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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Tinosorb S

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TABLE OF CONTENTS

FULL PUBLIC REPORT 4
1. APPLICANT AND NOTIFICATION DETAILS 4
2. IDENTITY OF CHEMICAL 4
3. COMPOSITION 4
4. INTRODUCTION AND USE INFORMATION 4
5. PROCESS AND RELEASE INFORMATION 5
5.1. Distribution, transport and storage 5
5.2. Operation description 5
5.3. Occupational exposure 5
5.4. Release 6
5.5. Disposal 6
5.6. Public exposure 6
6. PHYSICAL AND CHEMICAL PROPERTIES 6
7. TOXICOLOGICAL INVESTIGATIONS 9
7.1 Acute toxicity – oral 9
7.2 Acute toxicity – dermal 10
7.3 Phototoxicity 10
7.4 Acute toxicity – inhalation 11
7.5 Irritation – skin 11
7.6 Irritation – eye 11
7.7 Skin sensitisation 12
7.8 Photoallergenicity 12
7.9 Repeat dose toxicity 13
7.10 Toxicity to reproduction – one generation study 14
7.11. Genotoxicity – *S. typhimurium* 15
7.12 Genotoxicity – *E. coli* 16
7.13 Phototomutagenicity 17
7.14 Genotoxicity – in vitro 17
7.15 Genotoxicity – in vivo 18
7.16 Human skin penetration and distribution - in vitro 18
8. ENVIRONMENT 20
8.1. Environmental fate 20
8.1.1. Ready biodegradability 20
8.1.2. Bioaccumulation 20
8.2. Ecotoxicological investigations 21
8.2.1. Acute toxicity to fish 21
8.2.2. Acute toxicity to aquatic invertebrates 22
8.2.3. Algal growth inhibition test 23
8.2.4. Inhibition of microbial activity 24
9. RISK ASSESSMENT 25
9.1. Environment 25
9.1.1. Environment – exposure assessment 25
9.1.2. Environment – effects assessment 26
9.1.3. Environment – risk characterisation 26
9.2. Human health 27
9.2.1. Occupational health and safety – exposure assessment 27
9.2.2. Public health – exposure assessment 27
9.2.3. Human health – effects assessment 28
9.2.4. Occupational health and safety – risk characterisation 28
9.2.5. Public health – risk characterisation 28
10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS 29
10.1. Hazard classification 29
10.2. Environmental risk assessment 29
10.3. Human health risk assessment 29
10.3.1. Occupational health and safety 29
10.3.2. Public health 29
11. MATERIAL SAFETY DATA SHEET 29

11.1. Material Safety Data Sheet 29
11.2. Label 29
12. RECOMMENDATIONS 30
12.1. Secondary notification 30
13. BIBLIOGRAPHY 30

FULL PUBLIC REPORT

Tinosorb S

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Ciba Specialty Chemicals Pty Ltd (ABN: 97 005 061 469)
235 Settlement Road
Thomastown VIC 3074

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: Chemical identity, means of identification, identity of impurities and additives, import volume, identity of manufacturing sites.

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)
Assessed by Therapeutic Goods Administration for use in sunscreens at up to 10%.

NOTIFICATION IN OTHER COUNTRIES
China (2003)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Tinosorb S

METHODS OF DETECTION AND DETERMINATION

METHOD	High Performance Liquid Chromatography, Ultraviolet/Visible, Fourier Transform Infrared and ^{1}H-Nuclear Magnetic Resonance spectroscopy.
Remarks	Copies of the spectral data will be held by NICNAS.

3. COMPOSITION

DEGREE OF PURITY
High

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Imported in 20 and 50 kg plastic-lined metal drums.

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

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

USE
Broad-spectrum ultra-violet (UV) light absorber for daily moisturising creams (2-5%) and sunscreen preparations (10%).

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Melbourne.

TRANSPORTATION AND PACKAGING
The 20 and 50 kg drums are imported and stored at the notifier's warehouse, before being sold without repacking to customers for reformulation. Following reformulation, the sunscreens and moisturisers containing the notified chemical will be packaged in 100 or 200 mL containers.

5.2. Operation description

The notified chemical will be reformulated at a number of sites in Australia to produce moisturisers and sunscreens. The notified chemical (>99% purity) will be weighed out and manually poured into a stainless steel mixing vessel of up to 2000 L capacity. Mixing is achieved by slow mechanical stirring. Other ingredients are also added and the resulting mixture is tested for quality control. Once approved, the sunscreens (up to 10% notified chemical) and moisturisers (2-5% notified chemical) are pumped from the mixing vessel to a holding tank prior to packaging in 100 or 200 mL containers. Filling and packaging operations involving automated filling, capping and labelling.

The product will then be transported as required to various retail outlets. The cartons containing the product will be unpacked and products placed on the shelves.

Packages will be purchased by consumers. Sunscreens would be applied in anticipation of sun exposure and may be applied on almost all parts of the body. Moisturisers are expected to be used on a daily basis and applied to the face and neck.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Storage and transport	5-10	10 mins/week	12 weeks/year
Plant operators	15-30	3 hours/day	60 days/year
Laboratory	10-20	30 mins/day	30 days/year
Sales	1000	8 hours/day	240 days/year

Exposure Details
Storage and transport workers are not expected to be exposed to the notified chemical except in the event of an accident where the packaging may be breached.

Plant operators may be exposed to the notified chemical during weighing, addition to mixing vessels, and to products containing the notified chemical during packaging. Exposure will be limited through the use of local exhaust ventilation and PPE such as impervious gloves, coveralls and safety boots.

Laboratory workers may be exposed to 200 g samples of pure notified chemical, or to up to 1 L of finished product, during QA testing. Laboratory workers wear gloves and lab coats to minimise exposure.

Sales workers involved in shelf filling and sale of the product are not expected to be exposed to the notified chemical except in the event of an accident where the packaging may be breached. Sales representatives demonstrating will be dermally exposed to the products through application to potential customers or themselves.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Product containing the notified chemical at a concentration greater than 99% will be imported in 20 kg and 50 kg plastic-lined drums. These will be reformulated at a number of sites. Exposure may occur if import containers are accidentally breached, or there may be minor release from cleaning and maintenance of mixing equipment. The former scenario is considered unlikely. Minimal loss is expected through disposal of used packaging and maintenance of mixing equipment. It is estimated that 0.5% would remain in empty drums, totalling a release to wastewater of 5 kg annually. In addition, 40 kg a year is expected to end up in landfill through residue in cosmetic containers.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be present in creams and sunscreens, available nationally, and used daily. For this reason, release to wastewater and the ocean is expected to occur as the creams and sunscreens are washed off the skin.

