File No: NA/861

January 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Cetiol CC

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Cetiol CC

1. APPLICANT

Cognis Australia Pty Ltd of 83 Maffra Street Broadmeadows Melbourne VICTORIA 3047 (ACN 006 374 456) has submitted a standard notification statement in support of their application for an assessment certificate for Cetiol CC.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae have been exempted from publication in the Full Public Report and the Summary Report.

Marketing Names:	Cetiol CC Cetiol KE 3404 EW-POL 9535
Molecular Weight:	286
Method of Detection and Determination:	The chemical was identified and characterised using gas chromatography and Fourier Transform Infrared (IR), Ultraviolet (UV) and Nuclear Magnetic Resonance (NMR) spectroscopy.
Spectral Data:	IR peaks were located at 2957, 2923, 2873, 2858, 1744, 1468, 1402, 1379, 1262, 947, 793 and 723 cm^{-1}

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 25°C & 101.3 kPa:	White liquid.
Melting Point at 101.3 kPa:	-22°C
Boiling Point at 101.3 kPa:	330°C
Specific Gravity:	0.8906 $\pm$ 0.0002 at 20°C
Vapour Pressure:	2.1 x 10^{-5} kPa at 20°C
Water Solubility:	0.1 mg/L

Partition Co-efficient (n-octanol/water):	log P_{ow} = 4.2 $\pm$ 0.2 at 23.5°C
Hydrolysis as a Function of pH:	$T_{1/2}$ at pH 4.0 none $T_{1/2}$ at pH 7.0 none $T_{1/2}$ at pH 9.0 13.8 days
Adsorption/Desorption:	Not determined.
Dissociation Constant:	Not determined.
Particle Size:	Produced in liquid form.
Flash Point:	174°C
Flammability Limits:	Not flammable.
Autoignition Temperature:	Not determined.
Explosive Properties:	Not explosive.
Reactivity/Stability:	Stable and non reactive, can decompose to carbon dioxide, carbon monoxide and sulphur dioxide when mixed with strong acids and oxidising agents or when exposed to fire.

3.1 Comments on Physico-Chemical Properties

Only brief summaries have been provided for the tests which were carried out according to EU test guidelines which are essentially identical to those of the OECD.

The melting point, boiling point and vapour pressure were determined using the Dynamic Differential Calorimetry method using a 2 point calibration with water and Sn (Tilinski, 1999*a,b,c*). The vapour pressure of 2.1 x 10^{-5} kPa at 20˚C indicates that the chemical is moderately volatile (Mensink et al., 1995)

The relative density was determined using the Pycnometer method [based on OECD TG 109] of Gay-Lussac (Schmitt, 1999*a*).

Water solubility was measured by the column elution method [based on OECD TG 105] and analysed by gas chromatography (Schmitt, 1999*b*) with cold injection and flame ionisation detection.

Hydrolysis was measured using gas chromatography with cold injection and flame ionisation detection at pH 4, 7 and 9 (Schmitt, 1999*c*). No significant loss at pH 4 or 7 was detected after 6 days at 50ºC but a significant, measurable decrease in concentration occurred at pH 9. The temperature at which the half-life was estimated is unclear.

The partition coefficient for the notified substance was measured using the shake-flask method (based on OECD TG 107) with gas chromatography with cold injection and flame ionisation detection (Schmitt, 1999*d*).

The adsorption/desorption coefficient and dissociation constant have not been determined. The notifier expects the substance to adsorb strongly to soils and sediments due to its unpolar nature and does not expect it to dissociate. The low water solubility and high partition coefficient indicate that the chemical is likely to rapidly drop out of solution and associate with the organic component of sludges, soils and sediments.

4. PURITY OF THE CHEMICAL

Degree of Purity: 96.6%

The remainder 3.4% is made up of symmetric and unsymmetric carbonates of C_6, C_8 and C_{10}.

Hazardous Impurities: None

Non-hazardous Impurities (> 1% by weight): None

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical is used as an emollient in sun care products. It enhances the performance of the active ingredients in the formulation. The chemical is imported at 96.6%. One tonne of the notified chemical will be imported in the first year increasing to 5 tonnes/annum in years 2-5. In Australia the chemical will be formulated into sun creams containing up to 20% notified chemical. The chemical will be imported in 175 kg drums or 850 kg containers.

