final Report, August 2005, Study No. 05-E044. Givaudan Suisse SA, Ecotoxicological Laboratory, CH-1214 Vernier/Geneva, Switzerland (unpublished report provided by the notifier).

Givaudan Sussie SA (2005c) Partition Coefficient n-Octanol/water of GR-86-0999 According to OECD Guideline No. 117, Final Report, June 2005, Study No. 04-E105. Givaudan, Process Safety Laboratory, Switzerland (unpublished report provided by the notifier).

Givaudan Sussie SA (2005d) Ready Biodegadability of GR-86-0999 According to OECD Guideline No. 301 F, Final Report, June 2005, Study No. 04-E100. Givaudan Sussie SA, Process Safety Laboratory, Switzerland (unpublished report provided by the notifier).

Givaudan Sussie SA (2010a) Adsorption/desorption Study: Estimation of the Organic Carbon/water Partition Coefficient (K_{OC}) of Pepperwood with a QSAR, Final Report, March 2010, Project No. 10-E056/S. Givaudan, Process Safety Laboratory, Switzerland (unpublished report provided by the notifier).

Givaudan (2010b) Determination of the Auto-ignition Temperature of Pepperwood, Final Report, April 2010, Ref. No. 2010-042. Givaudan, Process Safety Laboratory, Switzerland (unpublished report provided by the notifier).

NOHSC (1994) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2003) National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd edition [NOHSC:2011(2003)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

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

NOTOX B.V. (2005a) Determination of the Vapour Pressure of GR-86-0999 by the Static Method , Final Report, Januray 2005, Project No. 424733 for Givaudan Suisse SA, CH-1214 Vernier/Geneva, Switzerland. NOTOX B.V. 5231 DD 's-Hertogenbosch, The Netherlands (unpublished report provided by the notifier).

NOTOX B.V. (2005b) Acute Toxicity Study in Daphnia Magna with GR-86-0999 (Flow-through), Final Report, March 2005, Project No. 424744 for Givaudan Suisse SA, CH-1214 Vernier/Geneva, Switzerland. NOTOX B.V. 5231 DD 's-Hertogenbosch, The Netherlands (unpublished report provided by the notifier).

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

RCC Ltd (2004a) Notified Chemical: Acute Oral Toxicity Study in Rats, Final Report, December 2004, Study No. 856927 for Givaudan Suisse SA, CH-1214 Vernier/Geneva, Switzerland. RCC Ltd, Toxicology, CH-4414 Fullinsdorf, Switzerland (unpublished report provided by the notifier).

RCC Ltd (2004b) Notified Chemical: Primary Skin Irritation Study in Rabbits (4-Hour Semi-Occlusive Application), Final Report, December 2004, Study No. 856928 for Givaudan Suisse SA, CH-1214 Vernier/Geneva, Switzerland. RCC Ltd, Toxicology, CH-4414 Fullinsdorf, Switzerland (unpublished report provided by the notifier).

RCC Ltd (2005a) Notified Chemical: Primary Eye Irritation Study in Rabbits, Final Report, January 2005, Study No. 856929 for Givaudan Suisse SA, CH-1214 Vernier/Geneva, Switzerland. RCC Ltd, Toxicology, CH-4414 Fullinsdorf, Switzerland (unpublished report provided by the notifier).

RCC Ltd (2005b) Notified Chemical: Local Lymph Node Assay (LLNA) in Mice (Identification of Contact Allergens), Final Report, January 2005, Study No. 856930 for Givaudan Suisse SA, CH-1214 Vernier/Geneva, Switzerland. RCC Ltd, Toxicology, CH-4414 Fullinsdorf, Switzerland (unpublished report provided by the notifier).

RCC Ltd (2005c) Notified Chemical: Salmonella Typhimurium Reverse Mutation Assay, Final Report, February 2005, Study No. 860100 for Givaudan Suisse SA, CH-1214 Vernier/Geneva, Switzerland. RCC Ltd, Toxicology, CH-4414 Fullinsdorf, Switzerland (unpublished report provided 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 >.