File No: LTD/1147

October 2004

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

MUSCENONE DELTA

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 and Heritage.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at:

Library
National Occupational Health and Safety Commission
25 Constitution Avenue
CANBERRA ACT 2600
AUSTRALIA

To arrange an appointment contact the Librarian on TEL + 61 2 6279 1161 or + 61 2 6279 1163.

This Full 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:

Street Address:	334 - 336 Illawarra Road MARRICKVILLE NSW 2204, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
Chemicals Notification and Assessment

TABLE OF CONTENTS

FULL PUBLIC REPORT

MUSCENONE DELTA

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Firmenich Ltd (ACN 002 964 794)
73 Kenneth Road
BALGOWLAH NSW 2093

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, CAS No., molecular weight, molecular and structural formulae, spectral data, purity and identity of impurities.

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)
Low Volume Chemical, Permit No. 33 (1994), No. 222 (1997), No. 365 (2001).

NOTIFICATION IN OTHER COUNTRIES

USA (PMN 92-1310P)	1993
Switzerland	1995
Japan	2000
Canada (DSL - Conf. 14905-1)	2003
EU (UK) :	
Annex VII-B	1992
Annex VII-A (429-900-5)	1999
Level 1A	2003

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Muscenone Delta

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	UV/visible spectrophotometry, Infrared (IR) spectroscopy, Mass spectroscopy, ^{1}H and ^{13}C NMR spectroscopy.
Remarks	Reference spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
90% (minimum).

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None.

ADDITIVES/ADJUVANTS
None.

4. 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 introduced as a small component (maximum 2%) of compounded fragrances.

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

Year	*1*	*2*	*3*	*4*	*5*
Kilograms	50	75	100	125	150

USE
The notified chemical will be used as a fragrance ingredient in a variety of cosmetic and domestic products. It will be imported in liquid compounded fragrances, which will be reformulated in Australia to produce the final consumer products. In the final products, the concentration of the notified chemical will be a maximum of 0.4% in fine perfumes, and a maximum of 0.025% in other cosmetic products and domestic products.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
The notified chemical is expected to initially be imported through Sydney, by wharf or airport.

IDENTITY OF MANUFACTURER/RECIPIENTS
The fragrance preparations containing the notified chemical will be imported by Firmenich Ltd and will be reformulated locally. The fragrance preparations containing the notified chemical will initially be stored and distributed from the notifier's site.

TRANSPORTATION AND PACKAGING
The fragrance preparations containing the notified chemical will be transported by road from the wharf or airport to the notifier's site and thence to the customer sites. The fragrance preparations will be imported and distributed in tightly closed lacquered drums, typically of 180 kg size, but also 100, 50, 25, 10 or 5 kg.

5.2. Operation description

The fragrance preparations containing the notified chemical will be reformulated to produce domestic products in a continuous mixing process, which will involve a regulated feed of the fragrance mixture into an automated system. Cosmetic products will be produced in a batch process, which may involve open vessels and manual addition of the fragrance preparations containing the notified chemical. Batches will be produced generally once a month, with fortnightly production on some occasions. Batch sizes will vary with product, but can be several thousand kilograms depending on the concentration of the notified chemical (maximum of 2%).

The products will be distributed to retail outlets, displayed and sold to the public.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Storage at notifier's warehouse	3	8 hours	1 day/year

At cosmetic, toiletries and household cleaning product manufacturing plants:

Mixer	5	4 hours/day	2 days/year
Drum handling	5	"	"
Drum cleaning/washing	8	"	"
Maintenance	3	"	"
Quality assurance	2	½ hour/day	1 day/year
Packaging	8	4 hours/day	2 days/year

Exposure Details
The notified chemical is contained in drums of 5 – 180 kg capacity in compounded fragrances at a maximum of 2%. It is then diluted into products at a maximum concentration of 0.4%. The fragrances are pumped to mixing vessels or to weighing vessels under local exhaust ventilation through closed lines. Therefore, inhalation exposure should be minimised. Dermal and ocular exposure may occur from spillage during transfer operations, maintenance of machinery and quality control testing. Packaging of final products is expected to be automated and should not result in appreciable worker exposure. Exposure during transport and storage of compounded fragrances or products is possible in the event of accidental rupture of containers. Workers in plants manufacturing cosmetics or domestic cleaning products typically wear personal protective equipment including overalls, safety glasses and impervious gloves.

5.4. Release

RELEASE OF CHEMICAL AT SITE
The containers of the fragrance preparations containing the notified chemical will be imported by Firmenich Australia Ltd and forwarded to their customers directly without being opened, except to repackage in case of damaged drums. At the customers' manufacturing plants for cosmetics, toiletries and household cleaning products, the containers are opened and the fragrance preparations containing the notified chemical are blended with other ingredients to form the final consumer product. Release to the environment during blending is expected to be minimal as closed lines are usually used limiting potential releases to accidental spills and estimated at 0.1%. Equipment is expected to be washed with water and washings reused. The average amount of container residues after vacuum pump removal is < 0.1%. Therefore the estimated total release of the notified chemical at manufacturing sites is about 0.2% or 0.3 kg/year of waste.

RELEASE OF CHEMICAL FROM USE
The range of containers for consumer products containing the notified chemical is very large, ranging from 20 - 30 mL for facial creams to 250 - 500 mL for body lotions and shampoos to about 1.5 L for liquid detergents. Almost all of the notified chemical will enter the aquatic compartment during use of the consumer products into which it is incorporated. Shampoos, perfumes and cosmetics will be washed off the hair and skin during bathing and cleaning agents will enter the sewage system during or after cleaning activities. A fraction of the chemical used in skin creams will be dermally absorbed and metabolised while any used in sprays and aerosols may volatilise. A proportion may enter stormwater from incorrect disposal of cleaning products or as runoff from cleaned surfaces.

5.5. Disposal
Empty containers at the blending plants will either be recycled or disposed of through an approved waste management capacity. Empty consumer product containers will be recycled or disposed of to municipal landfills. As a worst case, assuming that 3% of the products remain as residues inside "empty" containers at a maximum import volume of 150 kg/y, then 4.5 kg/y of the notified chemical would remain in consumer containers at disposal.

5.6. Public exposure
Widespread exposure of the public to shampoos, perfumes, cosmetics and cleaning agents will occur although the maximum concentration to which the public will be exposed is 0.4%.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa Colourless liquid.

Melting Point/Freezing Point < - 20°C

METHOD EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
TEST FACILITY SafePharm Laboratories Ltd (1995a).

Boiling Point 316.8 - 339.8°C

METHOD EC Directive 92/69/EEC A.2 Boiling Temperature.
TEST FACILITY Toxicol Laboratories Ltd (1992a).

Density 927.26 kg/m^3 at 20°C

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks Density was measured using the pycnometer method.
TEST FACILITY SafePharm Laboratories Ltd (1995a).

Vapour Pressure 4 x 10^{-5} kPa at 25°C

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks The vapour pressure was measured using a vapour pressure balance with measurements being made at several temperatures. Linear regression analysis was used to calculate the vapour pressure at 25°C. This was repeated three times. The vapour pressure indicates the chemical is moderately volatile (Mensink et al. 1995).

Based on various properties, the Henry's Law Constant was calculated to be 4.3 x 10^{-3} (log H = -2.4), which indicates it will tend to exhibit moderate volatility from water or moist soil surfaces (Mensink et al. 1995).
TEST FACILITY SafePharm Laboratories Ltd (1995b).

Water Solubility 0.899 mg/L at 20°C

METHOD EC Directive 92/69/EEC A.6 Water Solubility.
Remarks The determination was carried out using the flask method. The water solubility was determined by stirring excess test material into water at 30°C, equilibrating for 24 hours at 20°C, and then separating the aqueous and non aqueous layers by centrifugation and filtration. The concentration of the test substance in the aqueous phase was determined by gas chromatography and the average of 3 determinations taken as the solubility.
TEST FACILITY SafePharm Laboratories Ltd (2001a).

Hydrolysis as a Function of pH Not determined.

Remarks The chemical is readily biodegradable. There are no groups generally considered as hydrolysable.

Partition Coefficient (n-octanol/water) log Pow > 4.88 at 22.5 ±0.5°C

METHOD EC Directive 92/69/EEC A.8 Partition Coefficient – shake flask method.
Remarks Three determinations of different volumes of n-octanol containing dissolved material in water were conducted in duplicate. After shaking for 5 min, the aqueous and octanol phases were separated with no details of centrifugation, filtering or time to allow phase separation provided. The concentration of notified chemical was determined in each phase by gas chromatography.

TEST FACILITY SafePharm Laboratories Ltd (1994).

Fat Solubility Soluble in all proportions (coconut oil) at 37°C

METHOD OECD TG 116 Fat Solubility of Solid and Liquid Substances.
Remarks The determination was carried out using the flask method.
TEST FACILITY Toxicol Laboratories Ltd (1992a).

