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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Phenol, 2-methoxy-4-(tetrahydro-4-methylene-2H-pyran-2-yl) -(Eugewhite Isomer #2)

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FULL PUBLIC REPORT

Phenol, 2-methoxy-4-(tetrahydro-4-methylene-2H-pyran-2-yl) -(Eugewhite Isomer #2)

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
International Flavours and Fragrances Australia Ltd.
301 Frankton-Dandenong Road
Dandenong South
Victoria 3175

NOTIFICATION CATEGORY

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

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

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
US EPA: PMN 92-1033, 1992
EC, Ireland: 92-07-0037-02, 1992
Environment Canada: Schedule 1, NSN 11981, 2002

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
Phenol, 2-methoxy-4-(tetrahydro-4-methylene-2H-pyran-2-yl)-

OTHER NAME(S)
Not applicable

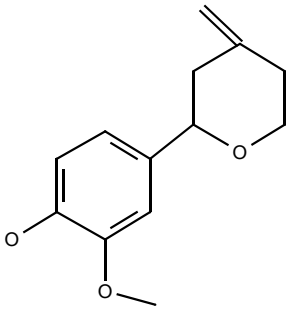
MARKETING NAME(S)
Eugewhite Isomer # 2

CAS NUMBER
128489-04-3

MOLECULAR FORMULA
$C_{13}H_{16}O_3$

MOLECULAR WEIGHT
236.31

STRUCTURAL FORMULA



SPECTRAL DATA

Eugewhite contains two closely related isomers (notified chemical and the chemical subject of LTD/1082). The spectra provided were for the mixed isomers.

ANALYTICAL METHOD	Infrared (IR) Spectroscopy		
Remarks	For mixed isomers Peaks at: 1518, 1465, 1452, 1434, 1270, 1238, 1205, 1152, 1118, 1035 cm^{-1}		
ANALYTICAL METHOD	UV/Visible Spectroscopy		
Remarks	For mixed isomers		
	Neutral solution	λmax = 277 nm	ε = 1878
		λmax = 226 nm	ε = 6198
	Basic solution	λmax = 290 nm	ε = 4077
		λmax = 246 nm	ε = 12238
	Acidic solution	λmax = 277 nm	ε = 1348
		λmax = 226 nm	ε = 6078
ANALYTICAL METHOD	^{1}H nmr spectrometry		
Remarks	Individual isomer peaks were partly resolved. Peaks at: 6.96-6.61, 5.61, 4.80, 4.21, 3.89, 3.54, 2.5-2.0 ppm		

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	IR Spectrum, NMR Spectrum, Gas Chromatography.
Remarks	Reference spectra were provided.

3. COMPOSITION

DEGREE OF PURITY

98 % (typical), 98-100% (range)

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS

Chemical Name Phenol, 4-(3,6-dihydro-4-methyl-2H-pyran-2-yl)-2-methoxy-
CAS No. 128489-02-1 *Weight %* 55 – 70 %
(Eugewhite isomer #1, subject of NICNAS notification LTD/1082 and present in test samples used for toxicity determination)

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

Chemical Name Unidentified minor closely related isomers and intermediates
CAS No. Unidentified *Weight %* 0 – 2 %

ADDITIVES/ADJUVANTS

Chemical Name Phenol, 2, 6-bis(1,1-dimethylethyl)-4-methyl-

CAS No. 128-37-0 *Weight %* 0.1 – 0.3 %

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Imported as part of a finished fragrance oil or in end-use consumer products.

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

Year	*1*	*2*	*3*	*4*	*5*
Quantity	68 kg	68 kg	158 kg	225 kg	225-450 kg

USE
The notified chemical will be used as an odourant in alcoholic perfumery, cosmetics, toiletries, household products, soaps and detergents. The resulting concentration of the Eugewhite in end-user consumer products is 0.04-0.4%, equating to a maximum of 0.18% notified chemical.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Melbourne

IDENTITY OF MANUFACTURER/RECIPIENTS
International Flavours and Fragrances Australia, Ltd.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported into Australia as a component of finished fragrance oils in sealed, polypropylene lined steel drums (200 L). The finished fragrance oils containing the notified chemical will be transported by road from docks to the notifiers warehouse and then to customers.

5.2. Operation Description

The notified chemical is imported as a component of finished fragrance oils at a maximum of 0.9% (2% Eugewhite mixed isomers) to be formulated to the finished product locally. Detailed information on the formulation process by customers was not provided. However, typical practices by cosmetic and consumer product manufacturers include the use of local exhaust ventilation and open mixing vessels and filling lines, although the processes are often automated.

During formulation, the main activity is blending of the ingredients with the notified chemical. The fragrance oil contained in drums will be transferred to a mixing tank and blended with various ingredient to make end-use consumer products such as alcoholic perfumes, cosmetics, toiletries, household cleaning products, soaps and detergents. The resulting concentration of the notified chemical in end-user consumer products will be up to a maximum of 0.18%.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Mixer	5	4 hr	2 days/year
Quality control worker	2	0.5 hr	2 days/year
Packager	10	4 hr	2 days/year
Maintenance	5	4 hr	2 days/year

Exposure Details
Waterside, transport and IFF warehouse workers will be exposed to the notified chemical only in the event of a spill. At the customer facilities, the nature of the work done is strictly a blending operation. It is expected that operations are mostly automated with large manufacturers. Small manufacturers are

likely to be less automated. Dermal contact with the notified chemical as a component of fragrance oils or finished products may occur during manual addition of ingredients and connection or disconnection of transfer lines.

The highest concentration of the notified chemical that workers may be exposed to is 0.9%. The final consumer products will contain a maximum of up to 0.18% of the notified chemical. Consumer product manufacturers typically have automated systems and coveralls, gloves and safety glasses are expected to be worn by workers at customer's facilities.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Release of the chemical is not expected at the notifier's warehouse site. Release from the reformulation facilities is anticipated to be extremely low given the concentration of Eugewhite in finished fragrance oils. Little material is expected to be lost during the formulation into the consumer product since the processes are mainly automated. It is assumed that if the process equipment is cleaned between batches, the washwater will be recycled or release to the sewer.