5.5. Disposal

Import containers will be recycled or disposed of to landfill. Domestic containers will be disposed of to landfill.

5.6. Public exposure

The concentration of the notified chemical in the finished products will range between 2 and 10%. It is anticipated that the finished products will have Australia-wide distribution.

The sunscreen products will used when sun exposure is anticipated and will be applied on the face and or other parts of the body depending on the formulation. The moisturiser products are “everyday” use formulations and will be applied on the face and neck on daily basis.

Thus there will extensive dermal exposure to the notified chemical amongst members of the public. Ocular and oral exposure are also possible.

The TGA regulates public health with respect to therapeutic goods. It is envisaged that most of the products containing the notified chemical would be classed as therapeutic. The notified chemical is permitted for use by the TGA as the active ingredient in sunscreens at a concentration of up to 10%.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Yellow solid

Melting Point/Freezing Point 80.4ºC

METHOD	OECD TG 102 Melting Point/Melting Range. EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	Capillary method.
TEST FACILITY	RCC (1998a)

Boiling Point >400ºC at 101.3 kPa

METHOD	OECD TG 103 Boiling Point. EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks	A differential scanning calorimeter was used.
TEST FACILITY	RCC (1998b)

Density 1.17 kg/m^3 at 20.4°C

METHOD OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.
Remarks Pycnometer method.
TEST FACILITY RCC (1998c)

Vapour Pressure 5.9 x 10^{-20} kPa at 25°C

METHOD OECD TG 104 Vapour Pressure.
EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Calculated from the boiling point using the Modified Watson Correlation. The boiling point was estimated as 664°C.
TEST FACILITY RCC (1997a)

Water Solubility <1.4 x 10^{-5} g/L at 20°C

METHOD OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Column Elution Method. An excess of the product was added to water. The preliminary test using a simplified flask method indicated that the concentration (as determined by HPLC) was less than 0.01151 mg/L. Therefore, the column elution method was used in the main test. In this test, the test column was filled with a finely ground mixture of 2.03g undissolved test substance and 5.04g of glass beads. A circulation pump was used to elute the notified chemical from the carrier material over 2 days in the first experiment. Results were confirmed in a second experiment that was run over 4 days, but at half the flow rate of the first experiment (0.26 mL/min vs 0.52 mL/min). 45 samples were analysed in the first experiment and 11 samples from the second experiment using HPLC. The water solubility was determined to be below the smallest calibration point of 0.014 mg/L.
TEST FACILITY RCC (1998d)

n-Octanol Solubility 6300 mg/L at room temperature

METHOD Simplified flask method.
Remarks Quantified in another study as part of method to calculate the partition coefficient (refer Partition Coefficient). 7.08 g and 7.10 g of the notified chemical were added to 25 mL n-octanol and stirred for 4 days. After centrifugation, the supernatant was filtrated and diluted with 1,4-dioxane, and analysed using HPLC.
TEST FACILITY RCC (1998j)

Hydrolysis as a Function of pH Not given.
Remarks The notified chemical does not contain any hydrolysable groups.

Partition Coefficient (n-octanol/water) log Pow > 5.7 at 20°C

METHOD EEC directive 92/69 Part A.8
Remarks Estimated from the ratio of its solubility in n-octanol (6300 mg/L) and in water (<0.014 mg/L). The authors claimed that analysis with HPLC could not be used because of the chemical structure and chromatographic behaviour of the test substance.
TEST FACILITY RCC (1998j)

Adsorption/Desorption Not given
– main test
Remarks It is estimated that the notified chemical is likely to adsorb to soil due to its low water solubility.

Dissociation Constant Not given.

METHOD OECD TG 112 Dissociation Constants in Water.
Remarks Estimated based on the molecular structure. The Hammett correlation equation is used to predict pK_a for aromatic substances, and the Taft correlation is used to estimate pK for aliphatic and alicyclic species. The notified substance has several sites that can be protonated, giving pK_as from –3.0 to 9.4. It was concluded that the notified chemical is not dissociated or protonated in the environmentally relevant pH range (5 to 8).
TEST FACILITY RCC (2000)

Particle Size 0.17% < 10 µm

METHOD OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.

Range (µm)	*Mass (%)*
<5	0.00
5-8	0.08
8-15	0.34
15-32	1.98
32-40	2.36
40-63	6.29
63-90	2.08
90-125	74.60
126-160	3.43
160-200	1.77
>200	7.06

Remarks Sieve method.
TEST FACILITY RCC (1998e)

Flash Point 284°C at 101.3 kPa

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks Pensky-Martens flash point tester (closed cup).
TEST FACILITY RCC (1998f)

Flammability Limits Not highly flammable

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks Test substance melted immediately under the flame.
TEST FACILITY RCC (1998g)

Autoignition Temperature Not auto-flammable.

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
Remarks None.
TEST FACILITY RCC (1998h)

Explosive Properties Not explosive by flame, shock or friction.

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks None.
TEST FACILITY ISS (1998)

Reactivity

Remarks The chemical is predicted to be stable under normal environmental conditions.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 >2000 mg/kg bw	low toxicity
Rat, acute dermal LD50 >2000 mg/kg bw	low toxicity
Guinea pig, phototoxicity	low toxicity
Rat, acute inhalation	not performed.
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Guinea pig, photoallergenicity – adjuvant test	no evidence of photoallergenicity
Rat, repeat dose oral toxicity – 90 days.	NOAEL = 1000 mg/kg bw/day
Rat, toxicity to reproduction – one generation study	NOAEL = 1000 mg/kg bw/day
Genotoxicity – bacterial reverse mutation - *S. typhimurium*	non mutagenic
Genotoxicity – bacterial reverse mutation - *E. coli*	non mutagenic
Phototomutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test	non genotoxic
Genotoxicity – in vivo mammalian erythrocyte micronucleus test	non genotoxic
Human skin penetration and distribution - in vitro	<0.08% absorbed

7.1 Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 401 Acute Oral Toxicity. EC Directive 92/69/EEC B.1 Acute Toxicity (Oral).
Species/Strain	Rat/HanIbm:WIST (SPF)
Vehicle	PEG 400
Remarks - Method	No significant protocol deviations.

RESULTS

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

LD50	>2000 mg/kg bw
Signs of Toxicity	None.
Effects in Organs	None.
Remarks - Results	No adverse effects observed.

CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	RCC (1997b)

7.2 Acute toxicity – dermal

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 402 Acute Dermal Toxicity. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal).
Species/Strain	Rat/HanIbm:WIST (SPF)
Vehicle	PEG 400
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

RESULTS

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

LD50	>2000 mg/kg bw
Signs of Toxicity - Local	None.
Signs of Toxicity - Systemic	None.
Effects in Organs	None.
Remarks - Results	No adverse effects observed.

CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	RCC (1997c)

7.3 Phototoxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD Draft TG, Acute Dermal Photoirritation Dose-Response Test, February 1995. CTFA Safety Testing Guidelines, Guidelines for Evaluating Photodermatitis, 1991.
Species/Strain	Guinea pig/Duncan Hartley
Number of Animals	15 females
Vehicle	PEG 400
Remarks - Method	The notified chemical (10%, 15%, 25%, 30%) was applied dermally to approximately 2 cm^2 on the shaven left flank 30 minutes prior to irradiation with 20 J/cm^2 UVA (320-400 nm). The test material was also applied to the right flank, which remained unexposed to light. Negative controls (5 animals) received only PEG 400 followed by illumination. Skin reactions were assessed at 24, 48 and 72 hours after application. All animals were pretreated with 2% DMSO in ethanol to enhance skin permeation.

RESULTS

Group	*Concentration*	*Number of Animals Showing Skin Reactions after:*					
		24 hours		*48 hours*		*72 hours*	
		Irradiated	*Not irradiated*	*Irradiated*	*Not irradiated*	*Irradiated*	*Not irradiated*
Test	10%	0/10	0/10	0/10	0/10	0/10	0/10
	15%	0/10	0/10	0/10	0/10	0/10	0/10
	25%	0/10	0/10	0/10	0/10	0/10	0/10
	30%	0/10	0/10	0/10	0/10	0/10	0/10
Control	0%	0/5	0/5	0/5	0/5	0/5	0/5

CONCLUSION The notified chemical showed no phototoxic potential under the conditions of this test.

TEST FACILITY RCC (1997d)

7.4 Acute toxicity – inhalation

Not performed.

7.5 Irritation – skin

TEST SUBSTANCE 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	3
Vehicle	None.
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

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	0	0	0
Oedema	0	0	0	0	0	0

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

Remarks - Results Pale yellow staining was observed at the 1-hour observation.

CONCLUSION The notified chemical is non-irritating to the skin.

TEST FACILITY RCC (1997e)

7.6 Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD 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	3
Observation Period	72 hours
Remarks - Method	No significant protocol deviations.

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	0.33	0.33	0.67	2	48 hours	0

Conjunctiva: chemosis	0	0	0	0	0	0
Corneal opacity	0	0	0	0	0	0
Iridial inflammation	0	0	0	0	0	0

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

Remarks - Results: Ocular discharge, and moderate redness and swelling of the conjunctivae were observed after 1 hour in all animals. Slight redness and slight watery discharge were observed at 24 hours in all animals. Slight redness persisted in one animal at the 48 hour observation, and had cleared by 72 hours.

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

TEST FACILITY: RCC (1997f)

7.7 Skin sensitisation

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 406 Skin Sensitisation – Maximisation Test.
EC Directive 96/54/EC B.6 Skin Sensitisation - Maximisation Test.

Species/Strain: Guinea pig/Himalayan spotted

PRELIMINARY STUDY: Maximum Non-irritating Concentration:
topical: 30%

MAIN STUDY

Number of Animals: Test Group: 10 male Control Group: 5 male

INDUCTION PHASE: Induction Concentration:
topical: 30%

Signs of Irritation: Four (out of ten) animals exhibited minor erythema at 24 hours, which remained at 48 animals in two animals.

CHALLENGE PHASE

1st challenge: topical: 30%

Remarks - Method: No significant protocol deviations.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	30%	0	0	-	-
Control Group	30%	0	0	-	-

Remarks - Results: None.

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

TEST FACILITY: RCC (1997g)

7.8 Photoallergenicity

TEST SUBSTANCE: Notified chemical

METHOD: OECD Draft TG, Acute Dermal Photoirritation Dose-Response Test, February 1995.
CTFA Safety Testing Guidelines, Guidelines for Evaluating Photodermatitis, 1991.

Species/Strain: Guinea pig/Duncan Hartley

Number of Animals	30 females
Vehicle	PEG 400
Remarks - Method	The notified chemical (0.1 mL, 30%) was applied epicutaneously to approximately 8 cm^2 of skin that was marked previously with Adjuvant. The test sites were then irradiated with 1.8 J/cm^2 UV-B and 10 J/cm^2 UV-A. This process was repeated 4 times within 2 weeks. The challenge was carried out by treating the test animals with the notified chemical (10%, 15%, 25%, 30%) followed by exposure to 20 J/cm^2 UVA (left flank) or no irradiation (right flank).

RESULTS

Group	*Concentration*	*Number of Animals Showing Skin Reactions after:*					
		24 hours		*48 hours*		*72 hours*	
		Irradiated	*Not irradiated*	*Irradiated*	*Not irradiated*	*Irradiated*	*Not irradiated*
Test (30% induction)	10%	0/20	0/20	0/20	0/20	0/20	0/20
	15%	0/20	0/20	0/20	0/20	0/20	0/20
	25%	0/20	0/20	0/20	0/20	0/20	0/20
	30%	0/20	0/20	0/20	0/20	0/20	0/20
Control	10%	0/10	0/10	0/10	0/10	0/10	0/10
	15%	0/10	0/10	0/10	0/10	0/10	0/10
	25%	0/10	0/10	0/10	0/10	0/10	0/10
	30%	0/10	0/10	0/10	0/10	0/10	0/10

CONCLUSION	There was no evidence of reactions indicative of photoallergenicity to the notified chemical under the conditions of the test.
TEST FACILITY	RCC (1997h)

7.9 Repeat dose toxicity

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Wistar
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week Post-exposure observation period: None.
Vehicle	PEG 400
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	20/sex	0	2
II (low dose)	20/sex	100	2
III (mid dose)	20/sex	500	2
IV (high dose)	20/sex	1000	1
V (control recovery)			
VI (high dose recovery)			

Mortality and Time to Death

A number of non-treatment related deaths occurred. There was no dose-response relationship for these deaths. Five animals died from possible improper gavage (day 44, 66, 81, two at day 91), one animal following blood

sampling (day 29), and one animal died during anaesthesia (day 86).