Adsorption/Desorption $K_{oc} > 3630$, $\log K_{oc} = 3.56$
Remarks The log Koc was calculated using QSAR for non-hydrophobic compounds as recommended by the EC for various classes of organic compounds according to the formula log Koc = 0.52 log Pow + 1.02. From this calculation, the Koc is greater than 3630.

Dissociation Constant Not determined.

Remarks The chemical does not contain any dissociable acidic or basic groups.

Particle Size Not determined.

Remarks The notified chemical is liquid at room temperature.

Flash Point 160°C

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks The determination was carried out using the distillation method.
TEST FACILITY Toxicol Laboratories Ltd (1992a).

Flammability Limits Not determined.

Autoignition Temperature 248°C

METHOD 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
TEST FACILITY SafePharm Laboratories Ltd (1996a).

Explosive Properties Not explosive.

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks A negative result was obtained for sensitivity to shock and to heat. The test for friction is not applicable to liquids.
TEST FACILITY SafePharm Laboratories Ltd (1996a).

Reactivity

Remarks The notified chemical is expected to be stable under normal environmental conditions. No test of oxidising properties was performed, however the notified chemical has not structural indications of oxidising properties or other unusual reactivity.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 > 2000 mg/kg bw	low toxicity
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	evidence of sensitisation
Guinea pig, skin sensitisation – non-adjuvant test.	no evidence of sensitisation
Human repeat insult patch test	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOEL = 250 mg/kg/day
Genotoxicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosomal aberration test	non genotoxic
Genotoxicity – in vitro mouse lymphoma mutation	non mutagenic
Developmental and reproductive effects	negative

7.1. Acute toxicity – oral

TEST SUBSTANCE — Notified chemical.

METHOD — EC Directive 84/449/EEC B.1 Acute toxicity (Oral).
- Species/Strain: Rat /Crl:CD(SD)Br (VAF plus).
- Vehicle: Polyethylene glycol (PEG 400).
- Remarks - Method: None.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2000	0/10

- LD50: > 2000 mg/kg bw
- Signs of Toxicity: No clinical signs of toxicity. No effect on bodyweight.
- Effects in Organs: No treatment related necropsy findings.
- Remarks - Results: None.

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

TEST FACILITY — Toxicol Laboratories Ltd (1992b).

7.2. Acute toxicity - dermal

TEST SUBSTANCE — Notified chemical.

METHOD — EC Directive 84/449/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
- Species/Strain: Rat/Crl:CD(SD)Br (VAF plus).
- Vehicle: Used as supplied.
- Type of dressing: Semi-occlusive.
- Remarks - Method: None.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2000	0/10

- LD50: > 2000 mg/kg bw
- Signs of Toxicity - Local: None.

Signs of Toxicity - Systemic	Perinasal staining noted in most animals, onset and recovery earlier in males than in females. Piloerection also noted in 4 males and 1 female, lasting from one to 5 days. No effect on bodyweight.
Effects in Organs	All abnormal findings at necropsy were of low incidence and were consistent with the background macroscopic pathology of this strain of rat.
Remarks - Results	Full recovery was observed by day 15.

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

TEST FACILITY Toxicol Laboratories Ltd (1991a).

7.3. Irritation – skin

TEST SUBSTANCE Notified chemical.

METHOD EC Directive 84/449/EEC B.4 Skin irritation.

Species/Strain	Rabbit/New Zealand White
Number of Animals	4 females
Vehicle	Used as supplied
Observation Period	7 days
Type of Dressing	Semi-occlusive
Remarks - Method	None.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	1.4	3	72 hours	0
Oedema	0.83	2	"	0

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

Remarks - Results 24 h after the end of the dosing period erythema varying in degree from slight to well defined and slight oedema were noted in all 4 treated rabbits. The incidence of irritation decreased during the following 48 h and at the 72 h observation period erythema and oedema were entirely absent in 2 of the rabbits. Seven days after dosing irritation had subsided in all the treated animals although skin thickening was observed in one animal.

CONCLUSION The notified chemical is slightly irritating to skin.

TEST FACILITY Toxicol Laboratories Ltd (1992c).

7.4. Irritation - eye

TEST SUBSTANCE Notified chemical.

METHOD EC Directive 84/449/EEC B.5 Eye irritation.

Species/Strain	Rabbit /New Zealand White
Number of Animals	4 females
Observation Period	72 hours
Remarks - Method	One animal was treated initially as a pilot.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0.42	3	48 hours	0
Conjunctiva: chemosis	0.25	2	"	0
Conjunctiva: discharge	0	2	1 hour	0
Corneal opacity	0	0		0
Iridial inflammation	0	0		0

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

Remarks - Results: Irritation was apparent one hour after dosing and consisted of slight discharge and chemosis with definite conjunctival redness in all animals. The irritation became less severe between 24 and 48 hours with slight chemosis and/or redness in some animals. At 72 hours, no signs of irritation were detected in any animals. No sign of corneal or iridal irritation was apparent in any animal at any of the examinations during the study.

CONCLUSION: The notified chemical is slightly irritating to the eye.

TEST FACILITY: Toxicol Laboratories Ltd (1992d).

7.5. Skin sensitisation
7.5.1 Maximisation test 1

TEST SUBSTANCE: Notified chemical.

METHOD: EC Directive 84/449/EEC B.6 Skin sensitisation, Maximisation Test.

Species/Strain: Guinea pig/Dunkin-Hartley.

PRELIMINARY STUDY: Maximum Non-irritating Concentration:
intradermal: 25% in liquid parafin
topical: 100%

MAIN STUDY

Number of Animals: Test Group: 20 Control Group: 10

INDUCTION PHASE: Induction Concentration:
intradermal: 25% in liquid parafin
topical: 100%

Signs of Irritation: Slight irritation in 4/20 test animals.

CHALLENGE PHASE

1st and 2nd challenge: topical: 50% and 100% in ethanol.

Remarks - Method: A second challenge was performed 4 days after the completion of the first challenge.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	100%	12/20	8/20	4/20	0/20
	50%	1/20	1/20	0/20	0/20
Control Group	100%	0/10	0/10	0/10	0/10
	50%	0/10	0/10	0/10	0/10

Remarks - Results: Scores of up to 2 (moderate diffuse redness) were seen in test animals; no dermal responses were recorded in control animals.

CONCLUSION: There was evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY Toxicol Laboratories Ltd (1992e).

7.5.2 Maximisation test 2

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 406 Skin Sensitisation – maximisation test.
USEPA Health Effects Test Guidelines, Subpart B: Dermal Sensitisation, 40 CFR 798.4100.

Species/Strain Guinea pig/Dunkin-Hartley.

PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 40% in mineral oil
topical: 100%

MAIN STUDY

Number of Animals Test Group: 20 Control Group: 10

INDUCTION PHASE Induction Concentration:
intradermal: 40% in mineral oil
topical: 100%

Signs of Irritation No topical irritation. Intradermal injection: 8 – 10 mm eschar with surrounding erythema at 50% and 100%.

CHALLENGE PHASE

1st challenge topical: 100%.

Remarks - Method Sodium lauryl sulfate (5%(w/w) in petrolatum) was applied 24 hours prior to topical induction.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	100%	0/20	0/20
Control Group	100%	0/10	0/10

Remarks - Results Scattered incidences of very faint erythema (score 0.5) were seen in both test and control animals.

CONCLUSION There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY Product Safety Labs (2000).

7.5.3 Buehler test

TEST SUBSTANCE

METHOD OECD TG 406 Skin Sensitisation - Buehler Test.

Species/Strain Guinea pig/Hartley - derived.

PRELIMINARY STUDY Maximum Non-irritating Concentration: 100%

MAIN STUDY

Number of Animals Test Group: 20 Control Group: 10

INDUCTION PHASE Induction Concentration: 100%

CHALLENGE PHASE

1st challenge topical: 50% in mineral oil.

Remarks - Method The test substance was dosed as supplied at the 3 induction phases of the test. Since very faint patchy erythema or faint confluent erythema was noted at the inductions, the test substance was challenged at 50% in mineral oil.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: Challenge*		
		24 h	*48 h*	*72 h*
Test Group	50%	0/20	0/20	0/20
Control Group	50%	0/10	0/10	0/10

Remarks - Results: Scattered incidences of very faint erythema (score 0.5) were seen in both test and control animals.

CONCLUSION: There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY: Celsis Laboratory Group (1999).

7.6. Skin sensitisation – human volunteers

7.6.1 Test 1

TEST SUBSTANCE: Notified chemical.

METHOD

Study Group: 118 subjects ranging in age from 18 to 74 (males and females) of which 102 completed the study.

Vehicle: The test substance was tested at 10% in diethyl phthalate.

Induction Procedure: The test substance was applied to the skin of the upper back in occluded patches, for a total of 9 applications. The patches were removed 24 hours after application.

Rest Period: 14 days.

Challenge Procedure: The challenge patch was applied to the original sites. Sites were evaluated at 48 and 72 hours after application.

Remarks - Method: Discontinuations were not test substance related.