RELEASE OF CHEMICAL FROM USE

Since Eugewhite will be used in household, laundry and personal cleaning products, almost all (~97%) of Eugewhite will end up in the sewer. Approximately 1% of the Eugewhite imported is expected to be lost as residues in consumer containers, which are primarily sent to land fill. Release to the environment during reformulation would result from residual material in the import container, which would be rinsed and most likely discharged to the sewer.

5.5. Disposal

The notified chemical will ultimately be disposed of in either the sewer (major) or landfill.

5.6. Public exposure

End-use products are designed to be sold to consumers. The general public will be repeatedly exposed to low levels of Eugewhite via a number of different consumer products, with typical levels of 0.04-0.4%, equating to a maximum of 0.18% notified chemical. Due to its low levels and the use patterns, the overall daily exposure to the notified chemical will be very low for a person using one or more consumer products containing the notified chemical.

Public exposure from transport, storage, reformulation or disposal is negligible.

6. PHYSICAL AND CHEMICAL PROPERTIES

The following data were obtained with the test substance Eugewhite, which contains Isomer # 2 (30-45%) and Isomer # 1 (55-70%). These isomers will not be used independently and Eugewhite is the finished product containing these isomers.

Appearance at 20°C and 101.3 kPa Viscous yellow-green liquid

Boiling Point Decomposes at 266-271°C at 101.3 kPa.

METHOD	EC Directive 84/449EEC A.2 Boiling Temperature.
Remarks	The test substance decomposes during preliminary microdistillation. The decomposition on heating meant that the vapour temperature could not be attributed to the test substance itself. Hence, it was decided to investigate the decomposition using an ebulliometer. In the first test, reflux commenced at 269°C and white fumed evolved at 271°C. In the second test, white fumes evolved immediately on refluxing at 266°C.
TEST FACILITY	Huntingdon Research Centre Ltd (1991a).

Density 1147.7 kg/cm^3

METHOD EC Directive 842/449/EEC A.3 Relative Density.
Remarks None
TEST FACILITY Huntingdon Research Centre Ltd (1991a)

Vapour Pressure 3.525×10^{-6} kPa at 25°C

METHOD EC Directive 84/449/EEC A.4 Vapour Pressure.
Remarks The vapour pressure was determined using vapour pressure balance in mass difference mode. The sample did not decompose at temperatures used in vapour pressure determination. The vapour pressure was calculated at 25°C using the mass difference method.

The result indicates that the test substance is slightly volatile (Mensink *et al* 1995).
TEST FACILITY University of Leeds (Huntingdon Research Centre Ltd, 1991a - addendum 1).

Water Solubility 2.065 g/L at 20°C

METHOD EC Directive 92/69/EEC A.6 Water Solubility.
Remarks The water solubility was determined by the flask stirring method. A preliminary test was conducted by stirring an excess of the test substance with distilled water overnight at 20°C. After centrifuging, the supernatant was analysed by GC. On the basis of the preliminary test, the solubility of the test substance was determined by pre-equilibrating the flasks (~1 g test substance in 100 mL water) in duplicate for 1, 2 and 3 days at 30°C prior to equilibration for 24 h at the test temperature of 20°C. The flasks were stirred continuously throughout the test. After centrifuging, the concentration of the test substance was determined by GC.

The result indicates that the test substance is readily soluble in water (Mensink *et al* 1995)
TEST FACILITY Huntingdon Research Centre Ltd (1991a)

Fat Solubility Miscible in all proportions with standard Fat HB 307 at 37°C

METHOD EEC Directive 84/449, Annex V, Method A7
Remarks Since Eugewhite was found to have infinite solubility in Standard fat, a modified test procedure was used. Mixtures containing from 4.96-95.0% w/w Eugewhite were liquefied and mixed in Standard Fat at 37°C. All the prepared mixtures were observed to form a homogeneous phase.
TEST FACILITY Huntingdon Research Centre Ltd (1991a)

Hydrolysis as a Function of pH

METHOD OECD TG 111 Hydrolysis as a Function of pH.
EC Directive 84/449 EEC C10 Abiotic Degradation: Hydrolysis as a Function of pH.

pH	*T (°C)*	$t_{½}$
4	25	> 1 year
7	25	> 1 year
9	25	31 days

Remarks In a preliminary test, no significant hydrolysis was observed at pH 4 and 7 over a period of 5 days at 50°C. The half-life was estimated to be between 1 day and 1 year at pH 9 and > 1 year at pH 4 and 7.
The test was rerun at pH 9. Test 1 of Method C7 carried out at 50°C showed pseudo first order reaction kinetics and test 3 was then carried out at 60°C and 70°C. Since the relative proportions of the two isomers of Eugewhite were found to differ between the calibration standards and the diluted test solutions, the two isomers were treated separately in calculations, with separate calibration curves.
The rate constants at 60°C and 70°C were calculated to be 8.787×10^{-3} hr^{-1} and

1.7278 x 10^{-2} hr^{-1}, respectively, for Isomer 1 and 1.0287 x 10^{-2} hr^{-1} and 1.8665 x 10^{-2} hr^{-1}, respectively, for Isomer 2. The rate constant extrapolated at 25°C was 5.7706 x 10^{-4} hr^{-1} for Isomer 1 and 9.3466 x 10^{-4} hr^{-1} for Isomer 2. The $t_{1/2}$ (25°C) at pH 9 for the notified chemical is 31 days.