6. OCCUPATIONAL EXPOSURE

Transport and Storage
Ten workers will be involved in transport and storage of the imported product. It will be packaged at 500 mL when mixed. Exposure will be limited to accidental spillage.

Dispensing and Compounding
The notifier has indicate that 8 workers will handle the notified chemical during manual weighing into smaller containers and transfer to 4000 L sealed mixing tanks. Dermal and ocular exposure to the chemical may occur. Exposure is expected for approximately 8 hours per day, 30 days per year. The notifier has indicated that the dispensary should be fitted with a vapour removal system. Disposable or PVC gloves and safety glasses should be worn by workers when required.

Reformulation
The notifier estimates 25 workers will be involved in the process. The notified chemical is blended with water and other ingredients in sealed 4000 L tanks at approximately 80°C and

cooled to 30°C after blending. The blended product containing 20% of the notified chemical is piped directly to sealed filling machines and automatically dispensed into 500 mL blow moulded plastic bottles for distribution. Due to the closed nature of the process it is unlikely that dermal or ocular exposure would occur. However exposure to drips and spills could occur when connecting and disconnecting hoses. The notifier has stated that safety glasses and protective gloves should be worn during reformulation and equipment cleaning. As estimated 50 batches will be made per year.

Laboratory and Quality Control Staff
During dispensing and reformulation, the notified chemical will be sampled and tested. Three research and development staff and 5 quality control staff will handle the notified chemical during these processes. During quality control testing, exposure to the notified chemical will be for 4 hours per day, 30 days per year and 6 hours per day, 15 days per year for trial batches.
The notified chemical is likely to be handled in small quantities. The probable route of exposure will be dermal or ocular. The notifier states that the laboratory will contain fume hoods and staff will wear safety glasses, laboratory coats and disposable gloves.

7. PUBLIC EXPOSURE

Since the final products will be sun creams containing up to 20% of the notified chemical, it is anticipated that the general public will come into contact with the notified chemical. Exposure to the notified chemical in a more concentrated (96.6%) form may occur in the event of an accident during transportation, prior to reformulation. According to the Material Safety Data Sheet (MSDS) for Cetiol CC, a spill should be prevented from flowing into the drainage system and should be removed with liquid-absorbing material.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

The notified chemical will be reformulated into suncare products at one site in Australia. The notifier expects that release volumes from the reformulation process will be low. Estimates are 0.3 kg/batch (up to 15 kg/annum) from residues of Cetiol CC remaining in the storage drums after emptying, 0.2 kg/batch (up to 10 kg/annum) from spills during reformulation and 0.2 kg/batch (up to 10 kg/annum) from cleaning of equipment. All the reformulation waste will be treated in the on-site treatment plant. It will be neutralised and the solids removed for landfill and the liquid effluent discharged to trade waste.

Release of the chemical to the environment through its proposed use as a consumer product is expected to be widespread. Consumers will apply the suncare products to the skin where the chemical will remain with very little absorption until it is washed off during swimming, bathing and showering. The notifier estimates that approximately 90% of the sun cream containing the notified chemical will be washed off the skin during showering (up to 4.5 tonnes/annum) and released to the sewer system.

The end use sun cream containers are expected to be disposed of with normal household garbage to landfill. The residues of notified polymer remaining in these bottles are expected to be 2% or up to 100 kg/annum.

8.2 Fate

It is likely that the majority of the imported volume will end up in the sewer, while the remainder will end up in landfill.

Estimated annual amounts and likely disposal sites of waste notified polymer from the reformulation process are:

Reformulation;	spills	10 kg	on-site TP/sewer
	storage container residues	15 kg	on-site TP/sewer
	equipment washings	10 kg	on-site TP/sewer
	consumer's container residue	100 kg	landfill

Approximately 0.7% (35 kg) of the notified chemical will enter the on-site treatment plant via container residues, spills and process equipment washing. The low water solubility and high partition coefficient suggest that the notified chemical is likely to adsorb to the sludge in the treatment plant. If it is presumed that 80% of the substance is removed in the treatment plant, 7 kg would enter the sewer in the effluent from the treatment plant.

Approximately 100 kg (2%) of the notified chemical will go to landfill as end use container residues. Given the low water solubility and high partition coefficient the notified chemical is not expected to leach from landfill but to remain associated with the soils and sediments until it is degraded by biotic and abiotic processes.