RESULTS

Remarks - Results: There were no evidence of sensitisation in the 102 subjects who completed the study.

CONCLUSION: A human repeat insult patch test was conducted using the notified chemical diluted with diethyl phthalate to 10% under occlusive dressing. The notified chemical was slightly irritating and non-sensitising under the conditions of the test.

TEST FACILITY: TKL Research, Inc. (1995).

7.6.2 Test 2

TEST SUBSTANCE: Notified chemical.

METHOD

Study Group: 110 subjects ranging in age from 20 to 74 (males and females) of which 108 completed the study.

Vehicle: The test substance was tested at 20% in diethyl phthalate.

Induction Procedure: The test substance was applied to the skin of the upper back in occluded patches, for a total of 9 applications. The patches were removed 24 hours after application.

Rest Period: 14 days.

Challenge Procedure: The challenge patch was applied to the original sites. Sites were evaluated at 48 and 72 hours after application.

Remarks - Method: Discontinuations were not test substance related.

RESULTS

Remarks - Results	There were no evidence of sensitisation in the 102 subjects who completed the study.

CONCLUSION	A human repeat insult patch test was conducted using the notified chemical diluted with diethyl phthalate to 20% under occlusive dressing. The notified chemical was slightly irritating and non-sensitising under the conditions of the test.
TEST FACILITY	TKL Research, Inc. (1999).

7.7. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Crl:CD(SD)BR (VAF plus).
Route of Administration	Oral – gavage.
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week;
Vehicle	0.5% carboxymethylcellulose.
Remarks - Method	None.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	6/ sex	0	0/12
II (low dose)	"	250	0/12
III (mid dose)	"	500	0/12
IV (high dose)	"	1000	0/12
V (control recovery)	"	0	0/12
VI (high dose recovery)	"	1000	0/12

Clinical Observations

No clinical signs related to treatment were noted. Hair loss was apparent in 1 female dosed at 250 mg/kg/day, 2 males and 3 females dosed at 1000 mg/kg/day. A female dosed at 1000 mg/kg/day had a swollen foot, this was considered to be coincidental and unrelated to treatment. Bodyweights and bodyweight gains were unaffected by administration of test substance. Food consumption values were those expected for animals of this age and strain. There were no treatment-related ocular findings.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Haematology Activated partial prothrombin time (PTT) levels were increased relative to the normal ranges for males dosed at 500 and 1000 mg/kg/day (21% and 34% respectively). Fibrinogen levels were also increased (15%) in males dosed at 1000 mg/kg/day. Following a 2-week treatment free period PTT levels were within the normal ranges and fibrinogen levels were reduced, showing that recovery had occurred.

Statistically significant changes were also seen in neutrophils, lymphocytes, monocytes, basophils and prothrombin time although the changes were minor and all group mean values were within the normal ranges.

Clinical Chemistry During week 4, non dose related increases in cholesterol levels were apparent in all treated females and in males dosed at 1000 mg/kg/day; however only 2 females dosed at 1000 mg/kg/day were outside the reference ranges. After a 2 week treatment free period, group 4 animals showed cholesterol levels within 10% of the control values.

Urinalysis Urinary parameters were unaffected by administration of the test substance.

Effects in Organs

Absolute and relative liver weights were statistically significantly higher in all treated males and female groups. After a 2 week treatment free period, group 4 values for absolute and bodyweight liver weights were within 10% of the controls.

A statistically significant increase was apparent in absolute ovary weights for females dosed at 1000 mg/kg/day. This was considered to be unrelated to treatment as the group mean value was within the normal range.

There were no treatment-related macroscopic and microscopic findings.

Remarks – Results	Haematological changes were considered not to be treatment related as all group mean values were within normal ranges. Observed changes in absolute and relative liver weights were attributed to the control values being lower than expected for animals of this age and strain.

CONCLUSION

The No Observed Effect Level (NOEL) was established as 250 mg/kg bw/day in this study, based on PTT and cholesterol changes.

TEST FACILITY Quintiles England Limited (1996).

7.8. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical.

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

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100.
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction.
Concentration Range in Main Test	a) With metabolic activation: 3.2, 16, 80, 400 and 2000 µg/plate. b) Without metabolic activation: 3.2, 16, 80, 400 and 2000 µg/plate.
Vehicle	DMSO
Remarks - Method	Two independent experiments were conducted in triplicate.

RESULTS

Remarks - Results	An increase in revertants was seen for TA1535 at 16 µg/plate in the absence of metabolic activation, giving statistically significance, in both experiments but the increase was not to double the solvent control and no dose response was seen. No other strain showed any increase in revertant numbers. A 3rd experiment carried out with TA1535 gave no indication of any significant increase in revertant numbers and it is concluded that the test substance is not a mutagen under the conditions of the test. Positive controls gave the appropriate increases indicating that the test system responded appropriately.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Toxicol Laboratories Ltd (1991b).

7.9. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 473 In vitro Mammalian Chromosomal Aberration Test.
Cell Type/Cell Line	Human lymphocytes.
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction.
Vehicle	Ethanol.
Remarks - Method	None.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Present			
Test 1	0, 17.81, 35.63*, 71.25*, 142.5*, 285, 570, 1140, 2280	4 h	20 h
Test 2	0, 17.81, 35.63, 71.25*, 142.5*, 213.5*	4 h	20 h
Test 2	0, 35.63, 71.25, 142.5, 213.8*	4 h	44 h
Absent			
Test 1	0, 4.45, 8.91*, 17.81*, 35.63*, 71.25	20 h	20 h
Test 2	0, 4.45, 8.91*, 17.81*, 35.63*, 53.44*	20 h	20 h
Test 2	0, 8.91, 17.81, 35.63*, 53.44*	20 h	44 h

*Cultures selected for metaphase analysis.

RESULTS

Remarks - Results	No statistically significant increases in the frequency of cells with aberrations or polyploid cells were observed either in the presence or absence of metabolic activation. Appropriate positive controls induced large increases in the number of aberrant cells, indicating that the test system responded appropriately. Mitotic index measurements indicated metaphases were present in test 1 up to 35.63 μg/mL without S9 and 142.5 μg/mL with S9. In test 2 approximately 50% mitotic inhibition was observed with 35.63 μg/mL without S9 and 142.5 μg/mL with S9 for the 20-hour harvest. For the 44-hour harvest approximately 50% mitotic inhibition was observed with 53.44 μg/mL without S9; mitotic inhibition was not observed with S9.
CONCLUSION	The notified chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.
TEST FACILITY	SafePharm Laboratories Ltd (1995c).

7.10. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 476 In vitro Mammalian Cell Gene Mutation Test.
Cell Type/Cell Line	Mouse lymphoma L5178Y TK+/- 3.7.2c cells.
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction.
Vehicle	DMSO.
Remarks - Method	Test was performed in duplicate, after a preliminary toxicity test. L5178Y TK+/- 3.7.2c mouse lymphoma cells were treated with the test material at 6 dose levels, in duplicate, together with vehicle (solvent) and positive controls. The entire experiment was repeated to confirm the result of the first experiment. Three-hour pulse exposures were used both with and without metabolic activation in Experiment 1. In Experiment 2, the exposure time without metabolic activation was increased to 24 h. The dose range of test material, plated out for expression of mutant colonies, was selected on the results of a preliminary toxicity test and was 2.5, 5, 10, 15, 20 and 25 μg/ml in the absence of S9 and 2.5, 5, 10, 20, 30 and 40

μg/ml in the presence of S9 for the first experiment. For the second experiment the dose range was 5 to 40 μg/ml with activation and 2.5 to 25 μg/ml without activation. The maximum dose level used was limited by test material-induced toxicity. A precipitate of test material was not observed at any dose levels used in the main experiment.

RESULTS

Remarks - Results	No statistically significant increases in the mutant frequency were observed either in the presence or absence of metabolic activation. Appropriate positive controls induced marked increases in the mutant frequency, indicating the satisfactory performance of the test and of the activity of the metabolising system. The vehicle (solvent) controls gave acceptable levels of mutant frequencies fro the L5178Y cell line at the TK +/- locus.
CONCLUSION	The notified chemical was not mutagenic to L5178Y treated in vitro under the conditions of the test.
TEST FACILITY	SafePharm Laboratories Ltd (2001b).

