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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Erythrulose

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Director
NICNAS

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FULL PUBLIC REPORT

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Bronson and Jacobs Pty Ltd (ABN: 81 000 063 249)
5 Parkview Drive
HOMEBUSH BAY NSW 2140

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

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

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

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
EU (2003).

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
2-butanone, 1,3,4-trihydroxy-

OTHER NAME(S)
Erythrulose

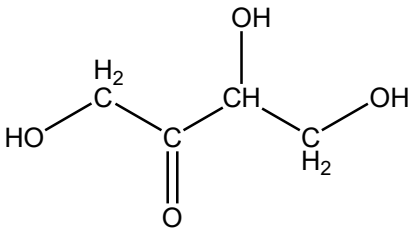
MARKETING NAME(S)
Erythrulose Pentapharm

CAS NUMBER
533-50-6*

MOLECULAR FORMULA
$C_4H_8O_4$

* =This is the CAS Number for L-Erythrulose which was the chemical assessed.

STRUCTURAL FORMULA



MOLECULAR WEIGHT
120

SPECTRAL DATA

ANALYTICAL METHOD	Ultraviolet/visible light (UV/VIS) Spectra
Remarks	λmax =278.77nm, ε=0.315 pH =7 λmax =279.20nm, ε= 0.286 pH =1.55 λmax=297.05nm, ε= 1.591 pH =11.90 Spectroscopy undertaken with sample from L-Erythrulose Lot 405045[307-01].
TEST FACILITY	Pentapharm (2002)

SPECTRAL DATA

ANALYTICAL METHOD	Infrared (IR) Spectrum
Remarks	Peaks at 3325.95, 2941.11, 2890.55, 2158.83, 1725.22, 1642.79, 1412.40, 1234.77, 1147.94, 1103.40, 1042.62, 998.54, 932.51, 881.06 cm^{-1}. Spectroscopy undertaken with sample from L-Erythrulose Lot 405045 [307-01]
TEST FACILITY	Pentapharm (2002)

SPECTRAL DATA

ANALYTICAL METHOD	Nuclear Magnetic Resonance (NMR) Spectra ^{1}H Spectrum Shifts: 4.78, 4.63, 4.58, 4.55, 4.50, 4.46, 4.45, 4.44, 3.87, 3.86 (3 peaks) ppm ^{13}C Spectrum Shifts: 212.37, 76.61, 66.44, 63.71, 40.22, 40.02, 39.81, 39.60, 39.39, 39.18 ppm
Remarks	Spectroscopy undertaken with sample from L-Erythrulose Lot 405045 [307-01]
TEST FACILITY	Pentapharm (2002)

SPECTRAL DATA

ANALYTICAL METHOD	Mass (MS) Spectrum Peaks observed at 58.9, 60.8, 72.0, 74.9, 86.9, 88.9, 98.7, 99.8, 100.9, 101.6, 118.1, 119.0, 120.0 m/z
Remarks	Spectroscopy undertaken with sample from L-Erythrulose Lot 405045 [307-01]
TEST FACILITY	Solvias (2002)

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD	High performance liquid chromatography
Remarks	A high performance liquid chromatographic (HPLC) method for the quantitative analysis of the test substance (Erythrulose Batch 405045/307-01 80% notified chemical and 20%water) was developed.

TEST FACILITY NOTOX (2003a)

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD UV/VIS, IR, NMR, and Mass spectroscopy

3. COMPOSITION

DEGREE OF PURITY
75-82%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

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

Chemical Name	Water		
CAS No.	7732-18-5	*Weight %*	13-20
Chemical Name	Sulphated ash		
CAS No.		*Weight %*	<1.5

ADDITIVES/ADJUVANTS
None

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported in 1 kg to 25 kg steel drums as a ready to use ingredient of cosmetic mixtures.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	1	1	1	1	1

USE
The notified chemical will be used as a self tanning agent (skin colourant) in topical applications such as tanning lotions and day tinting cremes at levels between 1.5% and 5.0%.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Sydney.

IDENTITY OF MANUFACTURER/RECIPIENTS
The imported chemical will be stored at Bronson and Jacobs warehouse Homebush Bay, New South Wales, for distribution to customers. The cosmetic products containing the notified chemical will be manufactured at various sites mainly in Sydney and Melbourne.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in polyethylene bags inside 1 kg and 25 kg steel containers.

The end use containers will be High Density Polyethylene (HDPE) and PVC bottles 50-500 mL in size.

5.2. Operation description

The notified chemical is weighed and pumped directly into a mixing tank, where it is blended with other ingredients of the tanning solutions or day cremes. During the mixing process, laboratory staff will sample end use product for quality control testing. Once approved, the final product will be transferred by filling lines to the end use containers. The end use product will be stored and despatched to the customers.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Laboratory Workers	2	2 hours/day	2 days/year
Manufacturing workers	4	8 hours/day	2 days/year
Filling	4	8 hours/day	2 days/ year

Exposure Details

Transport and Storage

Transport and storage workers handling the imported product, containing 78-82% (w/w) notified chemical, are not expected to be exposed to the notified chemical during transport except in the case of an accidental spill.

The finished product, containing 1.5-5.0% (w/w) of the notified chemical, will be transported to numerous sites.

Dermal exposure will be main route of exposure for transport and storage workers. Normally these workers are likely to wear overalls, safety boots, and gloves when handling containers.

Reformulation

At reformulation sites, the notified chemical will be weighed and pumped from steel containers into the blending tank. During the connection and disconnection of lines, incidental dermal and ocular contact from splashes, drips, and spills is possible.

Compounders will wear safety glasses with shields, gloves, apron, and coveralls.

Following blending the finished products are packaged into 50-500mL HDPE and PVC bottles. During the filling and capping of the bottles accidental dermal and ocular contact may occur. Packers monitoring the filling lines and capper would wear safety glasses, gloves and work uniforms.

The blending tank and the transfer lines are cleaned by rinsing with water and detergents. Maintenance workers handling the equipment used for blending and filling may come into dermal and ocular contact with residues containing the notified chemical (approximately 300-500 grams per tank). These workers will wear eye protection and gloves.

Laboratory Staff

Laboratory staff will take samples of the notified chemical as imported in the additive package as well as the final products for testing. During sampling and analysis there may be dermal contact. The laboratory testing will take a few minutes per batch. It is expected laboratory staff will wear adequate protection for the eyes, skin, body, and hands.