About 90% (4.5 tonnes/annum) of the chemical may end up in the sewer from consumer use, and likely to be removed in the metropolitan sewage treatment plant. If it is presumed that 80% of the substance is removed in the sewage treatment plant, approximately 900 kg may be released in sewer effluent in a very disperse manner throughout Australia. Incineration of the notified chemical will produce oxides of carbon and water.

The notified chemical has been determined to be readily biodegradable according to OECD criteria in the CO_2 headspace test (ISO 14593-similar to OECD TG 301D), displaying 89% CO_2 release within 28 days (Borner, 2000) with the reference substance, sodium benzoate, showing 99% degradation after 14 days.

The values for log Pow (4.2), water solubility (<1 mg/L) and molecular weight (286) of the notified chemical indicate significant potential for bioconcentration (Connell, 1989). However, the 89% biodegradable result in the CO_2 test should significantly mitigate this potential.

9. EVALUATION OF TOXICOLOGICAL DATA

Toxicological tests were conducted using the notified chemical. Tests were performed to corresponding OECD and EEC guidelines at testing facilities that comply with the OECD principles of good laboratory practice.

9.1 Acute Toxicity

Summary of the acute toxicity of Cetiol CC

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 5 000 mg/kg	(Haynes, 1999)
acute dermal toxicity	rat	LD_{50} > 5 000 mg/kg	(Schreiter, 1999a)
skin irritation	rabbit	slight irritant	(Schreiter, 1999b)
eye irritation	rabbit	slight irritant	(Schreiter, 1999c)
skin sensitisation	guinea pig	non-sensitiser	(Schreiter, 1999d)

9.1.1 Oral Toxicity (Haynes, 1999)

Species/strain:	Rats/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	5 000 mg/kg (maize oil) was administered by gavage
Test method:	OECD TG 401
Mortality:	no deaths were recorded during the study
Clinical observations:	piloerection was observed in males during the first week post dosing
Morphological findings:	no organ abnormalities were observed at necropsy
Comment:	no effect on body weight gain was observed
LD_{50}:	> 5 000 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Schreiter, 1999a)

Species/strain:	Rat/Wistar
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	the notified chemical (5 000 mg/kg) was applied under an occlusive dressing for 24 hours
Test method:	OECD TG 402
Mortality:	no deaths were recorded during the study
Clinical observations:	after dosing, all animals showed piloerection up to one hour
Morphological findings:	no organ abnormalities were observed at necropsy
Comment:	None
LD_{50}*:*	> 5 000 mg/kg
Result:	the notified chemical was of low acute dermal toxicity in rats

9.1.3 Inhalation Toxicity

Study not provided by the notifier.

9.1.4 Skin Irritation (Schreiter, 1999b)

Species/strain:	Rabbit/New Zealand albino
Number/sex of animals:	3 female
Observation period:	21 days
Method of administration:	0.5 mL test substance was applied to a clipped test site under semi-occlusive conditions for 4 hr
Test method:	OECD TG 404

Draize scores:

	Time after treatment (days)					
Animal	***1 hour***	***1 day***	***2 day***	***3 day***	***7 day***	***21 day***
Erythema						
1	[a]1	1	0	0	-	-
2	1	1	1	1	-	-
3	1	1	1	1	-	-
Oedema						
1	0	0	0	0	-	-
2	0	0	0	0	-	-
3	0	0	1	0	-	-

[a] see Attachment 1 for Draize scales

Individual mean scores: erythema 0.3, 1.00 and 1.00
oedema 0.00, 0.00 and 0.33

Comment: One hour after exposure all animals exhibited very slight erythema; erythema persisted up to days 3 in 2 animals; no significant oedema was noted, however scaling was persistent in all three animals

Result: the notified chemical was a slight irritant to the skin of rabbits

9.1.5 Eye Irritation (Schreiter, 1999c)

Species/strain: Rabbit/New Zealand albino

Number/sex of animals: 3 female

Observation period: 3 days

Method of administration: 0.1 mL test substance was placed in the conjunctival sac of the left eye ; the untreated eye served as control

Test method: OECD TG 405

Draize scores of unirrigated eyes:

