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May 2002

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

1-methyl-3-(2-methylpropyl)cyclohexan-1-ol

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Chemicals Notification and Assessment

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1. APPLICANT

Quest International Australia Pty Ltd (ACN 078 584 184) of 6 Britton St SMITHFIELD NSW 2164 has submitted a standard notification statement in support of their application for an assessment certificate and has not applied for any information relating to 1-methyl-3-(2-methylpropyl)cyclohexan-1-ol to be exempt from publication in the Full Public Report and Summary Report.

2. IDENTITY OF THE CHEMICAL

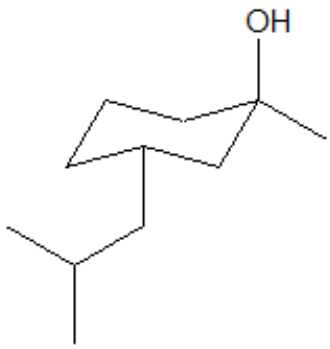
Chemical Name: 1-methyl-3-(2-methylpropyl)cyclohexan-1-ol.

Chemical Abstracts Service (CAS) Registry No.: 215231-33-7

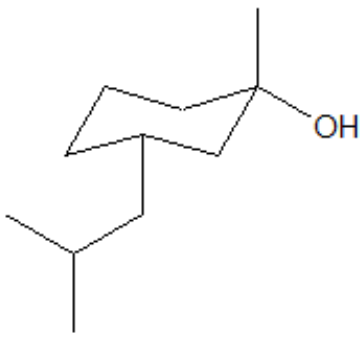
Marketing Name: Rossitol

Molecular Formula: C11H22O

Structural Formula:



trans (65%)



cis (35%)

Molecular Weight:	170
Method of Detection and Determination:	Nuclear Magnetic Resonance (NMR), ultraviolet (UV) and Mass (MS) spectroscopy, the latter coupling with Gas-Liquid Chromatography (GLC).
Spectral Data:	NMR, UV, IR and GLC-MS spectra were provided.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Clear colourless liquid.
Freezing Point:	- 94°C
Boiling Point:	204-214°C
Relative Density:	0.888 at 20.5°C
Vapour Pressure:	0.1 kPa at 20°C
Water Solubility:	189 mg/L at 20°C
Surface Tension:	48.4 mN/m
Partition Co-efficient (n-octanol/water):	log P_{ow} = 3.9
Hydrolysis as a Function of pH:	No data provided, however the chemical is not expected to readily hydrolyse as no hydrolysable groups are present.
Adsorption/Desorption:	log K_{oc} = 2.34
Dissociation Constant:	Not determined, however the chemical is not expected to dissociate in water.
Flash Point:	94°C
Flammability Limits:	Not highly flammable.
Autoignition Temperature:	256°C
Explosive Properties:	Not explosive.
Reactivity/Stability:	Stable under normal conditions.

3.1 Comments on Physico-Chemical Properties

All tests were performed by TNO Prins Maurits Laboratory, Rijswijk, the Netherlands or TNO Nutrition and Food Research Institute, DELFT, the Netherlands.

The vapour pressure provided was determined using a vapour pressure balance and Method A4 of Commission Directive 92/69/EEC. Linear regression analysis was used to calculate vapour pressure at 20 and 25°C. The high value determined indicates that the notified chemical is classified as being highly volatile (Mensink 1995).

The water solubility was determined using the flask method detailed in Method A6 of Commission Directive 92/69/EEC. The notified chemical is classified as being moderately soluble (Mensink 1995).

The partition coefficient has was determined using the GC method detailed in Method A8 of Commission Directive 92/69/EEC. The moderate water solubility is consistent with the relatively high log P_{ow}, indicating a high affinity for the organic component of soils and sediments. This is confirmed by the moderate high log K_{oc} determined by the HPLC method detailed in the 1997 OECD draft guideline. As such, the notified chemical is likely to be moderately mobile in soil.

Although no dissociation tests were conducted, the notified chemical is unlikely to undergo dissociation in the environmental pH range of 4 to 9 as no acidic or basic groups are present.