Clinical Observations
No test substance related findings.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Gamma globulin fraction was decreased by 21-22% in males receiving 1000 mg/kg bw/day as compared to controls, at all three clinical biochemistry observation points (5, 9, 13 weeks). This value was also reduced, by 30%, in 1000 mg/kg bw/day females at week 13. Also, urine output was increased, and specific gravity was decreased in females receiving 500 and 1000 mg/kg bw/day and males receiving 1000 mg/kg bw/day.

There was no evidence of morphological correlates, and the values were all within the ranges of normal background data. Thus, these changes are considered to be incidental and not toxicologically relevant. Other variations were slight and/or displayed no dose response relationship and/or were not consistently present in both sexes.

Effects in Organs
There were no dose-related differences between treated and control groups.

Remarks – Results
None.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 1000 mg/kg bw/day in this study based on minimal clinical chemistry effects at the high dose

TEST FACILITY RCC (1998k)

7.10 Toxicity to reproduction – one generation study

TEST SUBSTANCE Notified chemical

METHOD OECD TG 414 Teratogenicity.
Species/Strain Rat/WIST HanIbm
Route of Administration Oral – gavage
Exposure Information Exposure period - female: Days 6-17 post coitum
Vehicle PEG 400
Remarks – Method No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	22/f	0	0
2	21/f	100	0
3	21/f	300	0
4	21/f	1000	0

Mortality and Time to Death
No mortality observed.

Effects on Parental (P) animals:
In groups receiving 100 and 1000 mg/kg bw/day, there was a statistically significant increase in post-implantation loss (314% and 157% respectively), embryonic resorptions (389% and 154%), and consequently a decrease in the number of total foetuses (11% and 6%). This finding is not considered to be toxicologically relevant, as there is no dose-response, and the data is within the range of historical controls.

No other relevant toxicological abnormalities were observed between test and control animals.

Effects on 1st Filial Generation (F1)

No adverse effects were noted for offspring of the treated groups as compared with the control group. A slightly higher mean bodyweight in treated group offspring is possibly caused by the reduced number of foetuses per dam.

Remarks - Results

There was no evidence that the notified chemical caused teratogenicity at doses up to 1000 mg/kg bw/day administered during organogenesis in rats.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) with respect to teratogenicity was established as 1000 mg/kg bw/day in this study.

TEST FACILITY RCC (1997i)

7.11. Genotoxicity – *S. typhimurium*

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 92/69, L 383 A Mutagenicity – Reverse Mutation Test using Bacteria. Test 1: Plate incorporation procedure Test 2: Pre incubation procedure
Species/Strain	*S. typhimurium*: TA1538, TA1537, TA98, TA100
Metabolic Activation System	Liver microsomal fraction S9
Concentration Range in Main Test	a) With metabolic activation: 33.3-5000 µg/plate b) Without metabolic activation: 33.3-5000 µg/plate
Vehicle	DMSO
Remarks - Method	No significant protocol deviations.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity in Main Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	5000 (TA 1537)	Not reported.	None.
Test 2	None.	Not reported.	None.
Present			
Test 1	2500, 5000 (TA 1537); 1000, 5000 (TA 98)	Not reported.	None.
Test 2	None.	Not reported.	None.

Remarks - Results	Positive control substances had the appropriate response. Negative controls were within historical limits.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	RCC (1997j)

7.12 Genotoxicity – *E. coli*

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 92/69, L 383 A Mutagenicity – Reverse Mutation Test using Bacteria. Test 1: Plate incorporation procedure Test 2: Pre incubation procedure
Species/Strain	*E. coli*: WP2uvrA
Metabolic Activation System	Liver microsomal fraction S9
Concentration Range in Main Test	a) With metabolic activation: 33.3-5000 µg/plate b) Without metabolic activation: 33.3-5000 µg/plate
Vehicle	DMSO
Remarks - Method	No significant protocol deviations.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*		
	Cytotoxicity in Main Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	None.	None.	None.
Test 2	None.	None.	None.
Present			
Test 1	None.	None.	None.
Test 2	None.	None.	None.

Remarks - Results	Positive control substances had the appropriate response. Negative controls were within historical limits.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	RCC (1997k)

7.13 Phototomutagenicity

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. Test 1: Plate incorporation procedure Test 2: Pre incubation procedure
Species/Strain	*E. coli*: WP2*uvr*A *S. typhimurium*: TA102
Metabolic Activation System	Liver microsomal fraction S9
Concentration Range in Main Test	a) With metabolic activation: 33.3-5000 µg/plate b) Without metabolic activation: 33.3-5000 µg/plate
Vehicle	DMSO
Remarks - Method	Levels of UV irradiation were determined from a preliminary assay: WP2*uvr*A: 10 seconds of irradiation with 20 mJ/cm^2 UV-A, 1 mJ/cm^2 UV-B TA102: 40 seconds of irradiation with 80 mJ/cm^2 UV-A, 4 mJ/cm^2 UV-B

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	None.	None.	None.
Test 2	≥5000 µg/plate	None.	None.
Present			
Test 1	None.	None.	None.
Test 2	≥5000 µg/plate	None.	None.

Remarks - Results	Positive control substances had the appropriate response. Negative controls were within historical limits.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test in the presence of ultraviolet.
TEST FACILITY	RCC (1997l)

7.14 Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Cell Type/Cell Line	V79 Chinese hamster cells
Metabolic Activation System	Liver microsomal fraction S9
Vehicle	acetone
Remarks - Method	No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	6.5, 13.1, 26.3*, 52.5*, 105.0*, 210.0* µg/ml	4 hours	18 hours
Test 2a	6.5, 13.1, 26.3*, 52.5*, 105.0*, 210.0* µg/ml	18 hours	18 hours
Test 2b	26.3, 52.5*, 105.0, 210.0* µg/ml	28 hours	28 hours
Present			
Test 1	3.3, 6.5, 13.1*, 26.3*, 52.5*, 210.0* µg/ml	4 hours	18 hours
Test 2a	3.3, 6.5, 13.1*, 26.3*, 52.5*, 210.0* µg/ml	4 hours	18 hours
Test 2b	13.1, 26.3*, 52.5*, 210.0* µg/ml	4 hours	28 hours

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*		
	Cytotoxicity in Main Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	None.	≥105.0 µg/ml	None.
Test 2a	None.	≥105.0 µg/ml	None.
Test 2b	None.	≥105.0 µg/ml	None.
Present			
Test 1	None.	≥52.5 µg/ml	None.
Test 2a	None.	≥52.5 µg/ml	None.
Test 2b	None.	≥52.5 µg/ml	None.

Remarks - Results: Positive control substances had the appropriate response. Negative controls were within historical limits.

CONCLUSION: The notified chemical was not clastogenic to V79 Chinese hamster cells treated in vitro under the conditions of the test.