7.11. Toxicity to reproduction – one generation study

TEST SUBSTANCE	Notified chemical.
METHOD	OECD 415 One-Generation Reproduction Toxicity Study.
Species/Strain	Rat / Sprague-Dawley Crl:CD (SD) IGS BR
Route of Administration	Oral – gavage.
Exposure Information	Total exposure days : 70 (males) or 14 (females) prior to mating and then during mating, gestation and lactation. Dose regimen : 50, 250 and 1000 mg/kg/day bw, 7 days per week.
Vehicle	1% carboxymethylcellulose.
Remarks – Method	The test material was administered orally, by gavage, to groups of 28 male and 28 female rats throughout maturation, mating, gestation and lactation. The dose levels were 50, 250 and 1000 mg/kg/day of the test material, with a similar size control group receiving vehicle alone. Following at least 10 and 2 weeks of dosing respectively, male and female rats were paired within their dose groups to produce litters. At weaning of the offspring, all surviving animals were killed and examined macroscopically. Parental animals were observed daily for clinical signs of reaction to treatment. Bodyweights and food consumption were recorded weekly during the maturation phase which was continued for males after the mating phase. Mated females were weighed and food consumption recorded on specific days post coitum and post partum. The offspring were observed daily for clinical signs. The litter size and individual pup bodyweight were recorded on specific days post partum. During lactation period the offspring were observed for intra-litter onset and duration of landmark of physical development. On specific days of lactation, reflexological assessment of offspring were performed. Post mortem macroscopic examinations were performed on all adults and offspring, including decedents. Reproductive and potential target organs and any significant abnormalities from all parental animals were preserved in fixative. Histopathology was carried out on reproductive and target organs from control and high dose group parental animals. Histopathology

was extended to the low and intermediate dose groups for the liver (target organ) only.

RESULTS

Effects on Parental (P) animals:

At 1000 mg/kg/day in-life effects upon adults were limited to treatment-related increased salivation; pre and post dosing. There were no effects on fertility or reproductive performance.

Post mortem studies showed increased liver weights for males and an increased incidence of hepatocyte enlargement for both sexes. There were no effects upon reproductive organs.

At 250 mg/kg/day there was evidence of pre and post dosing salivation but at a lower incidence and frequency than at 1000 mg/kg/day. Post mortem studies showed an increased liver weight for males only and an increased incidence of hepatocyte enlargement for both sexes. There were no effects upon fertility or reproductive performance.

At 50 mg/kg/day there were isolated incidents of post dosing salivation. There were no effects upon adult fertility and reproductive performance. Post mortem studies showed an increased incidence of centrilobular hepatocyte enlargement for females only.

Effects on 1st Filial Generation (F1)

There were no treatment-related effects upon live litter size at birth and throughout lactation. There were no significant treatment-related differences in offspring growth and physical development during lactation. The statistically significant differences between control values and treated groups were incidental and unrelated to treatment.

Remarks - Results	The relationship of incidents of post dosing salivation at 50 mg/kg/day with test substance was questionable given their frequency. The reduction in offspring viability at 1000 mg/kg/day between days 7 and 14 of lactation was considered incidental as it was limited to a small number of females only. The administration of the test material to male and female rats throughout one reproductive cycle at dose levels up to 1000 mg/kg resulted in adult toxicity that can be generalised as adaptive, non-specific responses to the administration of a xenobiotic.

CONCLUSION

There were no toxicologically significant effects upon reproductive performance or fertility and no effects upon offspring viability, growth and development.

The No Observed Effect Level (NOEL) for reproduction and offspring viability development is 1000 mg/kg/bw.

TEST FACILITY	SafePharm Laboratories Ltd (2003a).

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability – closed bottle test

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Mixed population of activated sewage sludge microorganisms from the secondary stage of a sewage treatment plant.
Exposure Period	28 days.
Auxiliary Solvent	None.
Analytical Monitoring	Dissolved oxygen determined by a BOD probe and oxygen meter.
Remarks - Method	The test material was prepared in duplicate in inoculated culture medium at a nominal concentration of 1.5 mg/L. A control, positive control with sodium benzoate at 3 mg/L and a toxicity control with test material and sodium benzoate were incubated at 21°C for 28 days. Dissolved oxygen was measured at various times about every 3 days.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% degradation*	*Day*	*% degradation*
3	15	3	63
9	20	9	71
12	25	12	81
15	29	15	83
28	43	28	92

Remarks - Results	The test material did not achieve ≥ 60% biodegradation within 28 days and is not considered readily biodegradable according to this test. As the positive control of sodium benzoate achieved ≥ 60% biodegradation within 14 days, the results are considered valid. The toxicity control treatment attained ≥ 25% biodegradation within 14 days therefore the notified chemical is not considered inhibitory.
CONCLUSION	The notified chemical was not readily biodegradable under the conditions of this test.
TEST FACILITY	Safepharm Laboratories (1995g)

8.1.2. Ready biodegradability – manometric respirometry test

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 301F Ready Biodegradability: Manometric Respirometry Test
Inoculum	Mixed population of activated sewage sludge microorganisms from the aeration stage of a sewage treatment plant.
Exposure Period	28 days.
Auxiliary Solvent	None.
Analytical Monitoring	Dissolved organic carbon analysis with a carbon analyser at 900°C, pH.
Remarks - Method	The notified chemical was added directly to the culture medium to a nominal concentration of 100 mg/L. A control, positive control containing the standard material aniline at 100 mg/L and a toxicity control containing both aniline and the notified chemical were also prepared. All controls and treatments were made up in duplicate and inoculated at 30 mg/L of suspended solids. All flasks were incubated at 21°C in the dark in BOD cabinets measuring oxygen consumption.

RESULTS

Test substance		*Aniline positive control*	
Day	*% degradation*	*Day*	*% degradation*
6	12	4	5
16	52	5	45
20	55	6	60
23	60	7	70
28	61	28	92

Remarks - Results: According to the criteria of OECD TG 301F, > 60% biodegradation must be achieved after 28 days and within 10 days of exceeding 10%. As the notified chemical attained the first criterion (61% biodegradation after 28 days), but not the second (17 days elapsed, see above table), it was not considered readily biodegradable by this test methodology. The positive control confirmed the validity of the test and the toxicity control showed that the notified chemical was not toxic to the microorganisms.

CONCLUSION: Although the notified chemical was 61% biodegraded after 28 days, this was not attained within 10 days of achieving 10%. Therefore the notified chemical was not considered readily biodegradable under the conditions of this test.

TEST FACILITY: Safepharm Laboratories (1996b)

8.1.3. Ready biodegradability – CO_2 evolution test

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 301B Ready Biodegradability: CO_2 Evolution Test

Inoculum: Activated sludge from a wastewater treatment facility

Exposure Period: 29 days.

Auxiliary Solvent: None.

Analytical Monitoring: Inorganic carbon measured by a carbon analyser, dissolved organic carbon, pH

Remarks - Method: CO_2-free air was bubbled through bottles containing the notified chemical at 10 mg C/L, a positive control of sodium benzoate at the same concentration, a blank control and a toxicity control containing both notified chemical and sodium benzoate at 10 mg C/L each. Bottles were incubated at 19 - 21°C for 29 days with CO_2 traps connected and sampled regularly.

RESULTS

Test substance		*Sodium benzoate positive control*	
Day	*% degradation*	*Day*	*% degradation*
7	3.8	4	20.0
11	41.5	7	62.0
18	63.0	11	69.1
21	69.8	21	78.8
29	78.8	29	91.1

Remarks - Results: Reading from the graph supplied, the notified chemical was biodegraded by 10% at about 8 days and by 63% by 18 days, thus managing to fulfil the criteria of 60% biodegradation within a 10 day window of achieving 10%. Therefore the notified chemical was considered readily biodegradable according to this test method. The positive control confirmed the validity of the test and the toxicity control showed that the notified chemical was not toxic to the microorganisms.

CONCLUSION — The notified chemical was considered readily biodegradable under the conditions of this test as it achieved 60% biodegradation within a 10 day window of reaching 10%.

TEST FACILITY — Wildlife International (2000)

8.1.4. Inherent biodegradability – Modified MITI test (II)

TEST SUBSTANCE — Notified chemical. (95.64% purity)

METHOD — OECD TG 302C Modified MITI test (II)

Inoculum	Activated sludge collected from 10 locations of municipal and industrial sewage plants, surface water and surface soil.
Exposure Period	28 days.
Auxiliary Solvent	None.
Analytical Monitoring	Closed system oxygen consumption, GC.
Remarks – Method	Flasks containing the notified chemical at a nominal concentration of 30 mg/L in activated sludge or water, were incubated at 25 ± 1°C with positive controls (100 mg/L aniline and sludge) and control blanks for 28 days. Sludge was measured at 100 mg/L suspended solids for the treatment and control, but at 30 mg/L for the positive control. The notified chemical was observed not to be dissolved in both the water and sludge treatments at the start of the experiment and in the water treatment at termination.

RESULTS

Test substance		*Sodium benzoate positive control*	
Day	*% degradation*	*Day*	*% degradation*
7	15.3	7	69
14	85.7	14	75
21	77.0	No other data reported.	
28	84.7		
28	100*		

*Measured by GC, all other values measured by BOD

Remarks - Results — The notified chemical was biodegraded by 15% at 7 days and by 86% by 14 days. The two analytical methods determined the percentage biodegradation after 28 days to be 85 - 100%. Therefore the notified chemical was considered inherently biodegradable according to this test method. The positive control confirmed the validity of the test.

CONCLUSION — The notified chemical was considered ultimately biodegradable under the conditions of this test as > 70% degradation occurred.