The surface tension was determined using modified methodology from the Method A5 of Commission Directive 92/69/EEC. The concentration of solution of the test substance was 124 mg/L (90% of the saturated solution). The result indicated a surface tension of 48.4 mN/m indicating the notified substance may be considered to be surface active.

4. PURITY OF THE CHEMICAL

Degree of Purity:	Typically > 98%
Hazardous Impurities:	None
Non-hazardous Impurities (> 1% by weight):	None
Additives/Adjuvants:	None.

5. USE, VOLUME AND FORMULATION

The notified chemical will be used in personal and household products as an aroma chemical. It will be imported as a component of a fragrance compound at approximately 1% in 200 L steel kegs which are lacquer or polyethylene lined at a level of up to 1 tonne per year for the first five years. Personal and household products will generally contain 0.005% Rossitol with the exception of air fresheners which may contain up to 0.05% Rossitol.

6. OCCUPATIONAL EXPOSURE

Transport and storage of the steel kegs containing the fragrance compound incorporating the notified chemical should not result in exposure of transport and storage workers expect in the event of accidental rupture of the containers.

The notified chemical has a low vapour pressure and inhalation exposure during product formulation is unlikely particularly as aerosols should not be produced during mixing operations. The kegs containing the imported fragrance compound are unloaded into weighing vessels via a pump and drum spear and the contents added to closed or, occasionally, open mixing vessels. Exposure of the skin or eyes is possible during these processes and workers typically wear overalls, gloves and eye protection. Between 5 and 20 production workers can be exposed on 50 – 300 days per year, 1 hour per day.

Once in the mixing vessel the notified chemical is in an enclosed system and worker exposure is unlikely. This is also the case for dedicated lines used for containing filling. However, workers exposure to splashes and spills is possible during cleaning of lines and vessels and transfer equipment.

Worker exposure to the notified chemical in end use products is unlikely except in the event of accidental rupture of containers.

7. PUBLIC EXPOSURE

It is expected that public exposure to the notified chemical in blended fragrance mixtures containing ≤1% Rossitol will be minimal except in the rare event of an accidental spill.

Dermal, inhalation, oral and ocular exposure to the public will occur from personal and household products containing the notified chemical, most of which will contain 0.005%, but air-fresheners may contain up to 0.05%. The notified chemical is a severe skin and eye irritant. Air fresheners (containing up to 0.05%) are unlikely to pose an irritation hazard if used appropriately, and the irritation hazards posed by products containing 0.005% of the notified chemical are likely to be low.

The applicant supplied estimation of exposure for “leave-on”, “rinse-off”, and household products (all containing 0.005% Rossitol).

Ten gram of a “leave-on” product e.g. skin cream, applied once per day and assuming 100% absorption through the skin, would equate to an exposure of 8.3 microgram/kg/day for a 60 kg person.

Five gram of a “rinse-off” product e.g. soap, used once per day and assuming 10% is left on the skin and 100% is absorbed, would equate to an exposure of 0.42 microgram/kg/day for a 60 kg person.

Ten gram of a household product, used once per day, of which 1% is in contact with the skin and 100% is absorbed, would equate to an exposure of 0.083 microgram/kg/day for a 60 kg person.

The total of these 3 exposures is 8.8 microgram/kg/day.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

There is a possibility of spills during transport and use but the loss due to spillage is expected to be minimal.

The notifier has indicated that wastage of the compounded fragrance left as residue in the import containers would be less than 1% after emptying. It is likely that the containers would be rinsed and the rinseate added into the production or flushed down a drain (ie into the sewer). The cleaned containers would then be returned to the notifier. Release to the environment during reformulation and cleaning processes is expected to be low as closed, automated systems are used. The notifier anticipates approximately 1% or 10 kg of the notified chemical will be released in this fashion. Wastes from these processes will be disposed of either in landfill or into the sewer.

Approximately 1% of the contents will remain in the end-use container after it has been emptied. This represents 10 kg of Rossitol annually that would go into domestic rubbish and ultimately landfill.

Since Rossitol will be used in household, laundry and personal cleaning product approximately 97% (970 kg as a worst case) will eventually end up in the sewer. A small amount of the notified chemical will also be incorporated into air fresheners. The main release into air will result from the use of air fresheners and partitioning from water, based on the Simple Treat Model calculations conducted (see Section 8.2).