5.4. Release

RELEASE OF CHEMICAL AT SITE

There will be no release due to manufacture of the notified chemical as it will not be manufactured in Australia but will be used in the formulation of cosmetic products. In this process the potential sources of release include spills, process equipment cleaning, and import container residues. Loss due to spills will be minimal due to the size and type of the import containers. It is estimated that up to 3% (ie up to 30 kg) may be released annually due to equipment cleaning and up to 1% (ie up to 10 kg) via

residues in empty import containers. Equipment cleaning effluent will go into the onsite effluent treatment plant. Container residues may be rinsed into the batch or disposed of with the container via a licensed waste contractor.

RELEASE OF CHEMICAL FROM USE
The cosmetic product will be applied to the skin and then washed off during bathing into the aquatic environment. Up to 1% (10 kg) annually will remain in the empty container.

5.5. Disposal

Disposal from the product formulation plants, will consist of the release of treated effluent into the sewer system, containing up to 30 kg of notified chemical annually, and the disposal of containers and solid wastes (including cleanup rags), up to 10 kg annually, to landfill via a licensed waste contractor.

The empty container will be disposed of by the end user in the general domestic garbage the thence to landfill. Up to 95% of the imported notified chemical will be released into the aquatic environment during bathing.

5.6. Public exposure

The notified chemical as imported will not be available to the public. The finished self tanning lotions and crèmes containing the notified chemicals at 1.5 – 5% (w/w) will be widely available to the public. The cremes will be used twice daily and the lotions will be used once daily.

6. PHYSICAL AND CHEMICAL PROPERTIES

Erythrulose is approximately 80% notified chemical 20% water. Erythrulose (Batch 405045/307-01) was used to determine the freezing point, boiling point and flammability. Erythrulose (Batch 405829/307-01, composition not given) was used to determine the density, vapour pressure and flash point.

Appearance at 20ºC and 101.3 kPa Yellow viscous liquid.

Freezing Point <-80.5ºC

METHOD OECD TG 102 Melting Point/Melting Range
EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.

Remarks Erythrulose had no defined freezing point or freezing range. With a decrease in temperature, the viscosity of test substance increased without showing a clear phase transition of the liquid into the solid state.

TEST FACILITY NOTOX (2002a)

Boiling Point Not determined

METHOD OECD TG 103 Boiling Point.
EC Directive 92/69/EEC A.2 Boiling Temperature.

Remarks An exothermic effect was observed at temperatures above 180ºC, and in combination with observed changes of colour of the test substance, indicated reaction or decomposition of the test substance at these temperatures. Two endothermic effects that were observed at temperatures below 180ºC and were probably caused by evaporation of different components of the test substance. Reaction or decomposition, are likely to have started at a temperature below 180ºC and this probably interfered with the process that caused the second endothermic effect.

There was no indication for reaction or decomposition of the test substance, at temperatures up to 130ºC. Boiling of the test substance was not observed below the temperature at which reaction or decomposition started.

TEST FACILITY NOTOX (2002b)

Density 1390 kg/m^3 at 20ºC

METHOD OECD TG 109 Density of Liquids and Solids.

EC Directive 92/69/EEC A.3 Relative Density.

Remarks A glass pycnometer was used.

TEST FACILITY NOTOX (2003b)

Vapour Pressure 0.861 kPa at 20°C

METHOD OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.

Remarks The static technique was used with a capacitance manometer fitted. A measured amount of the test substance was placed in the sample vessel which was then attached to the mechanism. After evacuation the vessel was immersed in thermostatic water bath at various temperatures and the vapour pressure measured. The vapour pressure at 20°C was extrapolated from the curve. Since the measured vapour pressures were greater than 0.1 Pa, no correction for thermal transpiration was made.

The notified chemical is highly volatile (Mensink, 1995).

TEST FACILITY NOTOX (2003c)

Water Solubility ≥1331 mg/L at 19.6±1°C

METHOD OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.

Remarks A measured amount of test substance (1331 mg) was added to 1 mL of distilled water in a glass tube and was stirred magnetically for 12 days. After this the solution was visually checked for any undissolved material, of which none was observed.

TEST FACILITY NOTOX (2002d)

Hydrolysis as a Function of pH Not determined.

Remarks The notified chemical is stable for 18 months in water at low temperature. However, at pH greater than 5.5 it becomes unstable, and may eventually hydrate to an aliphatic tetra alcohol.

Partition Coefficient (n-octanol/water) log Pow = -2.16 at 20°C

METHOD OECD TG 107 Partition Coefficient (n-octanol/water)
EC Directive 92/69/EEC A.8 Partition Coefficient.

Remarks The notified chemical was added to three different ratios of n-octanol and water (1:1, 1:2 and 2:1). The test vessels were shaken by hand for 5 mins, centrifuged at 3500 g for 5 mins at 20°C and samples from each phase were analysed by HPLC.

The value derived by the Rekker calculation method was very similar at –2.5.

TEST FACILITY NOTOX (2003d)

Adsorption/Desorption log K_{oc} <1.32 at 35°C

METHOD OECD TG, Proposal for new guideline 121: "Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatograph (HPLC)".

Remarks The estimation software Pkalc version 5 was used to calculate the expected pKa values for the notified chemical. From this estimation it was determined that in the pH range 5.5–7.5 the substance would be in its non-ionised form. Therefore the HPLC mobile phase was not buffered in the study.

Phenol, at 1.3 g/L, with a known log K_{oc} of 1.32, was used as a reference substance.

TEST FACILITY NOTOX (2003e)

Dissociation Constant Not determined

Remarks While under extreme pH conditions the notified chemical may become ionised, in the environmental pH range of 4-9 this is unlikely.

Particle Size Not determined.

Remarks The notified chemical is a component of an aqueous solution.

Flash Point Not determined.