TEST FACILITY — Kurume Laboratory (2000)

8.1.5. Bioaccumulation

Although the notified chemical has a relatively high log Pow and may potentially bioaccumulate, it is also readily biodegradable which should limit any bioaccumulation.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE — Notified chemical.

METHOD — OECD TG 203 Fish, Acute Toxicity Test – semistatic conditions.

Species	Rainbow trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours.
Auxiliary Solvent	Tween 80/dimethylformamide
Water Hardness	100 mg $CaCO_3$/L
Analytical Monitoring	HPLC with external standard.
Remarks – Method	Following a preliminary range finding study, juvenile fish were exposed in groups of 10 (not replicated) to an aqueous dispersion of the test material at concentrations of 0.18 - 1.8 mg/L. Conditions during the exposure were 16 hours light photoperiod, 14°C, pH 7.3 - 7.4 and 7.8 - 10.1 mg/L dissolved oxygen. Test solutions were renewed daily and covered and sealed to reduce potential evaporation with no indication of undissolved test material. At the end of the exposure, fish had mean lengths of 4.5 cm and weights of 1.32 g.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0.18	0.181 - 0.0824	10	0	0	0	0	0
0.32	0.283 - 0.180	10	0	0	0	1	1
0.56	0.524 - 0.479	10	0	1	5	6	8
1.0	0.878 - 0.621	10	1	5	7	10	10
1.8	1.74 - 1.09	10	2	10	10	10	10

LC50 (mean measured)	0.53 (0.42, 0.69) mg/L at 24 h 0.36 (0.27, 0.49) mg/L at 48 h 0.24 (0.19, 0.31) mg/L at 72 h 0.22 (0.17, 0.27) mg/L at 96 h
NOEC	0.078 mg/L at 96 h
Remarks – Results	The concentration of notified chemical declined markedly after 24 hours, presumably due to adsorption to glassware. Therefore, the 96-hour LC50 was calculated based on mean measured concentrations over the 24-hour period before renewal of test solutions. However, based on the sublethal adverse effects of coughing, swimming at the surface, loss of equilibrium and moribundity, the mean measured concentrations of 0.078, 0.16 and 0.33 mg/L caused 0, 60 and 100% effect, respectively, indicating the 96-hour EC50 is likely between 0.078 and 0.16 mg/L.

CONCLUSION — The 96-hour LC50 was 0.22 (0.17, 0.27) mg/L at 96 hours, which is considered very toxic to aquatic life (United Nations 2003).

TEST FACILITY — SafePharm Laboratories (1995d)

8.2.2. Chronic toxicity to fish, early life stage

TEST SUBSTANCE — Notified chemical.

METHOD — OECD TG 210 Fish, Early-Life Stage Toxicity Test.

Species	Fathead minnow *(Pimephales promelas)*
Exposure Period	33 days.
Auxiliary Solvent	Tetrahydrofuran.
Water Hardness	132 - 142 mg $CaCO_3$/L
Analytical Monitoring	GLC with external standard.
Remarks – Method	Following a preliminary range finding test, newly laid eggs were exposed to the test material at nominal concentrations of 0.0020, 0.0063, 0.020, 0.063 and 0.20 mg/L for 33 days at 20.5 - 26.7°C and 16 hours light photoperiod under flowthrough conditions. Serial stock dilutions of test material in solvent were pumped into mixing chambers with diluent so that each replicate received individual exposure solutions. Each

	treatment contained two replicates of 30 eggs each. The range of pH and dissolved oxygen measurements was not reported but were recorded daily. No indication was given if any undissolved test material was present in the solutions. The number of mortalities or any sub-lethal effects of exposure in each test and control vessel were recorded daily until termination at 28 day post-hatch. The length and dry weight of the surviving fish were measured at termination. Observations of mortality and immobility were made daily.
RESULTS	
33-day NOEC	0.98 µg/L (based on growth)
33-day LOEC	2.65 µg/L (based on growth)
Remarks – Results	The NOEC and LOEC of 0.98 and 2.65 µg/L were based on mean measured concentrations and adverse effects on mean body length and weight relative to the solvent control. The mean fish length in the solvent control and 2.65 µg/L treatment were 20.9 and 19.4 mm with mean weights of 32.3 and 24.9 mg, respectively. In addition, 15% of larvae (eight out of 52) in the highest mean measured concentration of 31.6 µg/L had bent spines indicating potential teratogenesis. All larvae in this treatment were paler in colour than controls.
CONCLUSION	The 33-day NOEC and LOEC of 0.98 and 2.65 µg/L, respectively, indicate that the notified chemical is highly toxic to fish.
TEST FACILITY	SafePharm Laboratories (2003b)

8.2.3. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – static conditions.
Species	*Daphnia magna*
Exposure Period	48 hours.
Auxiliary Solvent	Tween 80/dimethylformamide
Water Hardness	270 mg $CaCO_3$/L
Analytical Monitoring	HPLC with external standard
Remarks - Method	First instar daphnids were exposed at 21°C, 16 hour light photoperiod, pH 7.4 - 7.7 and 7.9 - 8.5 mg/L dissolved oxygen under static conditions. The test material was dissolved in 10% Tween 80/dimethylformamide and the volume adjusted to 10 mL to give a 1.0 g/10 mL solvent stock solution. An aliquot (500 µL) of this stock solution was dispersed in reconstituted water and the volume adjusted to 5 L to give the 10 mg/L test concentration from which dilutions were made to give the test series. Test vessels were sealed to reduce evaporation and possible loss of the moderately volatile material. No indication was given if any undissolved test material was present in the solutions. Analytical measurements of nominal concentrations found a slight decrease after 48 hours with concentrations of 89 - 124% of nominal throughout the exposure.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*	*(two replicates of 10 daphnids)*	*24 h*	*48 h*
0.10	0.109-0.0951	20	0	0
0.18	Not reported	20	0	0
0.32	0.320-0.306	20	0	7
0.56	Not reported	20	0	16
1.0	1.07-0.949	20	5	20
1.8	Not reported	20	14	20
3.2	3.66-2.86	20	20	20

5.6	Not reported	20	20	20
10	12.4-8.91	20	20	20

EC50 1.4 (1.2, 1.6) mg/L at 24 hours
0.39 (0.33, 0.46) mg/L at 48 hours

NOEC 0.18 mg/L at 48 hours.

Remarks - Results The EC50 was calculated based on mean measured concentrations and the endpoint of immobilisation (inability to swim for about 15 seconds after gentle agitation). No other adverse behavioural observations were made.

CONCLUSION The 48-hour EC50 was 0.39 (0.33, 0.46) mg/L which is considered very toxic to aquatic life (United Nations 2003).

TEST FACILITY SafePharm Laboratories (1995e)

8.2.4. Chronic toxicity to aquatic invertebrates, reproduction test

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 211 *Daphnia magna* Reproduction Test.

Species *Daphnia magna*

Exposure Period 21 days.

Auxiliary Solvent None.

Water Hardness 243 - 283 mg $CaCO_3$/L

Analytical Monitoring GLC with external standard.

Remarks - Method First instar (≤ 24 hours old) *Daphnia magna* were individually exposed to mean measured concentrations of 0.0011 - 0.13 µg/L in beakers replicated 10 times per treatment. Saturated test solutions were made up and passed through a 0.2 µm filter preconditioned with 5 L of solution which was then discarded. This ensured an absence of undissolved material. Daphnids were fed daily and incubated for 21 days at 21°C, pH 7.8 - 8.1, dissolved oxygen 7.5 - 8.5 mg/L and 16 hours light photoperiod in test solutions that were renewed three times per week. Test vessels were covered with a plastic lid to reduce evaporation. The numbers of live and dead adult and young were determined daily.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number of survivors*	*Total number*
Nominal	*Actual*		*at 21 d*	*of live young*
Control		10	10	992
0.0040	0.0011	10	10	1025
0.013	0.0031	10	10	1035
0.040	0.011	10	10	1021
0.13	0.045	10	0	0
0.40	0.13	10	0	0

NOEC 0.011 mg/L (based on immobilisation and mortality)

LOEC 0.045 mg/L (based on immobilisation and mortality)

Remarks - Results Chemical analysis of the freshly prepared test solutions on days 0, 2, 5, 7, 9, 12, 14, 16 and 19 showed measured concentrations were 0.0040 - 0.374 mg/L (46 - 119% of nominal). Old solutions being replaced contained ≤ 15% of nominal indicating either volatilisation or adsorption of the chemical.