TEST FACILITY Huntingdon Research Centre Ltd (1992 and 1994)

Partition Coefficient (n-octanol/water) log Pow at 21°C = 2.31

METHOD EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks Octanol test solution (10 mL) and octanol saturated water (80 mL) were combined in a screw-capped glass jar and shaken mechanically for 15 minutes. The tests were performed in duplicate. The test phases were separated by allowing to stand for 1 h prior to centrifuging the samples. The final solutions were analysed by GC.

The log K_{ow} of 2.31 indicates that the test substance has a poor affinity for n-octanol.
TEST FACILITY Huntingdon Research Centre Ltd (1991a)

Adsorption/Desorption log K_{oc} = 2.81 (temperature not specified)

METHOD PCKOC Program (v1.66)

Remarks No details of the report was provided. The estimated Koc represents a best-fit to the majority of experimental values and the Koc was determined to be 2.81. However, the Koc may vary significantly with pH.

On the basis of the calculated Koc value, the notified chemical is likely to be of low mobility in soil (McCall *et al* 1980). However, the value should be treated with caution.

Dissociation Constant Not determined

Remarks The notified chemical includes a 2-methoxyphenol group which is likely to have typical acidity (pKa > 10, based on catechol) and therefore little dissociation is expected in the environmental pH range of 4 to 9.

Surface Tension 46.7 mN/m at 18.5°C

METHOD EC Directive 84/449/EEC A.5 Surface Tension
Remarks The surface tension of a 90% saturated aqueous solution was determined with a direct reading surface tension/torsion balance using OECD harmonised ring method at a test temperature of 18.5°C. Based on the determined surface tension of 46.7 mN/m, the test substance is considered to be surface active.
TEST FACILITY Huntingdon Research Centre Ltd (1991a)

Particle Size Not applicable.

Remarks The test substance is a liquid.

Flash Point 178°C at 1017 mbar

METHOD Pensky-Martens closed up method, as described in ASTM D93-80 was used.
Remarks None
TEST FACILITY Huntingdon Research Centre Ltd (1991a).

Flammability Limits Not flammable

METHOD Not stated.
Remarks The test substance did not evolve gas in any of the tests (flammability in contact with water or damp air). The notified chemical also did not ignite in air under the

conditions of the test.

TEST FACILITY Huntingdon Research Centre Ltd (1991a).

Autoignition Temperature >400°C

METHOD 84/449/EEC /A.16 Auto-Ignition Temperature

Remarks The test substance was too viscous to perform Test A15, therefore Test A16 (autoflammability solids) was used.

TEST FACILITY Huntingdon Research Centre Ltd (1991a).

Explosive Properties No explosive properties.

METHOD EC Directive 84/449/EEC A.14 Explosive Properties.

Remarks None.

TEST FACILITY TNO Prins Maurits Laboratory Rijswijk, The Netherlands (Huntingdon Research Centre Ltd, 1991a - addendum 2).

Reactivity

Remarks The notified chemical is expected to be stable in water and air under normal conditions of temperature and pressure

7. TOXICOLOGICAL INVESTIGATIONS

The following data were obtained with the test substance Eugewhite (mixed isomers), which contains Isomer # 2 (the notified chemical, 30-45%) and Isomer # 1 (55-70%). These isomers will not be used independently and Eugewhite is the finished product containing these isomers.

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	non-irritating
Rabbit, eye irritation	slight irritant
Guinea pig, skin sensitisation – Buehler test	limited evidence of sensitisation
Guinea pig, skin sensitisation – Maximisation test	evidence of sensitisation
Skin sensitisation-Repeat Insult Patch Test	no evidence of sensitisation
Rat, oral repeat dose toxicity - 28 days.	NOEL = 55 mg/kg/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosome aberration	non genotoxic

7.1. Acute toxicity – preliminary study

TEST SUBSTANCE — Eugewhite (mixed isomers)

METHOD — OECD TG 401 Acute Oral Toxicity – Limit Test.
EC Directive 84/449/EEC B.1 Acute Toxicity (Oral) – Limit Test.

Species/Strain — Rat/ Sprague-Dawley origin-Crl. CD (SD) BR VAF plus
Vehicle — None
Remarks – Method — The initial trial test was carried out by dosing four rats (2/sex) at 2500 mg/kg bw/day. The two males died during this study. Based on this results, further groups of rats (5/sex) were dosed at 3200, 5000 and 6400 g/kg bw.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	3200	6/10
2	5/sex	5000	4/10
3	5/sex	6400	3/10

LD50 — Not determined.
Signs of Toxicity — Deaths occurred from within 1 hour of dosing until day 2. Pilo-erection, abnormal body carriage (hunched posture), abnormal gait (waddling), lethargy, decreased respiratory rate, ptosis, pallor of the extremities, increased lacrimation, ataxia and prostration.
Effects in Organs — Terminal autopsy revealed no macroscopic lesions.
Remarks – Results — An inconsistent pattern of mortality with dose was observed.

CONCLUSION — An LD50 could not be determined in this study.

TEST FACILITY — Huntingdon Research Centre Ltd (1991b)

7.1. Acute toxicity – oral

TEST SUBSTANCE — Eugewhite (mixed isomers)

METHOD — OECD TG 401 Acute Oral Toxicity – Limit Test.
EC Directive 84/449/EEC B.1 Acute Toxicity (Oral) – Limit Test.

Species/Strain — Rat/ Sprague-Dawley origin-Crl. CD (SD) BR VAF plus
Vehicle — None
Remarks – Method — Based on the results of the preliminary study, rats in the main study were

treated with 2000 mg/kg bw/day.

RESULTS

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

LD50	> 2000 mg/kg bw
Signs of Toxicity	Pilo-erection, decreased respiratory rate, pallor of the extremities and ataxia were observed in all rats within ten minutes of dosing. These signs persisted in a majority of rats and were accompanied on day 1 only by abnormal body carriage (hunched posture), abnormal gait (waddling) and lethargy in a majority of rats; less common cases of increased lachrymation and prostration. Recovery, judged by appearance and behaviour, was complete by day 3.
Effects in Organs	Terminal autopsy revealed no macroscopic lesions.
Remarks – Results	None

CONCLUSION — The test substance is of low toxicity via the oral route.