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks The flashpoint of Erythrulose was determined using a Pensky-Martens closed cup flash point apparatus. In two separate tests no flash point was observed up to 122°C and 121°C, at which temperatures the test substance boiled out of the test cup. After the test, the test substance appeared to be a light brown liquid.
TEST FACILITY NOTOX (2003f)

Flammability Limits Not flammable

METHOD EC Directive 92/69/EEC A.12 Flammability (Contact with Water).
Remarks The notified chemical does not contain groups that might lead to evolution of highly flammable gases in dangerous quantities. No metals, transition metals, boron or silicon are present. Therefore it can be concluded that the test substance is incapable of developing a dangerous amount of (flammable) gas in contact with air, damp air or water. No spontaneous ignition nor evolution of gas occurred when a small quantity of the test substance was added to double distilled water. Erythrulose is know to be water soluble.
TEST FACILITY NOTOX (2002d)

Autoignition Temperature 340°C

METHOD 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks The lowest measured autoignition temperature was 342°C at an injection volume of 100 µL. Rounding down to the nearest 5°C gives an autoignition temperature of 340°C.
TEST FACILITY NOTOX (2003g)

Explosive Properties Not explosive

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks The calculated oxygen balance of the notified is -107%, which indicates potential for explodability. However, there are no bond groupings known to confer explosive properties (plosophores) and explosive enhancing groups (auxoploses) present in the structure. The relatively high oxygen balance is due the presence of the two hydroxyl groups and a carbonyl group in a relatively small molecule.
The notified chemical does not contain any chemically unstable or highly energetic groups that might lead to an explosion.
TEST FACILITY NOTOX (2002h)

Oxidising Properties No oxidising properties

METHOD EC Directive 92/69/EEC A.17 Oxidising Properties (Solids).
Remarks Erythrulose consists of 80% of the active ingredient and 20% water. Water is known not to be oxidising. On examination of the structure of the active ingredient, it was determined that the substance is incapable of burning, when mixed with cellulose, at a higher or equal rate with the maximum burning rate of a reference mixture of cellulose and barium nitrate. The oxygen in the molecule is chemically bonded to carbon atoms.
TEST FACILITY NOTOX (2003i)

Pyrophoric Properties Not pyrophoric.

METHOD	EC Directive 92/69/EEC A.13 Pyrophoric Properties of Solids and Liquids
Remarks	From the structural formula of the notified chemical, it can be concluded that it is not pyrophoric. The notified chemical does not contain any chemical group that might lead to spontaneous ignition a short time after coming into contact with airat room temperature. Experience in handling the test substance (80% notified chemical 20% water) shows that it does not ignite coming in contact with air.
TEST FACILITY	NOTOX (2002e)

Reactivity

Remarks	The notified chemical is expected to be stable under normal environmental conditions and has no oxidising potential.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion for test substance containing notified chemical*
Rat, acute oral LD50 >2000 mg/kg bw	low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly-irritating
Guinea pig, skin sensitisation – adjuvant test.	no evidence of sensitisation.
Rat, repeat dose oral toxicity – 28 days.	NOEL=1000 mg/kg bw/day
Phototoxicity and Photoallergic Potential	no evidence of phototoxicity or photoallergenicity
Repeat Application Dermal Irritation	non irritant
Genotoxicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosomal aberration	genotoxic
Dermal Drug Delivery and Percutaneous Absorption	did not penetrate human skin in vitro within 48 hours
Irritative potential in humans	extremely low potential

7.1. Acute toxicity – oral

TEST SUBSTANCE — Product No 7451/307-01 (81.5% notified chemical)

METHOD — OECD TG 401 Acute Oral Toxicity – Limit Test.
EC Directive 92/69/EEC B.1 Acute Toxicity (Oral) – Limit Test.

- Species/Strain: Rat/Sprague–Dawley
- Vehicle: None.
- Remarks - Method: No significant protocol deviation.

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: No signs of systemic toxicity were noted.
- Effects in Organs: No abnormalities were observed necroscopy.
- Remarks - Results: All animals showed expected gain in bodyweight.

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

TEST FACILITY — Safepharm Laboratories (1994a).

7.2. Irritation – skin

TEST SUBSTANCE — Product No. 7451/307-01 (81.5% notified chemical)

METHOD — OECD TG 404 Acute Dermal Irritation/Corrosion.
EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).

- Species/Strain: Rabbit/New Zealand White
- Number of Animals: Three
- Vehicle: Distilled water
- Observation Period: 14 days
- Type of Dressing: Semi-occlusive.
- Remarks - Method: No significant protocol deviation.

A 20% aqueous dilution of the test substance was used.

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 hour	1 hour
Oedema	0	0	0	-	-	-

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

Remarks - Results: Very slight erythema was noted at one treated skin site in one female one hour after patch removal. No skin reactions were noted at 24 hours. Yellow coloured staining was noted at all treated skin sites throughout the test and observation period. The staining did not affect the evaluation of skin responses.

CONCLUSION: A 20% aqueous dilution of the test substance is slightly irritating to the skin.

TEST FACILITY: Safepharm Laboratories (1994b).

7.3. Irritation – eye

TEST SUBSTANCE: Product No. 7451/307-01 (78.5% notified chemical)

METHOD: OEC D TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain: Rabbit/New Zealand White
Number of Animals: Three
Observation Period: 72 hours
Remarks - Method: No significant protocol deviation. A 20% aqueous dilution of the test substance was used.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0	0	0	1	1 hour	0
Conjunctiva: chemosis	0	0	0	0	-	0
Conjunctiva: discharge	0	0	0	1	1 hour	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results: No corneal or iridial effects were noted during the study. Minimal conjunctival irritation was noted in one treated eye one hour after treatment. All treated eyes appeared normal 24 hours after treatment.

CONCLUSION: A 20% aqueous dilution of the test substance is sightly irritating to the eye.

TEST FACILITY: Safepharm Laboratories (1994c).

7.4. Skin sensitisation

TEST SUBSTANCE: Product No 7451/307-01 (81.5% notified chemical)

METHOD: OECD TG 406 Skin Sensitisation – Magnusson & Kligman Maximisation.