Complete mortality occurred in the two highest treatments by day 8 with

	animals being markedly smaller and paler than controls prior to death. The NOEC and LOEC values were 0.011 and 0.045 mg/L, respectively, based on mean measured concentrations and mortality . The 21-day EC50 for parental daphnids was 0.022 (0.011, 0.045) mg/L based on mean measured test concentrations and immobilisation.
CONCLUSION	The 21-day NOEC and LOEC were 0.011 and 0.045 mg/L, respectively, which is considered highly toxic to aquatic invertebrates.
TEST FACILITY	SafePharm Laboratories (2003c)

8.2.5. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Scenedesmus subspicatus*
Exposure Period	72 hours.
Concentration Range	
Nominal	30 mg/L limit test
Actual	30.9 mg/L
Auxiliary Solvent	Tween 80/dimethylformamide.
Water Hardness	Not reported.
Analytical Monitoring	HPLC with external standard.
Remarks - Method	Although the water solubility of the notified chemical is 0.899 mg/L, a limit test was performed at a mean measured concentration of 30.9 mg/L with the aid of a solvent. Six replicate flasks were made up for the treatment with three flasks each for the control and solvent control. All flasks were shaken at 24°C under constant light at an initial cell density of 10^4 cells/mL and pH 8.0 - 10.2.

RESULTS

Biomass		*Growth*	
72-h E_bC50 > 30.9 mg/L	NOEC ≥ 30.9 mg/L	E_rC50 > 30.9 mg/L at 72 h	NOEC ≥ 30.9 mg/L

Remarks - Results	No adverse effects on biomass or growth rate were found during the exposure. There were also no abnormalities in cultures inspected microscopically at 72 hours.
CONCLUSION	Up to the limit of solubility of the notified chemical in this test of 30.9 mg/L, there were no adverse effects on the growth or biomass of the alga after 72 hours.
TEST FACILITY	SafePharm Laboratories (1995f)

8.2.6. Soil microorganisms: nitrogen transformation test

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 216 Soil microorganisms: nitrogen transformation test. EPPO (1994) Decision making scheme for the environmental risk assessment of plant protection products, Chapter 7: soil microflora. SETAC Europe (1995) Procedures for assessing the environmental fate and ecotoxicity of pesticides.
Inoculum	Mixed population of soil microorganisms sampled from a UK farm. No crop protection products had been used on the site for about 3 years and no organic fertiliser applied for about 5 years.
Exposure Period	28 days.
Nominal Concentration	1000 mg/kg soil dry weight limit test.

Remarks – Method	Following a preliminary range-finding test (conducted at concentrations of 1.0, 10, 100 and 1000 mg/kg soil), the test material in acetone was added to quartz sand, allowed to dry and mixed with 1.0 kg soil and 5 g powdered lucerne/green grass meal to act as a respiratory substrate. After adjusting to 40% of the water holding capacity, individual treatment (at 1000 mg/kg soil as a limit test), control and solvent control replicates were incubated at 21°C in the dark. Water was added regularly to maintain soil moisture and samples were taken at 0, 6 and 28 days for nitrate analysis.

RESULTS

NOEC	1000 mg/kg soil dw
Remarks – Results	There were no statistically significant differences between the solvent control and treatment groups, therefore the 28-day NOEC was 1000 mg/kg soil dw.

CONCLUSION	The 28-day NOEC was 1000 mg/kg soil dw in this limit test.
TEST FACILITY	SafePharm Laboratories (2002)

8.2.7. Seedling emergence and growth, acute toxicity

TEST SUBSTANCE	Notified chemical (90.6% purity).
METHOD	OECD TG 208 A (draft), Seedling Emergence and Seedling Growth Test
Species	Oat *(Avena sativa)*, Soybean *(Glycine max)*, Tomato *(Lycopersicon esculentum).*
Exposure Period	≤ 28 days.
Nominal treatment rate	Oat, soybean and tomato: 12, 37, 110, 330 and 1000 mg/kg soil.
Remarks - Method	Ten replicate pots for each species containing 1.2 kg of sandy loam soil (1.3% OC, pH not stated) were treated by topically applying 100 mL of the appropriate solution for test treatments, solvent controls (1% acetone solution) and controls (deionised water). Soils were not mixed to evenly distribute the chemical. For each pot, four seeds were planted at approximately 1 cm in each pot (40 seeds per treatment). Each pot was placed in a saucer and about 100 mL of nutrient solution was added to each saucer with replenishment as needed. Pots were incubated in a greenhouse at 15 - 35°C and 31 - 99% relative humidity with a 16 hours light photoperiod. Oat pots were observed on days 4, 11, 18 and 25 (test termination), soybean pots on days 5, 12, 19 and 26 (test termination), while tomato pots were observed on days 7, 14, 21 and 28 (test termination) to determine percent emergence, mortality and the morphological abnormalities (eg chlorosis of leaves) of the emerged shoots. At termination, the dry weights of shoots were determined.

RESULTS

Species	*EC25 (mg/kg soil)*	*EC50 (mg/kg soil)*	*NOEC (mg/kg soil)*	*LOEC (mg/kg soil)*
Oat	180 (sw)	>1000 (e, sw)	<12 (sw)	12
Soybean	>1000 (e, sw)	>1000 (e, sw)	1000 (e, sw)	>1000
Tomato	>1000 (e, sw)	>1000 (e, sw)	1000 (e, sw)	>1000

(as whole product) (e = percent emergence, sw = shoot weight)

NOEC	≤ 12 mg/kg soil
LOEC	12 mg/kg soil
Remarks - Results	The rating of morphological abnormalities and overall plant effect appeared to be subjective with no scale given for assessment. For oats, control mortality was < 8%. The authors discounted the statistically

significant 25 - 26% inhibition of emergence at 12 and 37 mg/kg soil because the next highest treatment of 110 mg/kg soil was not different from controls. Given that the two next highest treatments of 330 and 1000 mg/kg soil showed significantly higher inhibition of 37 and 41%, respectively, the non-significance of 110 mg/kg soil was considered questionable (rather than the significance of 12 and 37 mg/kg soil) and that the NOEC and LOEC values should be < 12 and 12 mg/kg soil, respectively.

Control mortality was relatively high in soybeans at 28 - 42% (with only 60 - 78% emergence) but was somewhat lower in tomato seedlings at 27%. However, OECD TG 208 stipulates that a maximum of 20% control mortality constitutes a valid test, compared to 35% in the draft method cited which is still the subject of discussion in the OECD Test Guidelines Program. Therefore the results for soybeans and tomatoes should be treated with caution. In each of the two highest treatments of 330 and 1,000 mg/kg soil, one replicate showed none of the four seeds emerged which was discounted from analysis by the author. However, given that other replicates in these treatments showed only one of four seeds emerged, these replicates should be regarded as valid. Therefore the mortality of 42% in these two treatments was similar to that of the controls.

CONCLUSION — The NOEC and LOEC for oats were < 12 and 12 mg/kg soil, respectively.

TEST FACILITY — Springborn Laboratories (2002)

8.2.8. Acute toxicity to earthworms

TEST SUBSTANCE — Notified chemical.

METHOD — OECD TG 207 Earthworm, acute toxicity test

Remarks - Method — Following a preliminary range-finding test (conducted at concentrations of 10, 100 and 1000 mg/kg soil), the earthworm *Eisenia foetida* was exposed for 14 d in groups of 40 (four replicates of 10 worms each) to concentrations of 100, 180, 320, 560 and 1000 mg/kg artificial soil. Worms were incubated for 14 days at 21°C, pH 5.6 - 6.0, continuous light and 26 - 30% soil moisture. Mortalities were determined after 7 and 14 days. A positive control using chloroacetamide, conducted approximately every 6 months, was reported for reference purposes.

RESULTS

Remarks - Results — Mortalities of 0, 95 and 100% were observed at the nominal concentrations of 180, 320 and 560 mg/kg soil indicating the 14-day LC50 was likely between 180 and 320 mg/kg soil. No sublethal effects were observed, including on body weights, aside from delayed time to burrow in treatments ≥ 320 mg/kg soil. The NOEC and LOEC were considered to be 180 and 320 mg/kg soil, respectively. The 14-day LC50 for the positive control was 23 (20, 25) mg/kg soil, confirming the validity of the test.

CONCLUSION — The 14-day NOEC and LOEC were 180 and 320 mg/kg soil, respectively.

TEST FACILITY — SafePharm Laboratories (2001c)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Nearly all of the imported notified chemical will eventually be released into the aquatic environment via the sewerage systems through formulation and use (washing off the skin, hair etc or cleaning activities) of the cosmetic and household products. Less than 100 g/y is expected to be disposed of to landfill as residue in empty containers via domestic garbage.

Based on maximum annual imports of 150 kg/y, and assuming a worst-case scenario that all of this is eventually released to sewers on a nationwide basis, the daily release to sewers is estimated to be 0.41 kg/d. Assuming a national population of 20 million with each person contributing an average 200 L/day to overall sewage flows and that the chemical is not removed during sewage treatment processes, the worst-case predicted environmental concentrations (PECs) in sewage effluent, ocean and inland river on a nationwide basis are estimated as follows:

Amount of notified chemical entering sewer annually	150 kg
Population of Australia	20 million
Amount of water used per person per day	200 L
Number of days of release in a year	365
Amount partitioned to water (based on solubility)	100%
$PEC_{aquatic}$ (sewage effluent)	0.10 µg/L
$PEC_{aquatic}$ (river)	0.10 µg/L
$PEC_{aquatic}$ (ocean)	0.01 µg/L

The worst-case PEC in sewage effluent on a nationwide basis is estimated as 0.10 µg/L (DEH 2003). Based on the respective dilution factors of 0 and 10 for inland and ocean discharges of effluents, the PECs of the notified chemical in freshwater and marine water may approximate 0.10 and 0.01 µg/L, respectively.