TEST FACILITY — Huntingdon Research Centre Ltd (1991b)

7.2. Acute toxicity – dermal

TEST SUBSTANCE — Eugewhite (mixed isomers)

METHOD — OECD TG 402 Acute Dermal Toxicity – Limit Test.
EC Directive 84/449/EEC B.3 Acute Toxicity (Dermal) – Limit Test.

Species/Strain	Rat/ Sprague-Dawley origin-Crl. CD (SD) BR VAF plus
Vehicle	None
Type of dressing	Occlusive
Remarks – Method	The test substance was applied by spreading it evenly over the prepared skin. At the end of 24-hour exposure period, the dressings were carefully removed and the treated area of skin decontaminated by washing in warm water and blotting dry with absorbent. The day of dosing was designated day 1.

RESULTS

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

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	There were no signs of dermal irritation at any of the application sites. Scores of zero for erythema and oedema were recorded for all animals.
Signs of Toxicity - Systemic	There were no signs of systemic reaction to treatment.
Effects in Organs	Terminal autopsy revealed no macroscopic abnormalities.
Remarks – Results	None

CONCLUSION — The test substance is of low toxicity via the dermal route.

TEST FACILITY — Huntingdon Research Centre Ltd (1991c)

7.3. Acute toxicity - inhalation

No test reports were submitted.

7.4. Irritation – skin

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	EC Directive 84/449/EEC B.4 Acute Toxicity (Skin Irritation). OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	Three
Vehicle	None
Observation Period	Four days
Type of Dressing	Semi-occlusive.
Remarks – Method	0.5 mL aliquot of the test substance was applied for a four hours period under a 2.5 cm square gauze pad to one intact skin site on each animal.

RESULTS

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

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

Remarks – Results	Very slight erythema, with or without very slight oedema, was evident at the treatment sites of all three animals approximately 30 minutes after removal of the dressings, four hours after application (Day 1). All reactions had resolved by the following day.
CONCLUSION	The test substance is non-irritating to skin.
TEST FACILITY	Huntingdon Research Centre Ltd (1991d)

7.5. Irritation – eye

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	EC Directive 84/449/EEC B.5 Acute Toxicity (Eye Irritation). OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	Three
Observation Period	Fourteen days
Remarks – Method	A 0.1 mL aliquot of the test substance was placed into the lower everted lid of one eye of each animal.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	1.0	1.3	1.0	2	4 days	0
Conjunctiva: chemosis	0.3	0.3	0.3	1	2 days	0
Corneal opacity	1.0	0.67	1.0	1	7 days	0

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

Remarks – Results	No irritation of the iris was observed in any animal.
CONCLUSION	The test substance is a slight irritant to rabbit eyes.

TEST FACILITY	Huntingdon Research Centre Ltd (1991e).

7.6. Skin sensitisation

7.6.1. Skin sensitisation- Buehler Test

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	EC Directive 84/449/EC B.6 Skin Sensitisation – Buehler
Species/Strain	Guinea pig/Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: topical: 100%
MAIN STUDY	
Number of Animals	Test Group: 20 (10/sex) Control Group: 10 (5/sex)
INDUCTION PHASE	Induction Concentration: topical application: 100%
Signs of Irritation	4/20 test animals showed slight irritation (slight patchy erythema, graded +) after the first induction treatment. Two of these animals plus one other showed similar changes after the second induction treatment. No evidence of irritation was seen following the third induction treatment.
CHALLENGE PHASE	
1st challenge	topical application: 100%
Remarks – Method	Fourteen days after the last induction exposure, the animals were challenged in the same manner on a naive site. Four naive animals (2/sex) were induced with the test substance on the challenge day in the same manner. The control group of 10 guinea pigs, treated with ethanol:distilled water, 80:20, during the induction phases of the study were also treated with ethanol:water at challenge, rather than with test substance.
RESULTS	
Remarks – Results	No erythema was observed in the animals treated with ethanol:distilled water (80:20) at 24 or 48 hours after challenge. No signs of erythema were observed in the naive group at 24 or 48 hours after challenge. No positive responses were observed at 24 or 48 hours after challenge in the animals receiving the test article at a 100% concentration. The effects seen at challenge in the test animals (4 at 24 hours & 3 at 48 hours), consisting of slight patchy erythema (grade +), were attributed by the study authors to irritation rather than sensitisation. While the incidence (confined to test animals) is consistent with a sensitisation reaction, the low severity of responses indicates that clear evidence of sensitisation was not obtained. Clear positive responses (grade 2 or 3) were elicited in a concurrent positive control group treated with 1-chloro-2,4-dinitrobenzene, indicating the sensitivity of the animal population.
CONCLUSION	There was limited evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test.
TEST FACILITY	Pharmakon Research International Inc., Waverly, PA (1991).

7.6.2. Skin sensitisation- Maximisation Test

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	EC Directive 92/69/EEC B.6 Skin Sensitisation – Magnusson and

	Kligman
Species/Strain	Guinea pig/Dunkin-Hartley
Number of Animals	Test Group: 10 Control Group: 5
INDUCTION PHASE	Induction Concentration: intradermal: 1% v/v in 5% acetone in Alembicol D topical: 100%
Signs of Irritation	Intradermal injection: Necrosis was recorded at sites receiving Freund's Complete Adjuvant in test and control animals. Slight irritation was seen in test animals at sites receiving 1% v/v in 5% acetone in Alembicol D and slight irritation was observed in control animals receiving 5% acetone in Alembicol D alone. Topical application: Moderate erythema was observed in test animals. Slight erythema was seen in control guinea pigs.
CHALLENGE PHASE	
1st challenge	topical application: 100% topical application: 50% v/v in acetone
Remarks – Method	The concentrations applied were determined in a preliminary study. Pretreatment with SLS was used to induce irritation prior to topical induction.