Species/Strain	Guinea pig/Dunkin-Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: <1% (w/v) in distilled water topical: 2% (v/v) in distilled water
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: 20% (w/v) in distilled water (maximum concentration requested by sponsor) topical: 20% (v/v) in distilled water
Signs of Irritation	Intradermal induction. Very slight to well defined erythema was noted at the intradermal induction sites of all test group animals at 24 hours with very slight erythema at 48 hours. No skin reactions were noted at the intradermal induction sites of control group animals at 24 hours. Due to a technical error, the 48-hour observation of the intradermal induction sites of control groups was not performed. This deviation was considered not to affect the purpose or integrity of the study Topical Induction Light brown/yellow coloured staining was noted at the induction sites of all test group animals at 1 and 24 hours. The staining did not affect evaluation of skin responses. Very slight to well defined erythema was noted at the induction sites of all test groups animals at 1 hour. Very slight erythema was noted at the induction sites of nine test group animals at the 24-hour observation. Bleeding from the intradermal induction sites was noted at the 1 hour. No skin reactions were noted at the treatment sites of controls group animals at 1 and 24 hours.
CHALLENGE PHASE	
1st challenge	topical: 20% and 10% (v/v)
Remarks - Method	None.

RESULTS

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

Remarks - Results	Light brown/ yellow coloured staining was noted at the challenge sites of all test and control group animals at 24 and 48 hours. The staining did not affect evaluation of skin responses. No skin reactions were noted at the challenge sites of the test and control group animals at 24 and 48 hours.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the test substance under the conditions of the test.
TEST FACILITY	SafePharm Laboratories (1994d)

7.5. Repeat dose toxicity

TEST SUBSTANCE	Product 405829/307-01 (80.3% notified chemical)
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents. EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).
Species/Strain	Rat/Wistar Crl (WF)

Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week; Post-exposure observation period: none
Vehicle	Water (Milli-U)
Remarks - Method	The dose levels used were based on the results of a 5-day range finding study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	5/sex	0	0/10
II (low dose)	5/sex	50	0/10
III (mid dose)	5/sex	150	0/10
IV (high dose)	5/sex	1000	0/10

Mortality and Time to Death

No mortality occurred during the study period.

Clinical Observations

There were no clinical signs of toxicity or behavioural changes over the 28-day observation period. Incidental findings observed included yellow staining of the fur, chromodacryorrhoea, a broken tail apex and alopecia on the shoulders. These incidental findings are commonly noted in rats of the age and strains used under the test conditions. No further corroborative findings and/or no dose response relationship were found and therefore these were considered of no toxicological significance.

No changes were observed in hearing ability, pupillary reflex, static righting reflex, and grip strength in the treated animals compared to control animals. There were no treatment related changes in motor activity observed.

Body weight of the treated animals remained within the same range as controls over the 4- week study period.

Statistically significant (Dunnett - test based on pooled variance significant at 1%) reductions of body weight gains in males at low and high doses until the end of the study and in males at mid dose during week 2 only were observed. The absence of a dose related reduction in weight gain and further corroborative findings in the study indicate these reductions were not of toxicological significance.

Statistically significant (Dunnett –test based on pooled variation significant at 5%) increases in body weight in females at mid dose during week 3 were considered to have occurred by chance and were not considered to be of toxicological significance.

Food consumption before and after allowance for body weight was similar between treated and control animals.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Males receiving the high dose showed a reduced partial thromboplastin time. A reduction of this parameter is generally considered not to be of toxicological significance. No toxicologically relevant changes occurred in haematological parameters of the other treated rats.

There were no differences noted between control and treated rats in clinical chemistry parameters that were considered to be treatment related. The decreased mean glucose values of males treated with the low dose was within the normal range and occurred in the absence of other supportive treatment related findings. It was thus concluded that this alteration was of no toxicological significance.

Effects in Organs

No toxicologically relevant alterations were observed at necroscopy.

Incidental findings among the animals included red foci on and/or red discolouration of the thymus, dark red

discolouration and/or enlargement of the mandibular lymph node, broken tails, a dark red papillary process of the liver and watery–clear fluid containing cysts on the uterus. These findings are occasionally seen among test and control animals. The absence of a treatment related distribution and/or the presence of these findings in controls as well as the treated groups, suggests these signs were not of toxicological significance. Watery fluid in the uterus, found in two high dose females, is related to the stage of the oestrous cycle and is a normal finding.

Organ weights and organ to body weight ratios of treated animals were considered similar to those of control animals.

Weight of the kidneys and spleen of females treated at mid dose showed a statistically significant increase (significance level not given). Based on the absence of the similar increases in the high dose group as well as the lack of related macroscopic or microscopic findings, these increases were considered not to be toxicologically significant.

There were no microscopic findings recorded which could be attributed to treatment with the test substance. All microscopic findings were within the range of the background pathology encountered in rats of the age and strain used and occurred at similar incidence and severity in both control and treated rats.

Remarks – Results
There were no changes in clinical appearance, performance of functional observation, body weight and food consumption measurements, or alteration during clinical laboratory investigations, macroscopic examination, organ weight determination, and microscopic examination that were considered to be treatment related.

CONCLUSION
The No Observed Effect Level (NOEL) was established as 1000 mg/kg bw/day in this study, due to absence of any toxicologically significant effects at this dose and lower doses.

TEST FACILITY NOTOX (2003j).

7.5. Repeat Application Dermal Irritation

TEST SUBSTANCE Product No.7451/307-01 (81.5% notified chemical)

METHOD Safepharm Standard Protocol Number SPL 50.

Remarks - Method Three male and three female albino Dunkin-Hartley guinea pigs had both flanks clipped with veterinary clippers and shaved using an electric razor. Fifty microlitres (μL) of a 20% (v/v) aqueous solution of the test substance was spread evenly over an approximately 2 cm x 2 cm area of the clipped skin on the left flank of each animal. The test site remained non-occluded. 0.05 mL of sterile distilled water (control substance) was applied to the right flank. The animals were returned to their cages. Approximately twenty-four hours after the first exposure, the test and control substances were re-applied to the appropriate sites. This was repeated over fourteen days. To prevent excessive staining by the test substance, the treatment sites were swabbed with cotton wool soaked in water to remove excessive residual test substance approximately two hours prior to reapplication. The control sites were treated in a similar manner. Shortly before each daily application and approximately 24 hours after the fourteenth application the test sites were examined for evidence of primary irritation and scored using the Draize scheme.

RESULTS

Remarks - Results There was no evidence of erythema or oedema at the test or control sites throughout the study period. There were no abnormal clinical observations made during the study period. All animals showed a bodyweight increase over the study period. Brown coloured staining was noted at the test sites throughout the study period. The staining did not affect the evaluation of the skin reactions.

CONCLUSION A 20% (v/v) aqueous solution of the test substance was considered non irritant to guinea pig skin under the conditions of the study.