TEST FACILITY: RCC (1998l)

7.15 Genotoxicity – in vivo

TEST SUBSTANCE: Notified chemical.

METHOD: OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
EC Directive 2000/32/EC B.12 Mutagenicity - Mammalian Erythrocyte Micronucleus Test.

Species/Strain: Mouse/Swiss Ico: OF1 (IOPS Caw)
Route of Administration: Intraperitoneal injection.
Vehicle: Corn oil
Remarks - Method: No significant protocol deviations.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5/sex	0	72 hours
II (low dose)	5/sex	500	72 hours
III (mid dose)	5/sex	1000	72 hours
IV (high dose)	5/sex	2000	72 hours
V (positive control, CP)	5/sex	0	24 hours.

CP=cyclophosphamide. M=mitomycin C.

RESULTS

Doses Producing Toxicity: None.
Genotoxic Effects: None.
Remarks - Results: Positive control substances had the appropriate response. Negative controls were within historical limits.

CONCLUSION: The notified chemical was not clastogenic under the conditions of this in vivo mammalian micronucleus microsome test.

TEST FACILITY: CIT (2003)

7.16 Human skin penetration and distribution - in vitro

TEST SUBSTANCE: Notified chemical

METHOD: This assay was conducted in accordance of COLIPA guidelines (1995)

for percutaneous penetration of cosmetic ingredients.

Epidermal membrane was removed from full-thickness human female breast and abdominal skin. The skin samples were mounted as a barrier between the halves of horizontal Franz-type diffusion cells, with the stratum corneum facing the donor chamber. The receptor chamber was filled with 6% (w/v) Oleth 20 in phosphate buffered saline (pH 7.4), which allows solubilisation of lipophilic compounds. A sunscreen-like formulation containing 10% notified chemical was applied to the donor side of the skin at 1.7-3.0 mg/cm^2 (mean of 211$\pm$12 µg/cm^2 notified chemical). Samples were taken from the receptor chamber at regular intervals over 24 hours, and the concentration of the notified chemical measured using HPLC. Following the 24-hour test period, the formulation remaining on the donor side was removed with cotton swabs and tape strips. Following the 20th tape strip, the skin was extracted into methylated spirits, and the amount of the notified chemical remaining was quantified. Skin surface temperature was maintained at 32$\pm$1°C.

RESULTS

The concentration of notified chemical in the receptor phase was, on average, close to the effective detection limit, and this leads to larger errors than if permeation had been greater.

Six out of twelve skin samples treated with the notified chemical showed any permeation over the course of the experiment. One of these samples was excluded from further consideration an anomalously high and early levels of permeation suggested that the integrity of the membrane had been compromised.

Permeation into the receptor phase plateaued between 12 and 24 hours. The average penetration after 24 hours was 0.04$\pm$0.02 µg/cm^2, or 0.02% of the applied dose. Extrapolation of the data at early time points resulted in a worst case value for total permeation of 0.004 µg/cm^2/hour, or total permeation for 24 hours of 0.1 µg/cm^2. This equates to <0.08% of the applied dose permeating through the skin after 24 hours.

After the experiment was completed >80% of the formulation was recovered on the skin surface or the first three tape strips. The remaining material was recovered in tape strips 4-20 (10.2% of the notified chemical) or the remaining skin (7.3%).

CONCLUSION

Penetration through the skin was very low, with a worst case estimate of 0.004 µg/cm^2/hour, or total permeation for 24 hours of 0.1 µg/cm^2 (<0.08% of the applied dose).

TEST FACILITY An-eX (1998)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge from a domestic wastewater treatment plant.
Exposure Period	28 days.
Auxiliary Solvent	None.
Analytical Monitoring	Biological oxygen demand was measured (O_2 drops and CO_2 is formed).
Remarks - Method	Two test suspensions were tested (24 mg and 26 mg test substance, corresponding to a concentration of 100 g/L, together with a toxicity control (25 mg test substance and 25.5 mg aniline), a procedure control (25.5 mg aniline), an inoculum control, and an abiotic control. There were no replicates.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
7	0.55	7	59.6
14	1.45	14	83.4
21	2.05	21	85.8
28	2.6	28	86.7

Remarks - Results	pH was 7.4 and 7.4 at day 0, and varied between 7.4 to 8.3 at day 28. Temperature was maintained at 22°C. The reference substance (aniline) was degraded by 83.4% by day 14, and 86.7% by day 28, thus validating the test. Degradation in the toxicity control (aniline plus test substance) followed a similar course to that of the procedure control (aniline only). Degradation was 36.6% (greater than 25%) within 14 days and therefore indicated that the test substance does not inhibit degradation.
CONCLUSION	Not readily biodegradable within 28 days.
TEST FACILITY	RCC (1998m)

8.1.2. Bioaccumulation

TEST SUBSTANCE	Notified chemical
METHOD	Non-standard method. "Method for Testing the degree of Accumulation of Chemical Substance in Fish Body", 1974, Planning and Coordination Bureau, Environment Agency, Pharmaceutical Affairs Bureau, Ministry of Health and Welfare, Basic Industries Bureau, Ministry of International Trade and Industry, Japan. This method is similar to OECD TG 305 Bioconcentration: Flow-through Fish Test.
Species	Carp, *Cyprinus carpio*
Exposure Period	Exposure: 8 weeks Depuration: Not done.
Auxiliary Solvent	HCO-20 (polyoxyethylene hardened castor oil).
Concentration Range	Nominal: 0.1 and 1.0 mg/L Actual: 0.101-0.103 and 0.948-0.981 mg/L
Analytical Monitoring	HPLC.

Remarks - Method	A preliminary test was run over 48 hours using the orange-red killifish, *Orvzias latipes*. The 48 h LC_{50} was greater than 205 mg/L. In the final test, fish were added to 3 tanks – 1 control tank containing 6 fish, and 2 tanks containing the test substance, with 25 fish.

RESULTS

Bioconcentration Factor	< 3 times at 1.0 mg/L < 19 times at 0.1 mg/L
CT50	Not given.
Remarks - Results	Fish and test water were tested weekly for the first 28 days. Only test water was tested on day 35 and day 49. Raw results indicate that a plateau was not reached, with a BCF of 19 reached in the lowest concentration in one sample on day 7, and all subsequent others below 11. Concentrations in fish were often below the detection peak area, and therefore taken to be the lowest calibration point, in 11 of 12 samples from the lower test concentration, and in 7 of 12 samples taken from the higher test concentration. This led to most BCFs being specified as below 9, 10 or 11 for the lower concentration.