Another worst-case scenario is considered assuming that products containing the notified chemical would only be used in a major metropolitan centre such as Sydney (with a population of 4.1 million) and the PECs for release to ocean and inland river are estimated to be 0.05 and 0.50 µg/L, respectively.

The notified chemical was considered readily biodegradable in one of three tests and was inherently biodegradable in another test. Using the SIMPLETREAT model (European Commission 2003) for modelling partitioning and losses in sewage treatment plants (STP) with an approximate log H of -2 and log Pow of 5, the amounts of chemical partitioning to sludge/biosolids and water are 56% and 28%, respectively, with 17% biodegraded (inherently biodegradable) and 47%, 8% and 45% if readily biodegradable.

Based on the partitioning if readily biodegradable, the revised worst-case PECs for freshwater and marine water from the nationwide release of the notified chemical into the sewage systems are 8 and 0.8 ng/L, respectively. On the metropolitan scale of Sydney, the PECs are 40 and 4 ng/L, respectively.

Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 0.5 mg/kg dry weight. Biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/y. Assuming a soil bulk density of 1,000 kg/m^3 and a soil-mixing zone of 0.1 m, the PEC of the notified chemical is 0.005 mg/kg in receiving soil. This assumes that degradation of the notified chemical occurs in the soil within 1 y from application.

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation rate is assumed to be 1,000 L/m^2/y (10 ML/ha/y). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 0.1 m of soil (density 1,000 kg/m^3). Using these assumptions, irrigation with a concentration of 0.01 µg/L is expected to give a soil PEC of 0.001 mg/kg soil.

Based on the ready/inherent biodegradability of the notified chemical, the relatively low volume imported and diffuse release to the sewer Australia wide, there is little expected potential for bioaccumulation.

9.1.2. Environment – effects assessment

The toxicity of the notified chemical to various organisms is summarised in the following table.

Organism	*Duration*	*Endpoint*	*Value (95% confidence limits)*
Rainbow trout (*Oncorhynchus mykiss*)	96 h	EC50 (coughing, swimming at the surface, loss of equilibrium, moribundity)	Between 0.078 and 0.16 mg/L
Fathead minnow (*Pimephales promelas*)	33 d	NOEC	0.98 µg/L
		LOEC	2.65 µg/L
		(based on mean body length and weight)	
Waterflea (*Daphnia magna*)	48 h	EC50	0.39 (0.33, 0.46) mg/L
	21 d	NOEC, LOEC	0.011, 0.045 mg/L
		(based on mortality and fecundity)	
Alga (*Scenedes-mus subspicatus*)	72 h	E_bC50	>30.9 mg/L
		E_rC50	>30.9 mg/L
Soil microorganisms	28 d	NOEC	1,000 mg/kg soil dw
Oat (*Avena sativa*)	≤28 d	NOEC	<12 mg/kg soil
		LOEC	12 mg/kg soil
		(based on inhibition of emergence)	
Earthworm (*Eisenia foetida*)	14 d	NOEC	180 mg/kg soil
		LOEC	320 mg/kg soil
		(based on mortality)	

An aquatic predicted no effect concentration (PNEC) of 0.098 µg/L was calculated by dividing the most sensitive endpoint of 0.98 µg/L (33-d NOEC for fathead minnows) by an assessment (safety) factor of 10 as chronic toxicity data were available for three species of three trophic levels – fish, invertebrates and algae (OECD 2003). For the terrestrial environment, the most sensitive endpoint of <12 mg/kg soil for oats divided by an uncertainty factor of 50 (chronic data available for two species of two trophic levels) gave a terrestrial PNEC of <0.24 mg/kg soil.

9.1.3. Environment – risk characterisation

Location	PEC (µg/L)	PNEC (µg/L)	Risk Quotient (Q)
Australia-wide STPs – no mitigation			
Ocean outfall	0.01	0.098	0.1
Inland River	0.10	0.098	1
Major metropolitan centre (eg. Sydney) – no mitigation			
Ocean outfall	0.05	0.098	0.5
Inland River	0.50	0.098	5
Australia-wide STPs – with mitigation*			
Ocean outfall	0.0007	0.098	0.007
Inland River	0.007	0.098	0.07
Major metropolitan centre (eg. Sydney) – with mitigation*			
Ocean outfall	0.004	0.098	0.04
Inland River	0.04	0.098	0.4

*PEC and Q values calculated assuming 47% of the notified chemical partitioned into biosolids, 1% to air, 44% biodegraded and 7% partitioned to water during the STP process based on the SIMPLETREAT model.

The worst-case risk quotients (Q = PEC/PNEC) with no mitigation for the freshwater environment if the notified chemical is used nation wide and in a major metropolitan centre such as Sydney are 1 and 5, respectively. The respective Q values for ocean are 0.1 and 0.5. Values greater than 1 indicate immediate concern to the aquatic compartment.

The biodegradability of the notified chemical will reduce the PEC in sewage effluent while the high log Pow indicates significant partitioning to soil/sediments and sewage sludge which will further reduce the PECs and the Q values. In the Sydney metropolitan area, these mitigation factors reduce the PECs for ocean and river to 0.004 and 0.04 µg/L with resultant Q values of 0.04 and 0.4, respectively. The risk for both rivers and the ocean is acceptable.

Given that the use pattern of the chemical indicates widespread and diffuse release, rather than within a single metropolitan base, the PECs and Q values will be lowered further. The PECs for ocean and river with nation-wide use, partitioning to sludge and biodegradation in the STP are 0.0007 and 0.007 µg/L, respectively. When divided by the PNEC of 0.098 µg/L, the Q values are 0.007 and 0.07, which indicate an acceptable risk. However, if import volumes rise to 1 tonne/y, the safety margins are significantly reduced to Q = PEC/PNEC = 0.0048/0.098 = 0.049 and0.048/0.098 = 0.49, respectively.

For the terrestrial environment, the worst case PEC of 0.005 mg/kg soil (from biosolid application to agricultural soils nationwide) and the PNEC of <0.24 mg/kg soil would give a Q value of 0.02, which is indicative of low risk. At an import volume of 1 tonne/y, the Q value is 0.03/0.24 = 0.12 which is of low risk but of a much smaller safety margin. Given the concerns with the terrestrial plant ecotoxicity test, a secondary notification and a better test which clearly defined the NOEC and LOEC should be required if the import volume reaches this level.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Occupational exposure to the notified chemical may occur during transport and storage of fragrance preparations containing the notified chemical at up to 2%. During reformulation of the fragrance preparations containing the notified chemical into cosmetics and domestic cleaning products, dermal exposure is the most likely route. Ocular exposure may occur due to accidental splashes. Exposure may occur when workers open the drums containing imported notified chemical at up to 2%, when weighing and transferring the imported fragrance preparations into mixing vessels, during blending operations and when cleaning up spills and equipment. Blending operations can be in open or closed systems, however, the process is often automated and local exhaust ventilation is usually employed. All workers handling perfume preparations containing the notified chemical and involved in open mixing operations may wear suitable gloves, eye and face protection and protective clothing to minimise exposure.

9.2.2. Public health – exposure assessment

It is expected that during import, transport, storage and reformulation of fragrance compositions containing the notified chemical, exposure of the public will be limited, except in the event of an accidental spill.

Consumer products containing the notified chemical (cosmetics, toiletries, household cleaning products) will be sold in the public domain, consequently there is the potential for widespread public exposure. Exposure will be principally via the dermal route. Exposure to the notified chemical is considered minimal given its concentration in the final consumer products (maximum 0.4%).

9.2.3. Human health - effects assessment

The notified chemical was of low acute oral and dermal toxicity in rats. It was a slight skin and eye irritant in rabbits. It was a skin sensitiser in guinea pigs in one of three tests but not in humans at 10% and 20%. It was not mutagenic in bacteria or clastogenic to human lymphocytes and was not mutagenic in a mouse lymphoma assay. In a 4-week repeat dose oral toxicity study

in rats, the NOEL was established to be 250 mg/kg/day bw. In an oral gavage one generation reproduction study in rats the NOEL for reproduction and offspring viability development was 1000 mg/kg bw.

9.2.4. Occupational health and safety – risk characterisation

Although the notified chemical has the potential to cause skin sensitisation in guinea pigs, this is unlikely to occur in humans at doses below 20% and is correspondingly less probable at the maximum concentration to be imported, ie 2%. Similarly, the slight skin and eye irritant potential of the notified chemical is unlikely to be elicited at 2%. Given the low likely occupational exposure (the imported fragrance preparations may be sensitising due to the content of components other than the notified chemical and, therefore, necessitate the use of impervious gloves, goggles and protective clothing) from mostly automated processes, the risk of skin or eye irritation or skin sensitisation is low. Inhalation exposure is controlled by local exhaust ventilation and the risk of respiratory irritation or sensitisation is low. The likely low exposure together with the results of the remaining toxicological studies suggests a low risk of acute or chronic toxic effects, genotoxic effects or reproductive effects.