TEST FACILITY Safepharm Laboratories (1995a).

7.6. Phototoxic and Photoallergic Potential

TEST SUBSTANCE Product No 7451/307-01 (81.5% notified chemical)

METHOD SafePharm Standard Method Number SPL 205

Remarks - Method Fifteen female albino Dunkin-Hartley guinea pigs were used for the main study. Five animals were allocated to the phototoxicity group (Group I), five to the photoallergy group (Group II) and five to the positive photoallergy group (Group III).

In order to assess the phototoxic potential of the test substance, the Group I animals received single topical applications of test substance at concentrations of 20% (v/v) in distilled water, with or without subsequent irradiation with ultraviolet light (UVA; 320-400 nm). The dosage of UVA was approximately 10Joules/cm^2 skin. These animals similarly received single topical applications of 0.005% (w/v) 8-methoxypsoralen in 95% aqueous ethanol (positive phototoxic substance) with and without subsequent UVA irradiation. Skin reactions were recorded 4, 24, and 48 hours after irradiation.

To assess the photoallergenic potential of the test substance, Group II animals received single topical applications of the test substance at a concentration of 20% (v/v) in distilled water, followed by exposure to UVA (approximately 10 Joules/cm^2 skin) on days 7, 8, 9, 10, and 11. This formed the induction phase of the photoallergenicity determination. On day 35 the same animals received topical applications of the test substance at concentrations of 20% and 10% (v/v) in distilled water followed by exposure to UVA (10 Joules/cm^2 skin). This formed the challenge phase of photoallergenicity determination. The challenge reactions were evaluated approximately 24 and 48 hours after irradiation.

Group III animals were used to validate the photoallergenicity phase. Group III animals were treated in a similar manner to the Group II animals but were treated topically with a 5% aqueous solution of the known photallergen 6-methylcoumarin.

RESULTS

Remarks - Results No evidence of erythema or oedema was noted in any Group I animal following treatment with 20% (v/v) of the test substance in distilled water. No skin reactions were apparent in the Group II animals after treatment with the test substance at concentrations of 20% and 10% (v/v) in distilled water during the photoallergenicity phase of the study. The positive controls used in test produced phototoxic and photoallergic reactions in animals under the conditions of the test.

CONCLUSION The test substance when applied at concentrations of up to 20%(v/v) in distilled water produced no evidence of phototoxicity or photoallergenicity under the conditions of the test.

TEST FACILITY SafePharm Laboratories (1995b).

7.7. Genotoxicity – bacteria

TEST SUBSTANCE Product No 7451/307-01 (81.5% notified chemical)

METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure.
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100. *E. coli*: WP2*uvr*A.
Metabolic Activation System	S9 fraction from Aroclor 1254 induced rat liver.
Concentration Range in Main Test	a) With metabolic activation: 0, 50, 150, 500, 1500, 5000 µg/plate. b) Without metabolic activation: 0, 50, 150, 500, 1500, 5000 µg/plate.
Vehicle	Distilled water.
Remarks - Method	No significant deviation in protocol.

RESULTS

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

Remarks – Results	No toxicity was exhibited in any of the strains of bacteria used. No significant increases in the numbers of revertant colonies of bacteria were recorded for any of the strains of bacteria used, at any dose level, either with or without metabolic activation. The positive control substances all produced marked increases in the number of revertant colonies and the activity of the S9 fraction was found to be satisfactory.
CONCLUSION	The test substance was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Safepharm Laboratories (1995c).

7.8. Genotoxicity – in vitro

TEST SUBSTANCE	Erythrulose (Batch 401089/307-01) (78.8% notified chemical)
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test. EC Directive 2000/32/EC B.10 Mutagenicity - In vitro Mammalian
Cell Type/Cell Line	Chinese Hamster/V79
Metabolic Activation System	S9 from β Naphthoflavone and Phenobarbital induced rat liver.
Vehicle	Distilled water.
Remarks – Method	

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	500*, 1000*, 2500*, 5000*	4	20
Test 2	500*, 1000*, 1500*, 2500*, 5000*	20	20
Present			
Test 1	500*, 1000*, 2500*, 5000*	4	20

*Cultures selected for metaphase analysis.

RESULTS

Remarks - Results

In Test 1, a clear and dose-dependent reduction of mitotic index and of the cell density was observed without metabolic activation (5000 μg/mL: mitotic index 12%, cell density 51% compared to control values). With metabolic activation, a reduction in only cell density was seen (5000 μg/mL: cell density 45% compared to control values). This differed to the pre experiment in which no toxicity occurred up to 5000 μg/mL.

In Test 2, reductions of mitotic index and cell density were seen (5000 μg/mL: mitotic index 38%, cell density 57% compared to control values). These reductions were not as severe as in Test 1 and may be attributable to experimental conditions. In Test 1, treatment with test substance was performed with serum free medium while Test 2 was undertaken in serum complete medium. This suggests that the reactive molecule(s) leading to cell toxicity are partially bound by serum proteins.

In Test 1 without metabolic activation, the test substance increased the frequency of cells with chromosomal aberrations in a biologically relevant and dose related manner. At the 2500 μg/mL concentration, 4.5% aberrant cells were found. At 5000 μg/mL, 18.5% aberrant cells were found in 130 metaphases scored. The aberration rates of the cells after treatment with the test item in Test 1 with metabolic activation and in Test 2 without metabolic activation were near the range of the negative control value and within the historical control range. These results indicate a strong correlation between cytotoxicity of the test item and clastogenic activity. Due to the clear effects observed without metabolic activation at 4 hours a delayed fixation time was not performed.

Positive controls used in the tests showed a distinct and biologically relevant increase in cells with structural chromosomal aberrations above the historical control data.

The testing laboratory after reviewing the same data have concluded that the notified chemical is non clastogenic. The laboratory noted that increases in chromosomal aberrations only occurred at the highest concentration. At this concentration the mitotic index was 12% and the testing laboratory suggested that it shouldn't be considered. The laboratory noted also that all concentrations which showed an acceptable mitotic index and cell density showed no increase in numbers of aberrations above the negative controls and historical data.

CONCLUSION

The test substance was clastogenic to Chinese Hamster V79 cells treated in vitro under the conditions of the test.

TEST FACILITY

Bioservice (2001).