RESULTS

Animal	*Challenge Concentration (%)*	*Number of Animals Showing Skin Reactions after: 1st challenge*		
		24 h	*48 h*	*72 hrs*
Test Group	100	10	10	10
	50	8	6	6
Control Group	100	0	0	0
	50	0	0	0

Remarks – Results	Both well defined erythema and well defined oedema were observed in the test animals at sites challenged at 100%. Responses were generally less for challenge with the 50% concentration.
CONCLUSION	In this study, the test substance produced evidence of skin sensitization in guinea pigs (10/10 at 100%, 8/10 at 50%).
TEST FACILITY	Huntingdon Research Centre Ltd (1995).

7.6.3. Skin sensitisation – Repeated Insult Patch Test

TEST SUBSTANCE	Eugewhite (mixed isomers), 10% in Alcohol SD 39C.
METHOD	
Study Design	Human Repeated Insult Patch Test
Study Group	A total of 54 subjects, 9 males and 45 females, ranging in age from 18 to 65 years, were examined for this study. A total of 51 individuals completed the test procedure.
Vehicle	10% in alcohol
INDUCTION PHASE	Approximately 0.2 mL of the test substance was placed directly onto a occlusive patch, which was applied to the back of each subject, between the scapulae and waist, adjacent to the spinal mid-lone. A total of nine applications were made. The patches were removed 24 hours after application. Rest periods consisted of either 24 hrs (if the day falls during the week) or 48 hrs (during the weekend).
CHALLENGE PHASE	After a rest period of 10 to 21 days following the ninth application, a challenge patch was applied to a virgin site. Sites were evaluated at 24

and 72 hrs after application

RESULTS

Remarks – Results	A single, transient, barely perceptible (+) non-specific patch test response was observed on one (1/51) test subject during the induction phase of the study. This non-specific response was not considered to be irritant or allergic in nature
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test.
TEST FACILITY	Essex Testing Clinic Inc., Verona, NJ (1991).

7.7. Repeat dose toxicity

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents. EC Directive 88/449/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).
Species/Strain	Rat, Charles River, Crl: CD(SD)VR VAF/Plus
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28days Dose regimen: 7 days per week Post-exposure observation period: 0
Vehicle	Corn Oil
Remarks – Method	A series of solutions were prepared freshly each day at concentrations of 0.1, 1.1 and 20% v/v. All animals were observed daily for signs of ill health, behavioural changes or toxicosis. Doses were determined on the basis of a 7 day preliminary test.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	5/sex	0	0
II (low dose)	5/sex	5	0
III (mid dose)	5/sex	55	0
IV (high dose)	5/sex	1000	0

Mortality and Time to Death

There were no mortalities.

Clinical Observations

Greasy fur persisted in all rats treated at 1000 mg/kg bw/day throughout the treatment period accompanied intermittently by slightly or moderately increased salivation. A low incidence of slightly greasy fur following dosing occasionally accompanied by slightly increased salivation was observed in all rats treated at 5 and 55 mg/kg bw/day and in the control group during week 1.

A sore was recorded on the left shoulder of one male rat from day 23 to termination. This was considered to be have been caused by fighting within the cage.

Pallor of the extremities was noted in all animals following blood sampling and is considered not to be treatment related.

Slightly lower bodyweight gains were recorded for male rats treated at 1000 mg/kg bw/day during week 3 and week 4 achieving statistical significance in comparison with controls. The change was minor and not seen in the females of the group. There were no other significant variations in bodyweight gain.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Haematology:

A slightly higher thrombotest time was recorded for male rats treated at 1000 mg/kg bw/day. Although achieving statistical significance, this change was very small in magnitude. Significantly

reduced neutrophil levels were recorded for female rats of all treated groups. Individual values for treated rats were all within 5 to 95 percentile range of background data for rats of this sex, age and strain, but high values were recorded among control rats. For all other haematological parameters measured, values for treated and control animals were similar.

Biochemistry:

Plasma protein values showed a slight increase in albumin levels among male rats treated at 55 and 1000 mg/kg bw/day and a decrease in globulin levels in all treated female rats resulting in significantly shifted A/G ratio for females only. No clear dose dependency could be established and all individual values were within the 5 to 95 percentile range of background data.

Urea nitrogen levels for male rats treated at 1000 mg/kg bw/day were significantly higher than for controls. Individual values for treated animals were all within the expected background range apart from one animal, which had higher than expected levels.

A small rise in creatinine level was recorded for male rats dosed at 1000 mg/kg bw/day, achieving statistical significance in comparison with controls. Significantly lower phosphorous levels were recorded for all treated female rats in comparison with controls.

Effects in Organs

Organ weights:

Adjusted liver weights for male and female rats treated at 1000 mg/kg bw/day were significantly higher than for concurrent controls. A marginal decrease in adrenal weight was recorded for treated male rats achieving statistically significance among rats treated at 1000 mg/kg/day. The change was minor and not considered to be treatment related.

Macroscopic pathology:

All macroscopic abnormalities were considered to be incidental and not related to treatment.

Microscopic pathology:

No treatment related changes were found in rats treated at 1000 mg/kg bw/day. In particular, there were no findings to account for the statistically significant increase in adjusted liver weights found in these animals when compared with controls. All findings were considered to be spontaneous in origin and therefore of no toxicological significance.

Remarks – Results

The observation of salivation and greasy fur in all groups was considered to be a response to the corn oil vehicle.

CONCLUSION

The No Observed Effect Level (NOEL) for the test substance was determined to be 55 mg/kg bw/day, based primarily on liver weight changes at 1000 mg/kg bw/day.