8.2 Fate

It is possible that up to 2% (20 kg) of the imported Rossitol would end up in landfill. Since the chemical has a moderate water solubility (182 mg/L) and is likely to be moderately mobile in soil (log K_{oc} = 2.34), it may leach but in a very dispersed manner.

The biodegradation of Rossitol was determined as described under the 'closed bottle test' in the OECD TG 301D for testing ready biodegradability using oxygen depletion as the test criterion in a 28-day test (TNO, 1999a). Biodegradation was determined using two nominal concentrations of 2.0 and 4.0 mg/L corresponding to a theoretical oxygen demand (ThOD) of 6.0 and 12.0 mg O_2/L respectively. Results indicated the reference substance sodium acetate reached the 60% pass level within 14 days. The maximum mean BOD value of 0.06 mg/L was found after 21 days. This value corresponds to a biodegradation of 2% based on the ThOD value. The highest value reached by the test subject was biodegradation of 6.2%. The study author concluded that given the test substance did not pass the level of 60% of the ThOD within 28 days it was considered as not readily biodegradable.

The notified chemical will eventually be released into the environment, and the majority could be expected to be discharged into sewerage systems and to air. For that proportion which reaches sewage treatment plants (ie is not volatilised or otherwise destroyed during passage to the plant), the proportions of the chemical which partition into the different

environmental compartments may be estimated using the Simple Treat Model (EEC, 1996). These estimates are based on a calculated Henry's constant of 1.94 Pa/m^3/mole based on the measured vapour pressure and water solubility, a log Pow of 3.9 and the chemical not being biodegradable. The chemical would be expected to partition into the air, water and sewer sludge compartments as 47%, 53% and 0%, respectively.

The notified chemical is relatively hydrophobic in nature with a log Pow of 3.9 and estimated log Koc of 2.34. This together with surface activity when released into the sewer system suggests some of the notified chemical may remain associated with the organic component of the particulate matter present in the raw sewage, and would eventually become incorporated into sediments. Here it would slowly degrade via biological and abiotic processes to water, carbon dioxide and methane. Hydrolysis in the sewer is not expected.

In the atmosphere it is likely that the notified chemical will degrade through reaction with hydroxyl radicals. An estimate of the half-life of the chemical in the atmosphere was calculated using the OECD Environmental Monographs No. 61. The calculation estimated that in the troposphere the new chemical would have a rate constant of 24 x 10^{-12} cm^3 $molecule^{-1}$ sec^{-1} leading to an estimated atmospheric half-life of 3.5 days.

Residual notified chemical disposed of to landfill with empty containers or with residual solids derived from water treatment at the production facilities is also expected to remain adsorbed to soil/sediment particles, and in this situation would be expected to be slowly destroyed by similar mechanisms to those operating in sediments. Incineration of the material would produce water vapour and oxides of carbon.

Although approximately half the chemical will remain in water compartment, its moderate water solubility indicate low potential for bioaccumulation (Connell, 1990).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Summary of Toxicological Investigations

Endpoint & Result	*Assessment Conclusion*
Rat, acute oral LD50 > 2000 mg/kg bw	very low toxicity
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rabbit, skin irritation	severely irritating
Rabbit, eye irritation	moderately to severely irritating
Guinea pig, skin sensitisation - adjuvant test	no evidence
Rat, oral route, Repeat Dose Toxicity - 28 Days	NOAEL, 15 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	Non mutagenic
Genotoxicity – in vitro chromosomal aberrations in CHO cells	Non genotoxic

9.2 Acute Toxicity

9.2.1 Acute Oral Toxicity (TNO, 1999b)

TEST SUBSTANCE	Rossitol QRM 2688
METHOD	OECD 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/Wistar
Vehicle	Maize oil

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3/sex	2000	*None*

LD50	> 2000 mg/kg bw
Signs of Toxicity	Sluggishness and ataxia in all animals at 4 hours post-dosing and ataxia in two females 1 hour after dosing.
Effects in Organs	None
Remarks - Results	All animals gained weight during the 14-day study period.