7.9. Dermal Drug Delivery and Percutaneous Absorption

TEST SUBSTANCE

Product 402303/307-01 (79.2% notified chemical)

METHOD

OECD Draft – New proposal "Dermal Delivery and Percutaneous Absorption: *in vitro* Method" May 1996.
ECETOC, Percutaneous Absorption, Monograph No 20, 1993.
CTFA Safety Testing Guidelines – *In vitro* penetration methods: summary of key literature and critical elements of design.
COLIPA – Cosmetic Ingredients: Guidelines for Percutaneous Absorption/Penetration, 1995.
Opinion concerning basic criteria for the in vitro assessment of percutaneous

absorption of cosmetic ingredients - Adopted by Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers during plenary sessions of 23 June 1999.

Remarks - Method: After equilibration of the skin membranes (450 µm thickness, 10 mm diameter consisting of the *stratum corneum*, epidermis and part of dermis from the human female abdomen) for at least 1 hour (adjustment for flow and temperature (32 ± 1°C). Forty µL of the test formulation corresponding to 2.22 mg test substance was applied to the skin surface and collecting of the acceptor fluid was started. The collection vessels were changed each 6 hours for a period of 48 hours. At the end of the exposure period excess test formulation and skin were collected in a vial and extracted with 2 mL PBS (pH 3.2). The amount of test item in the acceptor solution and in the extract of the quantitatively collected excess test substance and skin was analysed using a HPLC method with UV detection.

RESULTS

Remarks - Results: According to the results of the validation procedure the limit of quantitation of erythrulose in aqueous solution was 0.25 µg/mL. This reflects a detection limit of 0.04% of the applied dose during each time interval of the sample collection. The test item was not detected in receptor fluid in concentration higher than the threshold value. With the scope of limitation of quantitation, the test substance did not penetrate human skin in vitro within 48 hours. On the basis of the calculated applied amount of the test substance, the average recovery rate of the test substance and excessive formulation after 48 hours of penetration cell perfusion was 112.2% with a coefficient of variation (CV) of 11.1 (n=6). The CV which is mainly based on variable volumes during application of the gel and reflects the historical data and the validity of the experiment.

CONCLUSION: The test substance did not penetrate human skin *in vitro* within 48 hours.

TEST FACILITY: Bioservice (2000).

7.10. Irritative Potential in Humans

TEST SUBSTANCE: Erythrulose (78.5% notified chemical)

METHOD

Remarks - Method: A 20% solution of the test substance was applied under occlusive plastic test chambers for 48 hours on the backs of volunteers. After 48 hours the chambers were removed and the first inspections of reactions were done. A second inspection was done after 72 hours.

RESULTS

Remarks - Results: No results were provided

CONCLUSION: It was concluded that applied under regular conditions, the potency of test substance to act as an irritant is extremely low.

TEST FACILITY: Derma Consult (1993).

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Erythrulose
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test.
Inoculum	Secondary effluent organisms from municipal sewage treatment plant.
Exposure Period	28 days
Auxiliary Solvent	None.
Analytical Monitoring	WTW inolab Oxi Level 2 with WTW CellOx 325 oxygen electrode
Remarks - Method	Reference substance – sodium acetate Treatments: - test concentrations – notified chemical and inoculum - inoculum blank – inoculum only - positive control – reference substance and inoculum - toxicity control – notified chemical, reference substance and inoculum Oxygen concentrations measured at start, 7, 14, 21 and 28 days.

RESULTS

Test substance 2 mg/L		*Test substance 5 mg/L*		*Sodium acetate 2 mg/L*	
Day	*% degradation*	*Day*	*% degradation*	*Day*	*% degradation*
0	0	0	0	0	0
7	63	7	62	7	60
14	65	14	61	14	58
21	50	21	60	21	70
28	78	28	70	28	73

Remarks - Results	By day 7 both test samples reached 60% degradation, therefore, the notified chemical meets the criteria for ready biodegradability. In the positive control, the reference substance reached 60% degradation within 7 days indicating that the test conditions were acceptable. In the toxicity control degradation reached 25% within 14 days, indicating that the test substance did not inhibit microbial activity.
CONCLUSION	Under the study conditions, the notified chemical can be classified readily biodegradable.
TEST FACILITY	NOTOX (2003k)

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Erythrulose
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static. EC Directive 92/69/EEC C.1 Acute Toxicity for Fish – static.
Species	Carp (*Cyprinus carpio*)
Exposure Period	96 hours
Auxiliary Solvent	None.
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC

Remarks – Method	A 16-hour photoperiod was maintained throughout the study with aeration commencing at 24 hours. Temperature, dissolved oxygen and pH were measured daily in the blank control and 100 mg/L. Fish were not fed during the study. Analysis samples were taken from the blank control and the 100 mg/L sample at 0, 24, and 96 hours. The pH ranged from 7.3 to 8.0 in the blank control and 7.3 to 7.8 in the 100 mg/L sample. In both vessels the dissolved oxygen started at 8.6 mg/L but dropped to 6.4 mg/L on day 1 therefore aeration commenced, after which dissolved oxygen ranged from 8.0 to 8.7. Temperature ranged from 20.5 to 21.4°C in the blank control and 100 mg/L vessels. Pentachlorophenol was used as a reference substance at 0.06, 0.10, 0.15, 0.22 and 0.32 mg/L.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*2.5 h*	*24 h*	*48 h*	*72 h*	*96 h*
Blank control	0	7	0	0	0	0	0
0.1	-	3	0	0	0	0	0
1.0	-	3	0	0	0	0	0
10	-	3	0	0	0	0	0
100	97.9 (av 96 h)	7	0	0	0	0	0

LC50	>100 mg/L at 96 hours.
NOEC	100 mg/L at 96 hours.
Remarks – Results	No mortality or abnormal behaviour was observed at any of the concentrations. While the dissolved oxygen level dropped on day 1 it remained above 60% saturation therefore did not invalidate the study. The 96 h LC_{50} for the reference substance was 0.21 mg/L, which is within recorded 96 h LC_{50} values for this species of Carp and validates the test conditions.
CONCLUSION	Under the test conditions the notified chemical is not toxic to Carp.
TEST FACILITY	NOTOX (2003l)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Erythrulose
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test - Static. EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia - static.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	A 16 hour photoperiod was maintained throughout the study with no aeration. Daphnia were not fed during the study and immobility was observations were made at 24 and 48 hours. Temperature, dissolved oxygen and pH were measured daily in the blank control and 100 mg/L. Analysis samples were taken from the blank control and 100 mg/L at 0 and 48 hours.