CONCLUSION	The notified chemical does not accumulate in carp under these test conditions.
TEST FACILITY	Gakushin University (2000)

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static test *and* EC Directive 92/69/EEC C.1 Acute Toxicity for Fish - static test.
Species	Zebra fish, *Brachydario rerio.*
Exposure Period	96 hours.
Auxiliary Solvent	None.
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC with UV/VIS-detection.
Remarks – Method	Fish were acclimated for 10 days prior to commencement of testing. Mean body length was 3.0 ± 0.1 cm, and mean body weight was 0.27 ± 0.04 g. One aquarium containing test solution was used for each of the two treatments – the control and test medium (undiluted filtrate of the supersaturated stock suspension of the notified chemical). There were no replicates. The test medium was prepared in the following way: A supersaturated stock suspension with a nominal concentration of 100 mg/L (500 mg sonically dispersed in 5000 mL test water) was stirred for 72 hours, and then filtered through a Whatman GF/C glass microfibre filter (maximum pore size = 1.2 μm). The first 200 mL of filtrate were discarded. The undiluted filtrate, which was used as the test concentration, still contained very finely dispersed test article.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	0	7	0	0	0	0	0
Limit of water solubility	0.0013 (0 hrs), decreasing to 0.0005 (96 hrs)	7	0	0	0	0	0

LC50	Could not be quantified due to the absence of a toxic effect at the tested concentration.
NOEC (or LOEC)	= 0.8 μg/L (mean measured value) at 96 hours.
Remarks – Results	Higher concentrations were not tested, apparently because this concentration was the limit of solubility. There were no sublethal effects observed. The concentration at commencement of the test was 1.3 μg/L. However, it dropped to 0.5 μg/L after 4 days. The measured concentrations were within the determination limit of the analytical method. The decrease may be attributable to adsorption onto surfaces such as the fish and glass vessels. Treatment samples were extracted twice with dichloromethane before analysis using HPLC, and therefore were not additionally filtered. Temperature ranged from 21 to 22°C, pH from 7.8-8.1, and DO between 8.1-8.7 mg/L.
CONCLUSION	The toxicity of the notified chemical to fish cannot be accurately quantified. If a value of 0.9 μg/L were to be taken, the substance would be classified as very highly toxic to fish (United Nations 2003). However, consideration of solubility limits apply and it may be concluded that that the test substance is not toxic up to the limit of its water solubility.
TEST FACILITY	RCC (1998n)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – 48 hr immobilisation test *and* EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – 48 h static immobilisation test
Species	*Daphnia magna*
Exposure Period	48 hours.
Auxiliary Solvent	None.
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC with UV/VIS-detection.
Remarks - Method	There were two replicates of 10 animals tested. There were two treatments – a control and one test medium (undiluted filtrate of the supersaturated stock suspension of the notified chemical). This was prepared the same way as described in the fish test (section 8.2.1) except that 201 mg test article was dispersed in 2000 mL test water and then stirred. The first 100 mL of filtrate was discarded. Again, the undiluted filtrate, which was used as the test concentration, still contained very finely dispersed test article.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	0	20	0	0
Limit of water solubility	0.144	20	0	0

LC50	Not quantified due to absence of toxic effect at the tested concentration.
NOEC	144 μg/L at 48 hours.
Remarks - Results	Higher concentrations were not tested. The dissolved oxygen (DO) was 8.2 mg/L or higher throughout testing, temperature ranged from 20 to

21°C, and pH ranged between 8.1 and 8.7.

Sublethal effects were not noted at any concentration.
Samples of the test medium were taken just before the start of the test, and from test medium that had been incubated during the test period under the same conditions as the actual test (but without daphnia present). As described in section 8.2.1, the samples were not additionally filtered prior to analysis using HPLC.

CONCLUSION

The toxicity of this substance to *Daphnia* cannot be accurately quantified. If a value of 145 µg/L were to be taken, the substance would be classified as highly toxic to *Daphnia* (United Nations 2003). However, consideration of solubility limits apply and it may be concluded that that the test substance is not toxic up to the limit of its water solubility.

TEST FACILITY

RCC (1998o)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 201 Alga, Growth Inhibition Test *and*
EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species	*Scenedesmus subspicatus*
Exposure Period	72 hours.
Concentration Range	Nominal: 100 mg/L (supersaturated stock suspension, which was then filtered). Actual: 0.017 mg/L
Auxiliary Solvent	None.
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	HPLC with UV/VIS-detection.
Remarks - Method	There were 3 replicate flasks containing the test substance at a concentration of 17 µg/L, and 6 replicate control flasks. The test medium was prepared the same way as described in the *Daphnia* test (section 8.2.2), except only the first 50 mL of filtrate was discarded.

RESULTS

Biomass		*Growth*	
E_bC50	*NOEC*	*E_rC50*	*NOEC*
mg/L at 72 h	*ug/L*	*mg/L at 72 h*	*ug/L*
Not quantified	17	Not quantified	17

Remarks - Results

The LOEC and EC50 could not be quantified due to an absence of a toxic effect up to the water solubility limit (the tested concentration of 17 µg/L). No inhibitory effects were noted, with cell densities very slightly higher in the test medium than in control cultures. The NOEC was therefore 17 µg/L.

The cell density in the controls increased by a factor of 136 after 72 hours, thereby validating the test.pH was 8.0 at start of testing and 9.2-9.3 after 72 hours, possibly due to CO_2 consumption.

As described in section 8.2.1, the samples were not additionally filtered prior to analysis using HPLC.

CONCLUSION	The toxicity of this substance to algae cannot be accurately quantified. If a value of 18 µg/L were to be taken, the substance would be classified as very highly toxic to algae (United Nations 2003). However, consideration of solubility limits apply and it may be concluded that that the test substance is not toxic up to the limit of its water solubility.
TEST FACILITY	RCC (1998p)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Aerobic activated sludge
Exposure Period	3 hours.
Concentration Range	Nominal: 10, 32, 100, 320, 1000 mg/L Actual: not tested
Remarks – Method	There were 5 test substance treatments, 1 toxicity control and 1 inoculum control. There were no replicates. Test substance was directly weighted into test flasks and stirred for 72 hours, leading to finely dispersed test substance.
RESULTS	There was 12% inhibition at 1000 mg/L, however, this was considered to be within the limits of normal variability. pH ranged between 8.2 and 8.6. The 3 h EC50 of reference substance (3,5-dichlorophenol) was 23 mg/L, thereby validating the test.
IC50	> 1000 mg/L
NOEC	1000 mg/L
Remarks – Results	None.
CONCLUSION	There was no significant inhibitory effect on the respiration rate of activated sludge after 3 hours.
TEST FACILITY	RCC (1998q)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

The proposed use and disposal patterns for the notified chemical indicate that release to the environment will predominantly occur through release to wastewater from domestic use.