CONCLUSION	The notified chemical is of very low toxicity via the oral route.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.2.2 Acute Dermal Toxicity (TNO, 1999c)

TEST SUBSTANCE	Rossitol QRM 2688
METHOD	OECD 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rat/Wistar
Vehicle	Maize oil
Type of dressing	Occlusive.
Remarks - Method	24 hour treatment

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	2000	*None*

LD50	> 2000 mg/kg bw
Signs of Toxicity	None
Effects in Organs	None
Remarks - Results	Slight dip in body weight on day 3 of the study in most animals.

	Males showed very slight erythema on days 1 and 3, slight oedema on day 1 and very slight scaliness on day 3. Females showed very slight or slight erythema on days 1 and 3, slight oedema on day 1 and very slight or slight scaliness on day 3. No evidence of skin irritation was seen on day 14.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.2.3 Acute Inhalation Toxicity

Data not provided.

9.2.4 Skin Irritation (TNO, 1999d)

TEST SUBSTANCE	Rossitol QRM 2688
METHOD	OECD 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 males
Observation Period	14 days
Vehicle	None
Type of Dressing	Semi-occlusive.

RESULTS

[Use this table if 3 animals or less are used, otherwise delete]

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	4	4	4	4	7 days	0
Oedema	2	2	2	2	7 days	0

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

Remarks - Results	The following observations were made in addition to erythema/oedema: 24 hours, slight ischemic necrosis; 48 hours, slight incrustation; 72 hours, moderate incrustation.
CONCLUSION	The notified chemical is severely irritating to skin.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.2.5 Eye Irritation (TNO, 1999e)

TEST SUBSTANCE	Rossitol QRM 2688
METHOD	OECD 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	14 days

RESULTS

[Use this table if 3 animals or less used, otherwise delete]

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	*2*	*3*			
Conjunctiva: redness	1.3	3	1.3	3	7 days	0
Conjunctiva: chemosis	1.3	2	1.3	3	7 days	0
Conjunctiva: discharge	0.3	2	0.3	3	3 days	0
Corneal opacity	0.7	2	2	2	3 days	0
Iridial inflammation	0.3	0.3	0.3	1	1 day	0

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

CONCLUSION	The notified chemical is moderately to severely irritating to the eye.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.2.6 Skin Sensitisation (TNO, 1999f)

TEST SUBSTANCE	Rossitol QRM 2688	
METHOD	OECD 406 Skin Sensitisation – maximisation test.	
Species/Strain	Guinea pig/Dunkin-Hartley	
PRELIMINARY STUDY	Maximum non-irritating concentration: intradermal: 10% topical: 30%	
MAIN STUDY		
Number of Animals	Test Group: 10	Control Group: 5
INDUCTION PHASE	Induction Concentration intradermal: 10% topical: 30%	

Signs of Irritation	Topical pre-treatment with 10% SLS induced erythema in the controls and test animals; after topical application of the vehicle alone, slight erythema was observed in the controls. After the 48-hour topical application of the selected test concentration, slight or moderate erythema and scaliness were observed in the test animals.
CHALLENGE PHASE	
1st challenge	topical application: 30%

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	30%	0	0
Control Group		0	0

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.3 Repeated Dose Toxicity (TNO, 1999g)

TEST SUBSTANCE	Rossitol QRM 2688
METHOD	OECD 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Wistar
Route of Administration	Oral – gavage.
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week;
Vehicle	Corn oil

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	5/sex	0	*None*
2	5/sex	5	None
3	5/sex	15	None
4	5/sex	150	None

Clinical Observations
No treatment-related changes

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Clinical chemistry parameters were altered by treatment as follows: males of the high dose group exhibited elevated albumin/globulin ratio, males of the low to mid dose groups exhibited increased cholesterol and females of the high dose group exhibited increased urea.

No abnormal haematological findings were noted and no urinalysis parameters were measured.

Effects in Organs
No treatment related macroscopic findings were noted. High dose males exhibited statistically significant increases in relative kidney weights and both sexes exhibited statistically significant increases in relative liver weights in mid and high dose groups. No treatment-related histopathological changes were observed.

Remarks – Results
The increased cholesterol in males of the low and mid dose groups was within the normal range and the control levels were lower than normal. Therefore the increases were judged not to be treatment related.