For the blank control and 100 mg/L these were 4 replicate, while for the other concentrations there were only two replicates. Each replicate had 5 daphnia.

The chemical analysis indicated that the nominal concentrations were within 97-99% of the actual concentrations. The pH ranged from 7.7 to 8.0, while the dissolved oxygen started at 8.6 but dropped to 8.0 and temperature ranged from 20.2 to 20.7°C.

Potassium dichromate was used as a reference substance at 0.10, 0.18, 0.32, 0.56, 1.0 and 1.8 mg/L.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Blank control	0	20	0	0
0.1	-	10	0	0
1.0	-	10	0	0
10	-	10	0	0
100	96.9 (av 48 h)	20	0	0

LC50	> 100 mg/L at 48 hours
NOEC	100 mg/L at 48 hours
Remarks – Results	In one of the control and 0.1 mg/L replicates there were daphnia trapped at the medium surface. These were not counted as immobile individuals. No other abnormal behaviour or immobility was observed in any of the concentrations. The 96 h LC_{50} for the reference substance was 0.60 mg/L, this validated the study conditions.
CONCLUSION	Under the study conditions, the notified chemical is not toxic to daphnia.
TEST FACILITY	NOTOX (2003m).

8.2.3. Algal growth inhibition test

TEST SUBSTANCE	Erythrulose
METHOD	OECD TG 201 Alga, Growth Inhibition Test. EC Directive 92/69/EEC C.3 Algal Inhibition Test.
Species	*Selenastrum capricornutum*
Exposure Period	72 hours
Concentration Range	
Nominal	0, 0.1, 10 and 100 mg/L
Actual at 72 h	0, -, - and 79.8 mg/L
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	Initial cell density – 1 x 10^4 cells/mL. This study was a combined limit and range finding test. Continuous illumination was maintained throughout the study. Temperature was monitored continuously, while pH was measured at the beginning and end of the study in the blank control and 100 mg/L samples. Samples for analysis were taken from the blank control and 100 mg/L vessels at 0, 24 and 72 hours.

The pH ranged from 8.3 to 9.3 in the control and 8.4 to 9.0 in 100 mg/L sample and temperature ranged from 22.1 to 24.1ºC.

Potassium dichromate was used as a reference substance at 0.18, 0.32, 0.56, 1.0, 1.8 and 3.2 mg/L.

RESULTS

Biomass		*Growth*	
E_bC_{50} *mg/L at 72 h*	NOEC *mg/L*	E_rC_{50} *mg/L at 72 h*	NOEC *mg/L*
>100	100	>100	100

Remarks - Results

The E_bC_{50} for the reference substance was 0.73 mg/L and the E_rC_{50} was 1.2 mg/L. Both of these values were in the expected range and validated the study conditions.

CONCLUSION

Under the conditions of the study, the notified chemical is not toxic to freshwater algae.

TEST FACILITY

NOTOX (2003n)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

The majority of the notified chemical will eventually be released into the environment (up to 960 kg) via discharge into sewerage systems through bathing. It is expected that up to 10 kg per annum will remain in the consumer product containers and will be disposed of to landfill.

The notified chemical is expected to be highly soluble in water and as such will be mobile in both the aquatic and terrestrial compartment. It will not readily hydrolyse in natural waters at environmental pH values, however, is readily biodegradable. Residual chemical disposed of to landfill within empty containers will readily degrade.

As the majority of the notified chemical will be released into the aquatic environment via the sewerage systems the predicted environmental concentration (PEC) in the aquatic environment is estimated using a worst-case scenario including no removal or degradation:

National population	20 million
average water consumption per person per day	200 L
Number of days	365
Amount released to sewer	950 kg
PEC_{sewer}	$\frac{950\ 000\ 000}{20\ 000\ 000 \times 200 \times 365}$
	$= 6.5X10^{-4}$ mg/L
	= 0.65 µg/L
PEC_{inland} (dilution factor 1)	0.65 µg/L
PEC_{ocean} (dilution factor 10)	0.065 µg/L

The ready biodegradability test results showed that up to 70% of the notified chemical was eliminated after 28 days and therefore the notified chemical was considered to be readily biodegradable. The SIMPLETREAT model (European Commission, 2003) for modelling partitioning and losses in sewage treatment plants (STP) was used to estimate the proportions of the chemical partitioning into the different environmental compartments. The results indicate that when the chemical is released into the aqueous phase of a STP, about 13% would partition to water and 87% would degrade while there is no release to air through volatilisation or

partitioning to biosolids. These results are consistent with the non-volatility, high solubility and low log P_{ow} values of the notified chemical and the results of the adsorption/desorption test indicating that the test substance has no tendency to adsorb onto the sludge.

Assuming 13% of the notified chemical may potentially remain in solution, the PEC_{inland} and PEC_{ocean} become 0.0845 and 0.00845 µg/L respectively.

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 0.1 m of soil (density 1000 kg/m^3). Thus the soil concentration can be estimated in the following table.

Concentration in effluent		0.0845 µg/L
PECsoil (µg/kg) (assumes no degradation in soil or movement out of soil)		
Soil concentration	1 year	0.845
	5 years	4.225
	10 years	8.45

Bioaccumulation is not expected due to the high water solubility and low log P_{ow} of the notified chemical, which indicates a poor affinity to lipids. The readily biodegradable nature of the notified chemical would also limit its bioaccumulation potential.

9.1.2. Environment – effects assessment

The results of the aquatic toxicity tests are listed below.

Organism	*Duration*	*Outcome*
Fish	96 h	LC_{50} > 100 mg/L
Daphnia	48 h	EC_{50} > 100 mg/L
Algae	72 h	E_bC_{50} > 100 mg/L

Since data are available for three trophic levels a safety factor of 100 along with the LC_{50}/EC_{50} value of >100 mg/L are used to estimate a predicted no effect concentration (PNEC for aquatic ecosystems) of >1 mg/L by dividing the LC_{50} value by the safety factor.