	Time after instillation											
Animal	***1hour***			***1 days***			***2 days***			***3 days***		
Cornea	*All scores were zero*											
1												
2												
3												
Iris												
1	*All scores were zero*											
2												
3												
Conjunctiva	***r***	***c***	***d***	***R***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	1	1	0	1	0	0	1	0	0	0	0	0
2	1	1	0	1	0	0	0	0	0	0	0	0
3	2	1	0	1	1	0	0	0	0	0	0	0

[1] see Attachment 1 for Draize scales
o = opacity a = area r = redness c = chemosis d = discharge

Individual mean scores: erythema of conjunctiva 0.67, 0.33 and 0.33
oedema of conjunctiva 0.00, 0.00 and 0.33

Result: the notified chemical was a slight irritant to the eyes of rabbits

9.1.6 Skin Sensitisation (Schreiter, 1999d)

Species/strain: Guinea pig/Dunkin Hartley

Number of animals: 30 female
test animals 20
control animals 10

Induction procedure:

test group: days 1,7, 14 — 0.2 mL of 100% test substance in sesame oil was applied under occlusive patch to a clipped area of the left flank for 6 hours, the procedure was repeated in days 7 and 14

control group: treatment was as for the test group, using the vehicle as control

Challenge procedure:

day 28	0.2 mL of 75% test substance was applied by occlusive patch to a clipped area of the right flank for 6 hr, for both test and control groups

Test method: OECD TG 406 (Buehler test)

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
75%	0/20**	0/20	0/10	0/10

* time after patch removal
** number of animals exhibiting positive response

Comment: slight to moderate reactions of the skin and scales were observed in some animals during induction phase; no signs of irritation were observed during the challenge phase

Result: the test substance was not sensitising to the skin of guinea pigs under test conditions

9.2 13 Week Repeated Dose Toxicity (Biol, 2000)

Species/strain: rat/Sprague Dawley

Number/sex of animals: 10/sex/group: 3 test groups, 1 control group
5/sex/group: 2 recovery groups (high dose and control)

Method of administration: oral (gavage)

Dose/Study duration: control group: 0 mg/kg/day
low dose group: 75 mg/kg/day
mid dose group: 250 mg/kg/day
high dose group: 1 000 mg/kg/day
vehicle: corn oil

animals were fed for 13 consecutive weeks followed by a 4 week treatment free (recovery) period for the recovery groups

Test method: OECD TG 407

Clinical observations
No treatment-related responses were observed. Low and mid dose males demonstrated variations in motor activity at the end of treatment.

Clinical chemistry/Haematology
No treatment related responses were observed in clinical chemistry parameters. Variations

observed were within historical control values.

Pathology
Mid and high dose males demonstrated an increase in relative liver weights compared to the controls. However, increase in relative liver weights in high dose males showed a reduction at the end of the recovery period. The mid and high dose females had decreased relative liver weights at the end of the treatment period, with no changes in liver weight at the end of the recovery period.

Histopathology
No treatment related histopathological changes were observed.

Comment
No relevant treatment related changes were observed in males or females at any dose level. The variations observed in body weights of high dose males, clinical chemistry parameters and organ weights were slight, inconsistent between sexes and within historical control values.

Result
The NOEL was established to be ≥1000 mg/kg/day, the highest dose tested.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Wiebel, 1999)

Strains:	*Salmonella typhimurium* TA1538, TA1537, TA1535, TA100 and TA98
Metabolic activation:	liver fraction (S9 mix) from rats pretreated with phenobarbitol and 3-napthoflavone
Concentration range:	first and second assays: 0, 8, 40, 200, 1 000 and 5 000 μg/plate in the presence and absence of S9-mix (vehicle ethanol) positive controls: (without S9-mix); sodium azide for TA1535 and TA100; 9-aminoacridine for TA1537; 4-nitro-o-phenylendiamine TA1538 and TA98. (with S9-mix) 2-aminoanthracene for all strains
Test method:	OECD TG 471 (Direct Plate Incorporation Method)
Comment:	the notified chemical was not toxic to *S. typhimurium* strains up to 5 000 μg/plate; in both assays revertant frequencies for all doses and strains with or without S9 mix were comparable to concurrent negative control cultures

	all positive and negative controls responded appropriately; all conditions for a valid assay were met
Result:	the notified chemical was non mutagenic under the conditions of the test