The clinical chemistry results and organ weights pointed to effects on the kidneys and liver but there were no histopathological correlates.

CONCLUSION	The NOAEL for Rossitol was 15 mg/kg bw/ day on the basis of increased relative kidney weight in males, increased relative liver weight and albumin/ globulin ratio in males and increased urea in females. The NOEL was considered to be 5 mg/kg/day.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.4 Genotoxicity

9.4.1 Genotoxicity-Bacteria (TNO, 1999h)

TEST SUBSTANCE	Rossitol QRM 2688
METHOD	EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100.
Metabolic Activation System	S9 fraction from homogenised liver of rats induced with Aroclor 1254
Concentration Range in Main Test	With or without metabolic activation: 0, 62, 185, 556, 1667, 5000 microgram/plate (experiment 1) and 0, 31.3, 62.5, 125, 250, 500 microgram/plate (experiment 2).

Vehicle	dimethylsulfoxide
Remarks - Method	Toxicity was not expected and the toxicity test was incorporated in the first mutagenicity assay.

RESULTS

Metabolic Activation	*Test Substance Concentration (microgram/plate) resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	nd	185	-	-
Test 2	nd	250	-	-
Absent				
Test 1	nd	185	-	-
Test 2	nd	250	-	-

Remarks - Results	Toxicity, as determined by a reduction in the number of back mutants per plate, was observed in the first mutagenicity assay at 62 microgram/plate and above. Therefore the concentration range upper limit was reduced from 5000 to 500 microgram/plate. In the second assay, toxicity was observed at 250 and 500 microgram/plate but not at 125 microgram/plate.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.4.2 Genotoxicity-In Vitro (TNO, 1999i)

TEST SUBSTANCE	Rossitol QRM 2688
METHOD	OECD 473 In vitro Mammalian Chromosomal Aberration Test.
Cell Type/Cell Line	Chinese Hamster Ovary (CHO K-1) cells
Metabolic Activation System	S9 fraction from homogenised liver of rats induced with Aroclor 1254
Vehicle	dimethylsulfoxide

Metabolic Activation	*Test Substance Concentration (microgram/mL)*	*Exposure Period (h)*	*Harvest Time(h)*
Present			
Test 1	0*, 5, 10, 25*, 50*, 100*	4	18
Test 2	0*, 25, 50*, 100*, 150*, 200	4	18
Test 2	0*, 10, 25, 50, 100, 150*, 200	4	32
Absent			
Test 1	0*, 5, 10*, 25*, 50*, 100	18	18
Test 2	0*, 25, 50*, 100*, 150*, 200	18	18

Test 2	0*, 10, 25, 50, 100, 150*, 200	32	32

* selected for scoring chromosomal aberrations

RESULTS

Metabolic Activation	*Test Substance Concentration (microgram/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	50	5	-	-
Test 2	200 (4/18)	25 (4/18); 10 (4/32)	-	-
Absent				
Test 1	50	5	-	-
Test 2	150 (18/18); 200 (32/32)	50 (18/18); 10 (32/32)	-	-

CONCLUSION	The notified chemical was not clastogenic to CHO K-1 cells treated in vitro under the conditions of the test.
TEST FACILITY	TNO Nutrition and Food Research Institute.

9.5 Toxicokinetics (TNO, 1999j)

It was concluded that the notified chemical is expected to be extensively absorbed, distributed largely throughout the body, partly metabolised in the liver to non-mutagenic metabolites and readily excreted mainly via the urine.

9.6 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity in rats (LD50 > 2000 mg/kg) and was of low acute dermal toxicity in rats (LD50 > 2000 mg/kg). It was a severe irritant to rabbit skin and was a moderate to severe eye irritant. It was not sensitising in guinea pigs and was neither mutagenic in bacteria nor clastogenic in CHO cells in vitro. In a 28-day repeated dose oral toxicity test in rats no major organ toxicity was identified at the top dose of 150 mg/kg/day. The NOAEL was 15 mg/kg/day due to effects on the kidney and liver and the NOEL 5 mg/kg/day.

The notified chemical is classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999) and is assigned the risk phrases R36: Irritating to eyes and R38: Irritating to skin.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies have been supplied by the notifier. The tests were carried

out according to OECD Test Methods.