TEST FACILITY — Huntingdon Research Centre Ltd (1991f).

7.8. Genotoxicity - bacteria

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure/Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1538, TA1535, TA1537, TA98, TA100. *E. coli*: WP2 uvrA, WP2 uvrA (pKM101), WP2 (pKM101).
Metabolic Activation System	S9 fraction from livers of Aroclor-1254 induced rats.
Concentration Range in Main Test	a) With metabolic activation: 15 – 1500 µg/plate. b) Without metabolic activation: 15 – 1500 µg/plate.
Vehicle	DMSO
Remarks - Method	Two independent assays were performed. The highest final concentration, with no precipitate after incubation at 37°C, was 1500 µg/ml.

RESULTS

Remarks – Results

No significant increases in the numbers of revertants were seen for any strain either in the presence or absence of metabolic activation. No signs of toxicity were observed. Appropriate positive controls were used and

	led to large increases in revertants, indicating that the test system responded appropriately.
CONCLUSION	The test substance was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Huntingdon Research Centre (1991g).

7.9. Genotoxicity – in vitro

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	OECD TG 473 In vitro Mammalian Chromosomal Aberration Test. 84/449/EEC, Annex V, Method B10
Cell Type/Cell Line	Human lymphocytes
Metabolic Activation System	Liver Homogenates (S-9mix) from Arochlor 1254 induced rats
Vehicle	DMSO
Remarks - Method	The highest final concentration, with no precipitate after incubation at 37°C, was 1500 µg/ml.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Present			
Test 1	1500, 750, 375*, 188* and 46.9*, 23.4, 11.7, 5.9, 2.9	3 hr	24 hr
Absent			
Test 1	1500, 750, 375, 188*, 93.8*, 46.9, 23.4*, 11.7, 5.9, 2.9	3 hr	24 hr

*Cultures selected for metaphase analysis.

Remarks – Results	Toxicity as evidenced by reduction in mitotic index was seen at and above 188 µg/ml in the absence of S9 and at and above 375 µg/ml in its presence. No significant increases in the number of cells with chromosome aberrations were seen either in the presence or absence of metabolic activation. Appropriate positive controls were used and led to large increases in the number of cells with chromosome aberrations, indicating that the test system responded appropriately.
CONCLUSION	The test substance was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.
TEST FACILITY	Huntingdon Research Centre Ltd (1991h)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test. EEC Directive 84/449, Annex V, Method C6
Inoculum	Activated Sewage Sludge bacteria
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Dissolved Oxygen Concentrations were determined by means of a Yellow Spring BOD Probe (Model 54)
Remarks – Method	Test concentration of 2 mg/L was used. Each test included parallel series for the determination of oxygen depletion, without inoculum, in the presence of inoculum and with the positive control sodium benzoate at 3 mg/L. All bottles were incubated in the dark at 20°C during the test period. The oxygen concentration was determined using a Yellow Springs BOD Probe on days 0, 5, 15 and 28 in duplicate.

RESULTS

Test substance		*Sodium Benzoate*	
Day	*% degradation*	*Day*	*% degradation*
5	<1	5	53
15	4	15	74
28	9	28	83

Remarks – Results	After 28 days of incubation, the test substance attained only 9% biodegradation. The control substance attained 83% biodegradation within 28 days, thus satisfying the requirement that the reference substance had to attain >60% degradation, confirming the validity of the study.
CONCLUSION	The test substance cannot be classified as ready biodegradable.
TEST FACILITY	Huntingdon Research Centre Ltd (1991i)

8.1.2. Bioaccumulation

The log Kow for Eugewhite is 2.31 at 21°C. This indicates that Eugewhite is not expected to have a high potential to bioaccumulate. On the basis of the PBT Profiler data provided, the estimated bioconcentration factor of 30 further indicates that the notified chemical is not expected to bioaccumulate in the food chain as the BCF criteria are not exceeded.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Eugewhite (mixed isomers)
METHOD	OECD TG 203 Fish, Acute Toxicity Test Rainbow trout, flow-through EC Directive 84/449/EEC Annex V C.1 Acute Toxicity for Fish, Rainbow trout, semi-static
Species	*Oncorhynchus mykiss*
Exposure Period	96 hr

Auxiliary Solvent	None
Water Hardness	350 mg $CaCO_3$/L
Analytical Monitoring	Test concentration verified by HPLC analysis
Remarks – Method	A 96 h semi-static toxicity test was conducted with the renewal of the test media at 24 h intervals. The test vessel was glass aquarium containing 20 L of test medium. Nominal test concentrations of 1.8, 3.2, 5.6, 10, 18 and 32 mg/L for the test substance was used in the test aquaria. The other aquarium without the test substance was used as a control. Ten *Oncorhynchus mykiss* per test concentration were placed in each aquarium. The fish exhibiting toxic symptoms were recorded at 3, 6, 24, 48, 72 and 96 h. Marked reactions to exposure (other than death) were increased pigmentation, lethargy, loss of equilibrium, swimming near or lying on the bottom of the aquarium, exophthalmia and moribundity. Water quality parameters of temperature, dissolved oxygen and pH were measured throughout the test and were within acceptable limits.

RESULTS

Concentration mg/L Nominal	*Number of Fish*	*Cumulative Mortality*				
		3h	*24h*	*48h*	*72h*	*96h*
Control	10	0	0	0	0	0
1.8	10	0	0	0	0	0
3.2	10	0	0	0	0	0
5.6	10	0	0	0	0	0
10	10	0	0	0	0	0
18	10	0	0	0	0	0
32	10	0	7	10*	10*	10*

*Included 3 fish moribund from 24 hour to study termination. Moribundity assumed to be equivalent to mortality when this condition persists for longer than 24 h.