9.3.2 Chromosomal Aberration Assay in Chinese Hamster V79 Cells (Czich, 2000)

Cells:	chinese hamster (V79) cells
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with phenobarbitol and 3-napthoflavone

Dosing schedule:

Metabolic Activation	Experiment/ Study Number	Test concentration (µg/mL)	Controls
-S9	I	harvest time = 18 hours treatment time = 4 hours 0, 25.6, 64.0*, 160.0*, 400.0^{p*}, 1000.0^{p} and 2860^{p}	Positive: EMS Negative: ethanol
	II	harvest time = 18 hours treatment time = 18 hours 0, 6.3*, 12.5*, 25.0*, 50.0^{p}, 100.0^{p} and 200.0^{p}	
	II	harvest time = 18 hours treatment time = 28 hours 0, 25.0, 50.0, 100.0 and 200.0^{p*}	
+S9	I	harvest time = 18 hours treatment time = 4 hours 0, 25.6, 64.0, 160.0*, 400.0^{p*}, 1 000.0^{p*} and 2860.0^{p*}	Positive: CP Negative: ethanol
	II	harvest time = 28 hours treatment time = 4 hours 0, 25.6, 64.0, 160.0, 400.0^{p*}, 1 000.0^{p*} and 2860.0^{p*}	

EMS - ethyl methanesulphonate * doses selected for metaphase analysis
CP - cyclophosphamide
p – turbidity of the test item at the start of treatment, oily film on the surface of culture medium after 4 hours

Test method:	OECD TG 476
Comment:	in both experiments neither significant/biologically relevant increases in chromosomal aberrations nor an increase in the frequencies of polyploid metaphases were observed

Result:	the notified chemical was non clastogenic under test conditions

9.4 Human Patch Test (Kremer and Holz, 1999)

Three different chemicals were tested. Only findings relevant to the notified chemical are included in this report.

Species/strain:	Humans
Number and sex:	20 volunteers of both sexes
Doses and method of administration:	a single dose of the notified chemical (100%, 70 µL) was applied under a occlusive dressing for 24 hours on the backs of the test subjects positive controls: Texapon N28 1% AS sodium dodecyl sulphate 0.5% AS negative control: demineralised water
Test method:	according to COLIPA standard; evaluated according to Frosch scale (Frosch, 1979)
Comment:	skin reactions of erythema, oedema, scaling and fissures were used to determine skin tolerance to the test substance; no reactions were observed on exposure to the notified chemical all positive and negative controls responded appropriately
Result:	notified chemical was well tolerated by the human skin under test condition

9.5 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity (LD_{50} > 5 000 mg/kg) and low dermal toxicity (LD_{50} > 5 000 mg/kg) in rats. In rabbits, it was a slight skin and eye irritant. The notified chemical was not a skin sensitiser in a non-adjuvant type test in guinea pigs.

A 13 week repeat dose dietary study in rats established a NOEL of $\geq$ 1 000 mg/kg/day the highest dose tested. The notified chemical was not mutagenic in a reverse mutation assay in bacteria. It was non clastogenic in the *in vitro* chromosomal aberration assay in Chinese Hamster V79 cells.

The notified chemical was well tolerated in a human patch test.

The notified chemical is not classified as a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The notifier provided the following ecotoxicity data, which were performed in accordance with OECD Test Guidelines.

Test	Species	Results (Nominal, WAF)*
Acute Toxicity [OECD 203]	*Brachydanio rerio* (zebra fish)	LC_{50}(96 h) > 100 mg/L NOEC = 100 mg/L
Acute Immobilisation [OECD 202/1]	*Daphnia magna*	EC_{50}(48 h) > 100 mg/L NOEC = 100 mg/L
Inhibition of Algal Growth [OECD 201]	*Scenedesmus subspicatus*	EbC_{50} (72 h) > 100 mg/L ErC_{50} (72 h) > 100 mg/L NOEC = 100 mg/L
Inhibition of Bacterial Respiration [OECD 209]	Activated sludge bacteria	NOEC = 34 mg/L EC_{10} = 62 mg/L EC_{50} > 110 mg/L

*See actual concentrations below; WAF water accomodated function

Due to the low water solubility of the notified chemical, the test solutions used in the studies for fish, daphnia and algae were prepared by making solutions of the nominal concentrations of 1 to 100 mg/L in test medium one day before use, stirring for 24 h then filtering after a 2 h settling period. The filtered fractions were used for the tests and the actual concentrations of these filtrates (WAFs) were measured using gas chromatography after dichloromethane extraction.