Test	Species	Results
96 h Acute Toxicity	***Zebra fish*** BRACHYDANIO RERIO	LC50 = 7.5 mg/L NOEC = 3.2 mg/L
48 h Acute Toxicity	DAPHNIA MAGNA	EC50 = >10.0 mg/L NOEC = ≥10.0 mg/L
72 h Growth Inhibition	Algae SELENASTRUM CAPRICORNUTUM	EbC50 = 5.0 mg/L ErC50 = 14.0 mg/L NOEC = 1.0 mg/L
3 h Activated Sludge Respiration inhibition	Activated Sewage Sludge	EC50 = 496.0 mg/L NOEC = 10.0 mg/L

* NOEC - no observable effect concentration

Zebra fish *Brachydanio rerio* were used in a 96-hour semi-static acute toxicity study for the notified chemical (TNO,1999k). The study was set up using 10 fish per test vessel. The nominal concentrations of notified chemical were 0, 1.0, 1.8, 3.2, 5.6 and 10.0 mg/L. Observations were made at the start of the experiment, 3 hours and then at every 24-hour period to 96 hours. The observations included mortality, visible abnormalities (eg appearance and behaviour), oxygen, temperature and pH. No visible abnormalities and no mortalities were observed in the test vessels with concentrations of less than 3.2 mg/L over the period of the study. At 3.2 mg/L all the fish were observed swimming at the surface and pigmentation increased over time while at 5.6 mg/L all fish survived but their condition was poorer than the controls. At 10.0 mg/L all fish died. Therefore, the LC50 was determined to be 7.5 mg/L and the no observable effect concentration, 3.2 mg/L. This indicates that the notified chemical is moderately toxic to fish.

Daphnia magna was used in a 48-hour static acute toxicity study for the notified chemical (TNO,1999l). The study was set up using 20 animals per concentration distributed into 4 groups of 5 animals in glass beakers. The nominal concentrations of notified chemical were 0, 1.8, 3.2, 5.6 and 10 mg/L. Observations were made at the start of the experiment then at every 24-hour period. The observations included immobility, oxygen, temperature and pH. Allowing for 10% immobility in the control no agent-induced immobilisation was observed at any concentration. The EC50 was determined to be >10.0 mg/L and NOEC was ≥10.0 mg/L. These results indicate that the chemical is potentially slightly toxic to Daphnia.

Green algae *Selenastrum capricornutum* was used in a 72-hour growth inhibition study for the notified chemical (TNO, 1999m). The study was set up using glass flasks with an initial algal cell concentration of 4.8×10^3 cells/mL, with cell counts being performed every 24 hours. The nominal concentrations of notified chemical were 0, 1.0, 1.8, 3.2, 5.6, 10.0, 18.0 and 32.0 mg/L. Samples were taken at 0, 23, 49.5 and 72 hours. The EbC50 was determined to be 5.0 mg/L, and the ErC50 was 14.0 mg/L. These results indicate that the chemical is slightly to moderately toxic to algae.

A mixed population of activated sewage sludge microorganisms was used in the assessment of the inhibition of respiration in activated sewage sludge (TNO, 1999n). The test involved nominal concentrations of 0, 10, 32, 100, 320 and 1001 mg/L of Rossitol which were aerated

for a period of 3 hours at 20°C in the presence of activated sludge plus synthetic sewage as a respiratory substrate. The rate of respiration was measured after 30 minutes and 3 hours. The positive control used was 3,5-dichlorophenol. The 3-hour EC50 and NOEC for Rossitol were 466.0 and 10.0 mg/L, respectively.

The ecotoxicity data indicate the notified chemical is moderately toxic to fish and algae and slightly to toxic to daphnia.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified chemical will be used as a fragrance ingredient in domestic cleaning and personal care formulations, and most will eventually be released into domestic sewage systems as a consequence of product use. The compound is not readily biodegradable (2% over 28 days), has a high n-octanol/water partition coefficient of 3.9, a moderate log Koc of 2.34 and moderate water solubility (189 mg/L at 20ºC), all indicating that most of the material would remain in the sewage water. Accordingly, most of the released chemical is likely eventually to be discharged to receiving waters. However, some of the chemical will become associated with soils and sediments, and is expected to slowly degrade to water, carbon dioxide and methane through biological processes.