LC50	24 mg/L at 96 hours (CI: 18-32 mg/L).
NOEC (or LOEC)	1.8 mg/L at 96 hours.
Remarks – Results	Three fish survived the highest exposure level of 32 mg/L for the duration of the study. However, these fish were moribund from 24 h and consequently, are recorded as mortalities from 48 h onwards. Results at 48, 72 and 96 h are based on the assumption that moribundity persisting for > 24 h is equivalent to mortality. All results are expressed as nominal concentrations. All measured concentrations remained within the range of 90-100% of the nominal value throughout the study.

CONCLUSION — The test substance is harmful to Rainbow trout.

TEST FACILITY — Huntingdon Research Centre Ltd (1991j)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE — Eugewhite (mixed isomers)

METHOD — OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – *Daphnia magna* static
EC Directive 84/449/EEC Annex V C.2 Acute Toxicity for Daphnia – *Daphnia magna* static

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	350 mg $CaCO_3$/L
Analytical Monitoring	Test concentration verified by HPLC analysis
Remarks – Method	Nominal test concentrations ranging from 3.2-320 mg/L were used in the test. Daphnia were exposed for a maximum of 48 h and the test was performed in duplicate with 20 daphnia per test concentration plus a

control. The study area was maintained on a 16 h daylight photoperiod. No aeration of the test solution and no medium renewal were supplied during the test. The number of immobile daphnia were recorded after 24 and 48 h. Water quality parameters of temperature, dissolved oxygen and pH were measured throughout the test and were within acceptable limits.

RESULTS

Concentration mg/L		*Number of D. magna*	*Cumulative Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	-	20	0	0
3.2	-	20	0	0
5.6	-	20	0	0
10	-	20	0	1
18	-	20	4	8
32	-	20	11	17
56	-	20	16	20
100	-	20	20	20
180	-	20	20	20
320	-	20	20	20

EC50 20 mg/L (CI: 16-24 mg/L) at 48 h
NOEC (or LOEC) 10 mg/L at 48 h
Remarks – Results The lowest concentration resulting in 100% immobilisation at 48 h is 56 mg/L. All results are expressed in terms of nominal concentrations. All measured concentrations remained within the range of 103-110% of the nominal value throughout the study.

CONCLUSION The notified chemical is harmful to *Daphnia magna*.

TEST FACILITY Huntingdon Research Centre, Ltd (1991k)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE Eugewhite (mixed isomers)

METHOD ECOSAR Program (v0.99f)

RESULTS
Remarks – Results The predicted 96 h EC50 of 9.255 and 24.213 mg/L for green algae were derived from vinyl/allyl ethers and phenols, respectively, by using the ECOSAR Program. These were calculated by assuming a Log Kow of 2.74 and a water solubility of 172.2 mg/L. The predicted values of 9.255 and 24.213 mg/L would respectively lead to the conclusions that the notified chemical would be toxic or harmful to green algae.

CONCLUSION The test substance is considered to be toxic to harmful to green algae.

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Based on the release described in Section 5.4, the majority of the notified chemical will be discharged to sewer. For that proportion of the chemical 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 Technical Guidance Document, 1996). These estimates, based on the chemical having a calculated Henry's constant of 4.03 x 10^{-4} Pa/m^3/mole based on measured

vapour pressure, water solubility and a Log Pow of 2.31, indicate that the chemical would be expected to partition into the air, water and sewer sludge compartments and degrade as follows:

Air	Water	sludge
0%	99%	1%

Using a worst-case scenario, it has been assumed that all 1000 kg of Eugewhite (mixed isomers) used is discharged through sewerage systems throughout Australia and none is attenuated within these systems. Assuming a national population of 19.5 million and that each person contributes an average 200 L/day to overall sewage flows and 99% partition into water, the predicted Eugewhite concentration in sewage effluent on a nationwide basis is estimated as 0.7 µg/L.

Amount entering sewer annually	1000 kg
Population of Australia	19.5 million
Amount of water used per person per day	200 L
Number of days in a year	365
Estimated PEC	0.7 µg/L

Based on the respective dilution factors of 1 and 10 for inland and ocean discharges of effluents, the PECs of Eugewhite in freshwater and marine water may approximate 0.7 µg/L or 0.07 µg/L, respectively, ie a maximum of 0.32 µg/L or 0.032 µg/L notified chemical in freshwater or marine water, respectively.

Fate

The notified chemical is considered to be slightly volatile. Therefore, its loss to the atmosphere is unlikely to be significant. In view of the low log Pow and the ready solubility of the notified chemical, the bioaccumulation potential is considered to be low (Connell 1990). The calculated log K_{oc} of 2.81 appears to indicate that the notified chemical is likely to be of low mobility. Thus leaching in landfill is unlikely to occur and abiotic or slow biotic processes are likely to be largely responsible for the degradation of the notified chemical disposed of to landfill.

9.1.2. Environment – effects assessment

In summary the aquatic toxicity data indicate:

Rainbow trout (*Oncorhynchus mykiss)*: 96 h LC50	24 mg/L
Daphnia magna: 48 h EC50	20 mg/L
Green algae: 72 h LC50 (calculated)	9.2-24.2mg/L

Using the lowest EC50 of 20 mg/L for *Daphnia magna*, a predicted no effect concentration (PNEC) of 20 µg/L for Eugewhite (mixed isomers) has been derived by dividing the LC50 value by a safety factor of 1000 since toxicity data are available for two trophic levels. It should be noted that the results for algae were calculated values which should be treated with caution.