Minimal loss is expected through disposal of used packaging and maintenance of mixing equipment. It is estimated that 0.5% would remain in empty drums, totalling a release to wastewater of 5 kg annually. In addition, 40 kg a year is expected to end up in landfill through residue in cosmetic containers.

The notified chemical will be present in creams and sunscreens, available nationally, and used daily. For this reason, release to wastewater and the ocean is expected to occur as the creams and sunscreens are washed off the skin and pass through the sewage system. The notifier has estimated a worst-case daily release of 2.74 kg/day to sewage systems.

The estimated Predicted Environmental Concentration (PEC) has been estimated as follows:

Amount entering sewer annually (Worst Case)	1000 kg/y
Number of days used per year	365 d/y
Amount entering sewer per day (Worst Case)	2.74 kg/d
Population of Australia	20,100,000 persons
Daily water use per person	200 L/person/d
Daily water entering sewer	4020 ML/d
Predicted Environmental Concentration	0.682 µg/L

Based on dilution factors of 1 and 10 for inland and ocean discharges of STP-treated effluents, the PECs of the notified chemical in freshwater and marine water may approximate 0.682 and 0.068 µg/L respectively.

The notified chemical is not readily biodegradable. The partition coefficient is greater than 5.7, indicating that the notified chemical is much more soluble in n-octanol than in water. Using SIMPLETREAT, the notifier assumed that 8% partitions to water and 92% partitions to biosolids (sludge) in sewage treatment plants. Under this scenario, the PEC would be decreased to 0.055 µg/L in freshwater.

The SIMPLETREAT model (European Commission, 2003) is used for modelling partitioning and losses in sewage treatment plants (STP). Using EPIWIN to calculate Henry's Law Constant = 3.745×10^{-17} atm-m^3/mole and using the tables for chemicals that are not readily biodegradable, the DEH can make a conservative estimate that when the chemical is released into the aqueous phase of a STP, none is lost through volatilisation, 15% partitions to water, none degrades, and 85% will partition to biosolids (using the lowest values for log H and the highest values for log Pow available on the table).

Assuming that 15% of the notified chemical remains in solution, the following revised worst-case PEC values were obtained (Environment Australia 2003). The worst-case PEC for the aquatic environment resulting from the nationwide release of the notified chemical into the sewage systems is reduced to 0.102 µg/L prior to any dilution. The respective concentrations in freshwater and marine water are expected to be approximately 0.10 and 0.01 µg/L.

Biosolids from sewage treatment plants are commonly incinerated or used as soil conditioners. Partitioning to biosolids in STPs Australia-wide may result in an average biosolids concentration of 5.793 mg/kg (dry wt). As a soil conditioner, biosolids are applied to agricultural soils, with an assumed average rate of 10 t/ha/year. Assuming a soil bulk density of 1000 kg/m^3 and a soil-mixing zone of 0.1 m, the concentration of the notified chemical may approximate 0.06 mg/kg in applied soil. This assumes that degradation of the notified chemical occurs in the soil within 1 year from application. Assuming accumulation of the notified chemical in soil under repeated application of biosolids, the concentration of notified chemical

in the applied soil in 5 years may be approximately 0.3 mg/kg, and 0.6 mg/kg after 10 years.

In addition, STP effluent can also be used for irrigation. 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). Using these assumptions, irrigation with a concentration of 0.102 mg/L may potentially result in a soil concentration of approximately 1.02×10^{-3} mg/kg. Assuming accumulation of the notified chemical in soil under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 0.01 mg/kg and 0.02×10^{-4} mg/kg, respectively.

It is estimated that the notified chemical is likely to adsorb to soil due to its low water solubility. There is potential for the notified chemical to bioaccumulate due to its high log P_{ow} and the low water solubility but will be limited due to the relatively low volume imported and diffuse release to the sewer Australia wide.

9.1.2. Environment – effects assessment

Aquatic toxicity data were submitted for 3 taxa (fish, Daphnia and algae). Three studies commented that an EC_{50} could not be set because toxic effects were not observed at concentrations up to the solubility limit (nominal concentration 100 mg/L). However, it is also noted that the purported solubility limits are quite different in each of the studies (0.8 µg/L, 144 µg/L and 17 µg/L, respectively). These differences likely reflect analytical and method variations, particularly as finely dispersed article was present in all test media (itself indicating inadequate filtration).

Modelling data using ECOSAR, based on the chemical structure of the notified chemical, indicate that the 48 h LC_{50} for Daphnids is 0.116 µg/L, the 96 h EC_{50} for green algae is 0.11 µg/L, and the 96 h EC_{50} for fish is 0.508 µg/L. However, it is also noted that the chemical may not be soluble enough to measure this predicted effect, with a calculated solubility of 0.1023 µg/L, and a measured solubility of less than 0.014 mg/L. It is therefore concluded that it is not toxic to the limit of solubility (<0.014 mg/L).

In addition, there was no indication of aquatic toxicity in any test at a nominal concentration of 100 mg/L.

9.1.3. Environment – risk characterisation

In order to evaluate the environmental risk, data on measured concentrations in the environment, or alternatively, predictions of environmental concentrations (PEC), are compared with predicted no effect concentrations (PNEC). The PNEC is a concentration that is expected to cause no harm to organisms. The PNEC value of the notified chemical is <0.14 µg/L, using the limit of solubility, and a safety factor of 100. A safety factor is used to account for intra and inter-species variability, and it decreases from 1000 as more data for different trophic levels are provided. A risk quotient (RQ) is calculated where RQ = PEC/PNEC. Any RQ less than 1 (that is, where the concentration in the environment is less than the concentration that would cause harm) is considered safe for the environment.

Location	PEC (µg/L)	PNEC (µg/L)	Risk Quotient (RQ)
Australia-wide STPs (worst case)			
Inland river	0.682	0.14	4.87
Ocean outfall	0.068	0.14	0.49
After mitigation using SIMPLETREAT model (15% remains in solution)			
Inland river	0.102	0.14	0.73
Ocean outfall	0.01	0.14	0.07

Overall, this indicates an acceptable risk to the aquatic environment from release of the notified chemical after mitigation. Nevertheless, even after mitigation, the RQ value is approaching 1,

and exceeds 1 if release to STPs is concentrated into a smaller fraction of the population rather than assuming national use.