9.1.3. Environment – risk characterisation

The risk to the environment of the of notified chemical can be estimated by determining the aquatic risk quotient (RQ = PEC/PNEC).

Aquatic release – Australia-wide STPs

Location	PEC	PNEC	Risk Quotient (RQ)
Worst case scenario – No decomposition			
Ocean outfall	0.065 µg/L	>1 mg/L	<0.000065
Inland River	0.65 µg/L	>1 mg/L	<0.00065
Likely scenario - 87% decomposition			
Ocean outfall	0.00845 µg/L	>1 mg/L	<0.00000845
Inland River	0.0845 µg/L	>1 mg/L	<0.0000845

Since the RQ values are much less than 1, the proposed use of the notified chemical is unlikely to pose an unacceptable risk to aquatic life. Even if the chemical's degradation was not taken into account the RQ value is much less than 1.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Transport and Storage

The potential of exposure to the notified chemical as imported (78-82% (w/w)) and in the final products (1.5-5.0% (w/w) notified chemical) during transport and storage is minimal, except in the event of an accident if the packaging is breached. Worker exposure will be minimised by the use of overalls, safety boots and gloves.

Reformulation

During the reformulation process, there is expected to be minimal worker exposure. Incidental dermal exposure to splashes, drips, and spills of notified chemical as imported may occur during the charging of the blending vessels.

During filling and capping, worker exposure is expected to be limited. Packers monitoring the filling lines and the capper would wear safety glasses, gloves and work uniforms.

Maintenance workers involved in cleaning blending and filling equipment may be dermally exposed to residues containing the notified chemical (300-500 grams per tank). These workers will wear eye protection and gloves.

Laboratory Staff

Laboratory staff are expected to have minimal exposure due to the brief sampling periods and the small quantities involved. Dermal exposure due to drips may occur during sampling. It is expected laboratory staff will wear adequate protection for the eyes, skin, body, and hands.

9.2.2. Public health – exposure assessment

Public exposure will be restricted to those persons using the self tanning products. The notified chemical will be present up to 5% (w/w) in the final product. The tanning cremes will be used twice daily, while the body lotions will be used once daily. Persons using the final product will be dermally exposed to the notified chemical. Accidental ocular exposure to the notified chemical may also occur.

Direct public exposure during transport and storage or from manufacturing waste is unlikely.

9.2.3. Human health - effects assessment

The notified chemical exhibits low acute oral toxicity in rats and was found to be slightly irritating to the eyes and skin of rabbits. There was no evidence that the notified chemical was a skin sensitiser in the guinea pig maximisation test. The notified chemical produced no evidence of phototoxicity or photoallergenicity in guinea pigs.

The NOEL for the notified chemical a 28-day repeat dose oral toxicity study in rats was 1000 mg/kg bw/day based on the absence of any treatment related effects at any dose. In a repeat application dermal test, the notified chemical was found to be non-irritant in guinea pigs.

The notified chemical was not mutagenic in bacterial reverse mutation assays but was found to be clastogenic in an *in vitro* in Chinese Hamster V79 cells. However there is insufficient evidence to classify the notified chemical as R46 (mutagenic) or R40 (possible risk of irreversible effects) in accordance with the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999b).

The notified chemical did not penetrate human skin *in vitro* within 48 hours and was found to have low irritative potential in humans.

Based on the available data, the notified chemical is not classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2002).

9.2.4. Occupational health and safety – risk characterisation

Occupational exposure can occur when handling the notified chemical as imported (78-82% notified chemical). During the formulation process, dermal and accidental ocular exposure to notified chemical may occur during charging of the blending vessel, QC testing and cleaning of the blending tank. The notified chemical is slightly irritating to the eyes and skin and therefore operators should wear, gloves, safety glasses, and overalls.

Once the final product is packed, exposure should be low. Hence, exposure for warehousing and distribution workers and retail workers is unlikely unless the packaging is breached.

9.2.5. Public health – risk characterisation

The level of the notified chemical in finished product 1.5-5% (w/w). Dermal absorption of the notified chemical is likely to be low based on the in vitro test using human skin. Data from animal and human studies indicate that notified chemical is not a skin sensitiser and repeated dermal exposure is not of concern.

The self tanning body lotions are used once daily and crème products twice daily. The notifier has calculated dermal exposure using:

Systemic exposure = [dp*c*a*f]/bw

Where
a= amt of product applied per application (mg)
c = concentration in product
dp = dermal penetration
f = frequency of application
bw = body weight

The following assumptions were made:
c = 5% maximum concentration of notified chemical in products
bw = 60 kg
dp = 10% worst case scenario.

For Body Lotion:
8 gram of product per application once a day
[dp*c*a*f]/bw
= (10% x 5% x 8000 x 1)/60
= 0.67 mg/kg bw/day

For general purpose creme:
1.2 gram of product per application twice a day
[dp*c*a*f]/bw
= (10% x 5% x 1200 x 2)/60
= 0.2 mg/kg bw/day

For general purpose creme:
0.8 gram of product per application twice a day
[dp*c*a*f]/bw
= (10% x 5% x 800 x 2)/60
= 0.13 mg/kg bw/day

Margin of Exposure (MOE) calculations were undertaken, based on the NOEL of 1000 mg/kg bw/day from the 28-day oral repeat dose subchronic study in rats and the highest exposure scenario of 0.67 mg/kg bw/day for the daily use of the body lotion given above.

MOE = NOEL/systemic exposure
= 1000/0.67

= 1492.53

The Margin of Exposure exceeds 100, and is hence acceptable.

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

10.1. Hazard classification

Based on the available data the notified chemical is not classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*.

and

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. Under this system the notified chemical would not be classified for either human health or environmental end points.

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.

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 in the notification.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical 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 the notified chemical 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

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced:
  - Minimise drips and spills

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - Safety glasses, gloves and coveralls

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

- A copy of the MSDS should be easily accessible to employees.
- If products and mixtures containing the notified chemical 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

- The following control measures should be implemented by cosmetic manufacturer to minimise environmental exposure during formulation of the notified chemical:
  - Process equipment should be within bunded areas with only process drains in the vicinity.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

- Spills/release of the notified chemical should be contained and either pumped into sealable containers or absorbent material used, which should then be placed in sealable labelled containers ready for disposal to landfill.

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 exceeds one tonne per annum notified chemical;

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.

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