9.2.5. Public health – risk characterisation

The maximum concentration to which the public can be exposed is 0.4% in perfumes. This is unlikely to elicit skin or eye irritation or skin sensitisation after repeated or prolonged exposure from the notified chemical content. The margin of safety should be greater than 100 for the notified chemical to be considered safe and can be calculated as:

NOEL/Systemic Exposure Dosage:

250 mg/kg/day/ ((0.75 g/day x 1000 mg/g x 0.4/100)/ 60 kg) =

250/750 x 0.4/6000 = 250/300/6000 = 250/1/20 = 5000

This assumes 100% absorption and 0.75 g applied once per day with no removal.

It can be concluded that there is negligible public health risk from repeated dose or reproductive effects.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2002). The classification and labelling details are:

R43: May cause sensitisation by skin contact

As a comparison only, the classification of notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

Category 2: Sensitiser

The environmental hazard classification is:

Acute hazard category 1: Very toxic to aquatic life; and

Chronic hazard category 1: Very toxic to aquatic life with long lasting effects.

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio, the chemical is not considered to pose a risk to the environment based on its reported use pattern.

However, this assessment is based on the maximum annual use of 150 kg/year. If this amount increases significantly, the chemical may pose a risk to the environment based on the notified use pattern. Further work or actions, such as additional testing in the area of concern (chronic effects on fish and terrestrial phytoxicity), detailed exposure analysis, in-depth risk assessment or further risk management actions may be necessary if import levels are predicted to rise above 1 tonne/year.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is Negligible Concern to public health when used as described.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical and products containing the notified chemical provided by the notifier were in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 2003). They are published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for the notified chemical and products containing the notified chemical provided by the notifier were in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS
Hazard Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:
  - R43: May cause sensitisation by skin contact

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - > 1%: R43: May cause sensitisation by skin contact

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced:
  - Local exhaust ventilation should be provided at points of likely release during product formulation.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - To preclude contact with hazardous components of the imported formulations containing the notified chemical, natural rubber gloves, safety goggles and

protective clothing. Respiratory protection should be provided where general ventilation is inadequate.

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 are classified as hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Environment

Disposal

- The notified chemical should be disposed of to landfill and not discharged to drains, soil or the aquatic environment.

Storage

- The following precautions should be taken regarding storage of the notified chemical:
  - Store in closed, preferably full, containers away from heat sources and protected from extremes of temperature. Do not reuse the empty container.

Emergency procedures

- Spills/release of the notified chemical should be cleaned up by using any absorbent which should be disposed of promptly, preferably by incineration as some cases of spontaneous combustion of rags soaked with similar materials have been reported.
- Gross spillages should be contained by the use of sand or inert powder, and disposal should be to landfill in accordance with government regulations.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment 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 of the notified chemical is predicted to exceed that notified.

or

(2) Under Section 64(2) of the Act:
  - if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required. If a significant increase in import volume is notified, the Director may require data on the chronic effects on fish and further data on terrestrial phytotoxicity at this time.

13. BIBLIOGRAPHY

Celsis Laboratories Group (1999) Delayed Contact Hypersensitivity - Modified Buehler Method, Project Number 830171, Celsis Laboratories Group, New Jersey, USA (unpublished report submitted by notifier).

DEH (Australian Government Department of the Environment and Heritage) (2003) Model and Guidance for Estimating Predicted Environmental Concentrations to Surface Water and Soil from Chemicals Released to the Environment Through a Sewage Treatment Plant. Chemical Assessment Section, Canberra, Australia.

European Commission (2003) Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances - Parts II and III.

Kurume Laboratory, Chemical Evaluation and Research Institute (2000) Biodegradation Test of Muscenone 962191 by Microorganisms. Project Number 13609, Kurume Laboratory, Chemical Evaluation and Research Institute, Japan (unpublished report submitted by 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 (2002) Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2002)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

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

Product Safety Labs (2000) ST 19 C 99 Dermal Sensitization Test - Magnusson-Kligman Method (OECD 406), Project Number 8809, Products Safety Labs, New Jersey, USA (unpublished report submitted by notifier).

Quintiles England Limited (1996) ST 04 C 91 - 4 Week Oral (Gavage) Toxicity Study in the Rat Followed By a 2 Week Treatment-Free Period , Project Number FCH/13/96, Quintiles England Limited, Ledbury, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1994) ST 04 C 91 Determination of Partition Coefficient, Project Number 161/011, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1995a) ST 04 C 91 Determination of General Physico-Chemical Properties, Project Number 161/052, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1995b) ST 04 C 91 Determination of Vapour Pressure, Project Number 161/054, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1995c) ST 04 C 91 Chromosome Aberration Test in Human Lymphocytes In Vitro, Project Number 161/055, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1995d) ST 04 C 91 Acute Toxicity to Rainbow trout *(Oncorhynchus mykiss)*, Project Number 161/056, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1995e) ST 04 C 91 Acute Toxicity to *Daphnia magna*, Project Number 161/057, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1995f) ST 04 C 91 Algal Inhibition Test, Project Number 161/058, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1995g) ST 04 C 91 Assessment of Ready Biodegradation, Closed bottle test, Project Number 161/059, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1996a) ST 04 C 91 Determination of Hazardous Physico-Chemical Properties, Project Number 161/053, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (1996b) ST 04 C 91 Assessment of Ready Biodegradation, Manometric Respirometry Test, Project Number 161/073, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (2001a) ST 45 C 00 Determination of Water Solubility, Project Number 161/279, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (2001b) ST 16 C 01 L5178Y TK +/- Mouse Lymphoma Assay, Project Number 161/313, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (2001c) ST 16 C 01 Acute Toxicity to Earthworms *(Eisenia foetida)*, Project Number 161/311, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (2002) ST 16 C 01 Soil Microorganisms : Nitrogen Transformation Test, Project Number 161/312, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (2003a) ST 16 C 01 Oral Gavage One Generation Reproduction Study in the Rat, Project Number 161/314, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (2003b) ST 16 C 01 Fish, Early-Life Stage Toxicity Test, Project Number 161/309, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories (2003c) ST 16 C 01 *Daphnia magna* Reproduction Test, Project Number 161/310, Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Springborn Laboratories, Inc. (2002) ST 16 C 01 - Determination of Effects on Seedling Emergence and Seedling Growth of Three Plant Species, Project Number 13768.6101, Springborn Laboratories, Inc., Massachusetts, USA (unpublished report submitted by notifier).

TKL Research, Inc. (1995) Repeated Insult Patch Study, Project Number 951005, TKL Research Inc, New Jersey, USA (unpublished report submitted by notifier).

TKL Research, Inc. (1999) Repeated Insult Patch Study, Project Number 991018, TKL Research Inc, New Jersey, USA (unpublished report submitted by notifier).

Toxicol Laboratories (1991a) ST 04 C 91 Acute Dermal Toxicity Study, Project Number A/D/31639, Toxicol Laboratories Limited, Ledbury, UK (unpublished report submitted by notifier).

Toxicol Laboratories (1991b) Bacterial Reverse Mutation Assay - ST 04 C 91, Project Number M/Ames/31640, Toxicol Laboratories Limited, Ledbury, UK (unpublished report submitted by notifier).

Toxicol Laboratories (1992a) Determination of Physico-Chemical Parameters (EEC Annex V) on ST 04 C 91, Project Number N/M/32662, 32650, Toxicol Laboratories Limited, Ledbury, UK (unpublished report submitted by notifier).

Toxicol Laboratories (1992b) ST 04 C 91 Acute Oral Toxicity Study, Project Number A/O/31638, Toxicol Laboratories Limited, Ledbury, UK (unpublished report submitted by notifier).

Toxicol Laboratories (1992c) ST 04 C 91 Acute Dermal Irritation/Corrosion Study, Project Number A/S/31635, Toxicol Laboratories Limited, Ledbury, UK (unpublished report submitted by notifier).

Toxicol Laboratories (1992d) ST 04 C 91 Acute Eye Irritation Study, Project Number A/E/31636, Toxicol Laboratories Limited, Ledbury, UK (unpublished report submitted by notifier).

Toxicol Laboratories (1992e) ST 04 C 91 Guinea Pig Maximisation Test, Project Number A/M/31637, Toxicol Laboratories Limited, Ledbury, UK (unpublished report submitted by notifier).

United Nations (2003) Globally Harmonised System of Classification and Labelling of Chemicals (GHS). United Nations Economic Commission for Europe (UN/ECE), New York and Geneva.

Wildlife International, Ltd. (2000) ST 19 C 99 Ready Biodegradability by the Carbon Dioxide Evolution Test Method, Project Number 498E-104, Wildlife International, Ltd., Maryland, USA (unpublished report submitted by notifier).