9.1.3. Environment – risk characterisation

On the basis of the low volumes used (ie. 1000 kg/year total for mixed isomers) and nationwide and diffuse use of the notified chemical, it is not considered to pose an unacceptable risk to the health of aquatic life based on its reported use and estimated disposal patterns. The PEC/PNEC ratio for the mixed isomers for the aquatic environment, assuming nationwide use, is 3.5×10^{-2} (0.7/20) and 3.5×10^{-3} (0.07/20), for freshwater and marine water, respectively. These values are significantly less than 1, further indicating no immediate concern to the aquatic compartment.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

The maximum occupational exposure is expected for workers handling the highest concentration

of the notified chemical (0.9%) as a component of fragrance oil, during formulation of the finished product. Dermal/eye exposure to drips and spills may occur while blending of the ingredients with the notified chemical from drums to mixing vessels. This is expected to be infrequent (approximately 2 days/year) and the use of gloves and other protective equipments should minimise exposure.

All other workers (waterside, transport & warehouse) are expected to handle the highest concentrate of the notified chemical (0.9%) only in sealed containers, or handle only the finished products containing up to 0.18% notified chemical. Exposure of waterside, transport & warehouse workers is likely to occur only in the event of an accident/spill.

9.2.2. Public health – exposure assessment

Public exposure to the notified chemical is expected to be low and will occur through the use of the cosmetic and domestic products containing 0.018 – 0.18% notified chemical. The highest exposure is expected to arise from the use of skin creams, which may be applied to large skin areas.

9.2.3. Human health - effects assessment

The substance used in toxicity testing, Eugewhite (mixed isomers), is of low acute oral toxicity in rats (LD50 > 2000 mg/kg bw, no mortality at this dose), although mortalities were seen on testing levels slightly higher than this, eg 2/4 animals at 2500 mg/kg bw. It is of low dermal toxicity in rats with dermal LD50 > 2000 mg/kg bw. No inhalation toxicity data was provided. It is essentially non-irritant to rabbit skin, but is irritating to rabbit eyes, with corneal effect persisting beyond 7 days. The eye irritation scores are sufficiently low as to not require the test substance to be classified as an eye irritant.

A number of skin sensitisation test reports were submitted. In a Buehler test, slight responses were seen in test animals only, and the results did not give a clear indication of whether a true sensitisation potential exists. However, in a Maximisation test, clear-cut results indicating sensitisation potential were obtained. Testing in a human repeat insult patch test at 10% did not show any sensitisation potential.

In a 28 day repeat dose study in rats, a NOEL of 55 mg/kg bw/day was established. At the next highest dose, 1000 mg/kg bw/day, only slight effects were seen, particularly a (probably adaptive) increase in liver weights. Supporting biochemical and histopathological evidence of toxicity was not seen.

The test substance was not found to be mutagenic or clastogenic in two in vitro mutagenicity studies.

It is not possible to classify the notified chemical based on the data provided, as all data refers to the mixed isomers and it is not possible to apportion the effects between the two isomers. However, as the mixed isomers (in fixed proportion) are the only form in which the notified chemical will be used, it is relevant to classify the mixed isomers. Under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999), Eugewhite (mixed isomers) is classified as a skin sensitiser, with the risk phrase R43 “May cause sensitisation by skin contact”.

9.2.4. Occupational health and safety – risk characterisation

The main hazard presented by the notified chemical arises from sensitisation on repeated skin contact; however human repeat insult patch testing indicated that the notified chemical is not a highly potent sensitiser under these conditions. The low vapour pressure indicates that inhalation is not likely to be a significant exposure route.

Occupational exposure is expected to be low for workers handling the highest concentration of the notified chemical (0.9%), as workers who handle it in concentrated form will do so on an infrequent basis. Although occupational exposure to workers handling the notified chemical is expected to be low, appropriate personal protection should be worn during handling of the

fragrance oil containing the notified chemical due to the skin sensitisation risk.

Waterside, warehouse and transport workers will only be exposed to the notified chemical in the event of an accident or damage to packaging.

The notified chemical is expected to have low hazard at the concentration used in finished products (maximum of 0.18% in perfumes), resulting in low occupational risk for handlers of the finished products.

9.2.5. Public health – risk characterisation

While there may be widespread exposure to products containing the notified chemical, it is expected to have low hazard at the concentration used in cosmetics and domestic products. This is the only form in which the public will use the notified chemical, and the products containing higher concentration of the notified chemical (eg perfumes) will only be used in extremely small quantities. Therefore, the risk to the public resulting from the use of the notified chemical is expected to be very low.

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

10.1. Hazard classification

Eugewhite (mixed isomers) is classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999). The classification details are:

R43 May cause sensitisation by skin contact

According to the OECD (2002) Globally Harmonised System for the Classification and Labelling of Chemicals, Eugewhite (mixed isomers) is categorised as **Chronic III** for effects on aquatic organisms. For human health effects, the classification is:
Skin sensitiser Category 1
Symbol: Exclamation Mark
Signal word: Warning
Hazard statement: May cause allergic skin reaction

10.2. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

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 No Significant Concern to public health when used as a fragrance ingredient in cosmetic and domestic products.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of Eugewhite (mixed isomers) provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets*

(NOHSC, 2003). It is 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 Eugewhite (mixed isomers) provided by the notifier was 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 Eugewhite (mixed isomers):
  - R43 May cause sensitisation by skin contact

- Use the following risk phrases for products/mixtures containing >1% Eugewhite (mixed isomers):
  - R43 May cause sensitisation by skin contact
  - S24 Avoid contact with skin
  - S37 Wear suitable gloves

CONTROL MEASURES
Occupational Health and Safety

- Workers who become sensitised to Eugewhite (mixed isomers) should not handle products containing the notified chemical in the workplace

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - Protective gloves, safety glasses or goggles, industrial clothing and footwear

  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

- Do not allow concentrated fragrance oils or contaminated packaging to enter drains, sewers or water courses.

Disposal

- Eugewhite (mixed isomers) should be disposed of by placing material and absorbent into sealed container and dispose of to landfill.

Emergency procedures

- In case of a spill, remove ignition sources. Contain using sand or inert powder and earth. Collect and seal in properly labelled drums for disposal in accordance with

relevant Government regulations. Prevent runoff into drains or waterways.

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(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.

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