However, it is noted that the value used to calculate PNEC reflects the limit of solubility rather than an actual harmful effect. Indeed, because the notified chemical has very low solubility, it is unlikely to be available at concentrations that would cause harmful effects to aquatic organisms. In addition, only about 25% of treated sewer effluent is released to inland rivers or streams. However if greater volumes of the notified substance were to be imported and used, the PEC would correspondingly increase. In this case, the DEH may have concerns regarding risk to the aquatic environment.

The risks associated with environmental exposure from remaining notified chemical in biosolids (sludge) are also likely to be very low. According to the DEH model, and given the quantity of notified chemical to be used in formulations nationally over a year, the concentrations in biosolids if applied to soil at a rate of 10 tonnes/ha/year should not exceed 0.06 mg/kg soil.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Occupational exposure to the notified chemical during transport and storage of the imported product (pure notified chemical), or of finished products containing up to 10% notified chemical, is only likely in the event of accidental container spillage involving breach of import packaging.

During reformulation, the most likely exposure route is dermal. Ocular exposure may also occur as a result of accidental drips or spills. Exposure is expected to be minimal due to the use of PPE such as impervious gloves, coveralls and safety boots. Inhalation exposure will be limited by sufficient ventilation, including local exhaust ventilation fitted to mixing and filling machines, and the low vapour pressure and relatively large particle size (less than 0.17% < 10μm).

Intermittent, wide-dispersive use with direct handling may occur when sales staff demonstrate the product. Assuming twenty applications a day, exposure could be up to 24 g/day (EU SCCNFP/0690/03) of product containing up to 10% notified chemical.

Anticipated systemic human exposure to the notified chemical:

General equation:

$$= \frac{\text{(amount of sunscreen applied daily) x (\% dermal absorption) x (concentration of chemical in sunscreen)}}{\text{body weight}}$$

Amount of sunscreen applied daily = 24 g
Assumed dermal absorption = 0.08%
Assumed maximum concentration of notified polymer in finished product = 10%
Average adult body weight = 60 kg

$$= \frac{24 \text{ g} \times 0.08\% \times 10\%}{60\,000 \text{ g}}$$

$$= 3.2 \text{ ng/kg bw}$$

9.2.2. Public health – exposure assessment

Direct public exposure during transport and storage is unlikely, and therefore, public exposure will be restricted to those persons using the products containing the notified chemical. There will be two types of products that the notified chemical will be incorporated into; moisturising formulas (2-5% notified chemical), that are used on a daily basis and applied on the face and neck; and sunscreens (10% notified chemical) in anticipation of sun exposure to the face and/or other parts of the body depending on formulation.

The applicant has suggested that on average the products will be used be approximately once a day. Persons using the final product will be dermally exposed to the notified chemical through several areas including the arms, legs, face, neck, back, and chest. Up to 18 g of sunscreen containing 10% notified chemical may be applied per day (EU SCCNFP/0690/03). Accidental direct ocular exposure and ingestion of the notified chemical may also occur.

Anticipated human exposure to the notified chemical:

General equation:

$$= \frac{\text{(amount of sunscreen applied daily) x (\% dermal absorption) x (concentration of chemical in sunscreen)}}{\text{body weight}}$$

Assumed dermal absorption = 0.08%
Assumed maximum concentration of notified polymer in finished product = 10%
Amount of sunscreen applied daily = 18 g
Average adult body weight = 60 kg

$$= \frac{18 \text{ x } 0.08\% \text{ x } 10\%}{60 \text{ kg}}$$

$$= 2.4 \text{ ng/kg bw}$$

9.2.3. Human health – effects assessment

The percutaneous absorption of notified chemical was measured *in vitro* using human skin. Absorption values of <0.08% were obtained from this study.

The notified chemical was found to have low acute oral and dermal toxicity in rats. No phototoxicity was observed in Guinea pigs.

The notified chemical was not irritating to the skin of rabbits. Slight eye irritation was observed in rabbits, with slight redness and slight watery discharge observed at 24 hours, with redness persisting to 48 hours in some cases. The notified chemical was not a skin sensitiser and did not cause photoallergenicity in Guinea pigs.

No treatment related effects were observed in a 90-day repeat dose study in rats, with the NOAEL found to be >1000 mg/kg bw/day. No treatment related effects were seen in a teratogenicity study in pregnant rats.

The notified chemical was not found to be genotoxic in an in vivo mammalian erythrocyte micronucleus test, or an in vitro mammalian chromosomal aberration test, or bacterial reverse mutation tests carried out on *E. coli* and *S. typhimurium*, the latter in the presence or absence of UV illumination.

Based on the available data the notified chemical is not classified as a hazardous substance under the NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 1999).

9.2.4. Occupational health and safety – risk characterisation

The low toxicity of the notified chemical indicates that the risk to occupational health and safety will be low. Plant operators and laboratory workers may be exposed to small amounts of the pure notified polymer or products containing up to 10% notified chemical. There is likely to be widespread exposure of retail workers to this product. However, the low dermal absorption limits systemic exposure, and there is no evidence of skin sensitisation or irritation.

9.2.5. Public health – risk characterisation

The primary source of exposure to the notified chemical will by dermal exposure. Other routes of accidental or incidental exposure will be ocular or oral exposure.

The notified chemical is of low acute oral and dermal toxicity, does not cause skin irritation and may cause slight eye irritation.

Using a NOAEL of the 1000 mg/kg bw/day, the expected daily dose of 3.2 ng/kg bw/day calculated in Section 9.2.2, the Margin of Exposure (MOE) is greater than 1 million. The high MOE is due to the low toxicity, and low dermal absorption of the notified chemical. The high Margin of Exposure, and no indication of genotoxicity or teratogenicity, indicates the notified chemical poses a low public health regulatory concern.

The OTC Medicines Section, Therapeutic Good Administration, following its evaluation of the safety of Tinosorb S in November 2004 concluded that it:

"can now be included in sunscreen products which are proposed for registration or listing in the Australia Register of Therapeutic Goods without the need for further evaluation of safety of the substance per se, subject to the following conditions:

For use in topical (dermal) sunscreen products only; the concentration is not to exceed 10%."

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*.

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.

The notified chemical is not classified under the GHS.

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 a component of sunscreen and moisturisers.

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

- 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

- Use of the chemical must remain within the parameters specified by this notification.

Disposal

- The notified chemical should be disposed of to landfill or by incineration.

Emergency procedures

- Spills/release of the notified chemical should be handled by adsorption on to an inert material, and then disposed of via a licensed waste disposal operator to a suitable 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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