The ecotoxicity data indicates that the notified chemical is slightly toxic to daphnia and moderately toxic to fish and algae. However, based on annual imports of 1 tonne/annum, and assuming the majority of this is eventually released to sewer and not removed during sewage treatment processes, the daily release on a nationwide basis to receiving waters is estimated to be 2.74 kg/day. Assuming a national population of 18,000,000 and that each person contributes an average 150 L/day to overall sewage flows, the predicted concentration in sewage effluent on a nationwide basis is estimated as 1 microgram/L.

Amount of Rossitol entering sewer annually	970 kg
Population of Australia	*18 million*
Amount of water used per person per day	150 L
Number of days in a year	365
Estimated PEC	0.001 mg/L (1.0 ppb)

When released to receiving waters the concentration is generally understood to be reduced by a further factor of at least 10, and so the Predicted Environmental Concentration (PEC) is around 0.1 microgram/L. The company also provided a PEC based on 100% use of the compound in Melbourne. This calculation gave a PEC value of 0.16 microgram/L after released to receiving waters.

Both PEC estimates indicate that after discharge to receiving waters the environmental concentration of the new compound will be several orders of magnitude less than the demonstrated toxicity to the green algae (EbC50 = 5.0 mg/L) the most sensitive organism tested.

The above considerations indicate minimal hazard to the environment when the notified chemical is used as a component of domestic products in the manner and levels indicated by the notifier.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment

The notified chemical was of very low acute oral toxicity in rats (LD50 > 2000 mg/kg) and was of low acute dermal toxicity in rats (LD50 > 2000 mg/kg). It was a severe irritant to rabbit skin and was a moderate to severe eye irritant. It was not sensitising in guinea pigs and was neither mutagenic in bacteria nor clastogenic in CHO cells in vitro. In a 28-day repeated dose oral toxicity test in rats no major organ toxicity was identified at the top dose of 150 mg/kg/day. The NOAEL was 15 mg/kg/day due to effects on the kidney and liver.

The notified chemical is classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999) and is assigned the risk phrases R36: Irritating to eyes and R38: Irritating to skin. However, the notified chemical will not render the imported fragrance compound a skin or an eye irritant as it is present at a concentration of 1% or less.

Occupational Health and Safety

Transport and storage of the steel kegs containing the fragrance compound incorporating the notified chemical should not result in exposure of transport and storage workers expect in the event of accidental rupture of the containers.

The notified chemical has a low vapour pressure and inhalation exposure during product formulation is unlikely. Unloading of the kegs containing the imported fragrance compound into weighing vessels and thence to mixing vessels can result in exposure of the skin or eyes if personal protective equipment is not worn but there is minimal risk of adverse health effects.

Once in the mixing vessel the notified chemical is in an enclosed system and worker exposure is unlikely. This is also the case for dedicated lines used for filling containers. Although workers may be exposed to splashes and spills during cleaning of lines, vessels and transfer equipment, the low concentration of the notified chemical in finished products (less than 0.05%) would serve to minimise the risk of adverse health effects even in the absence of personal protective equipment.

Worker exposure to the notified chemical in end use products is unlikely except in the event of accidental rupture of containers.

Public Health

The total public exposure was calculated to be 8.8 microgram/kg/day. When divided into the NOEL from the 28-day study (5 mg/kg/day), this gives a safety margin of 568. Consequently the hazard from typical systemic exposure to products in the public domain is likely to be low. Overall, the public hazard from exposure to the notified chemical through all phases of its life-cycle, is considered to be low.

13. RECOMMENDATIONS

CONTROL MEASURES

Occupational Health and Safety

- The MSDS for the fragrance compound to be imported should be prepared in accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994). A copy of this 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.

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

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical and an example of a fragrance formulation were provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994). An MSDS for a fragrance formulation containing the notified chemical was not finalised at the time of assessment.

These MSDS were provided by the applicant as part of the notification statement. They are reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

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Attachment 1

The Draize Scale (Draize, 1959) for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale (Draize *et al*., 1944) for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
Diffuse beefy red	3 severe	Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
		Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe

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