Zebra Fish

The ecotoxicity tests on the zebra fish were performed using a semi-static test methodology (Weirich, 2000*a.*). Groups of 10 fish were exposed to the nominal concentrations of 1 and 100 mg/L of test substance and the control solution. During the test the dissolved oxygen was always >73% saturation and pH ranged from 7.8-8.3. The temperature of the test solutions ranged from 22-21.5ºC. In the control and test concentrations, all fish were observed at 2, 24, 48, 72 and 96 hours and no deaths occurred. The measured concentrations of the nominal 1 and 100 mg/L solutions were between 0.03 and 0.09 for the nominal 1 mg/L and between 0.02 to 0.04 for the nominal 100 mg/L.

Daphnia magna

The ecotoxicity tests on daphnia were performed using a static test methodology (Weirich, 2000*b)*. Two groups of 10 organisms were exposed to each of the nominal concentrations of 1, 10 and 100 mg/L of test substance and the control solution. During the test the dissolved oxygen was always >94% saturation and pH ranged from 7.6-7.8. The temperature of the test solutions was 21ºC. In the control and test concentrations all daphnia were observed at 24 and 48 hours and no deaths occurred. The measured concentrations of the nominal 1, 10 and 100

mg/L solutions were between 0.01 and 0.03 for the nominal 1 mg/L, between 0.01 and 0.02 for the nominal 10 mg/L and between 0.01 to 0.03 for the nominal 100 mg/L.

Algal Growth Inhibition

The chronic algae toxicity tests were performed using a static test methodology (Weirich, 2000*c*). Three replicates at the nominal concentrations of 1, 3, 10, 30 and 100 mg/L of test substance and the control solution were innoculated with algae. During the test the pH ranged from 7.4-9.0 (pH increase likely caused by growth of the test algae) and the temperature of the test solutions was 24.5ºC. Aliquots were removed from each vessel at 24, 48 and 72 h and the algae cell concentrations determined. No inhibition occurred at any WAF but the measured concentrations of the nominal 1, 10 and 100 mg/L solutions were between 0.03 and 0.05 for the nominal 1 mg/L, between 0.04 and 0.06 for the nominal 10 mg/L and between 0.05 to 0.44 for the nominal 100 mg/L.

Activated Sludge Inhibition

Due to the low water solubility of the notified chemical the test solutions used in the study for sludge inhibition were prepared by making solutions of the nominal concentrations of 20, 60 and 200 mg/L in test medium one day before use, stirring for 24 h then filtering after a 2 h settling period, except the 20 mg/L which was siphoned instead of filtered. The filtered fractions were used for the tests and the concentrations of these filtrates (WAFs) were further diluted by the inoculum and nutrient media by a factor of 56.8/100 so that the final concentrations were nominally 11.4, 34.1 and 114 mg/L. The actual concentrations of the solutions were not measured in the test.

The respiration rate of an activated sludge suspension mixed with each of the test solutions and the control solutions (containing 3,5-dichlorophenol as the reference substance) was measured after 180 minutes. The oxygen consumption and inhibition of the test solutions were compared with the controls. The EC50 (3h) of the reference substance was 23 mg/L hence the criteria for the validity of the test was fulfilled.

Conclusion

The substance is not toxic to fish, daphnia and algae up to the limits of its water solubility. However, some toxic effects may be expected on sewage micro-organisms below this concentration.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The majority of notified chemical will be incorporated into suncare products. Consumer use is expected to be widespread across Australia, resulting in release of a portion of the chemical directly to the aquatic compartments. Some release of the chemical in sunscreens may occur in natural waterways, e.g. oceans, lakes and rivers. However, release is expected to be very diffuse.

The notifier indicates that most of the suncare products (up to 90% of the total volume of the notified chemical), may be discharged directly into the sewer through washing. The calculated PEC for a worst case scenario predicts a concentration of 4.5 µg/L in the sewage outflow assuming all the imported chemical remains dissolved in sewage waters. Parameters include: 4500 kg maximum annual release by consumers (12.33 kg/day), an Australian population of 18 million and a daily per capita waste water discharge of 150 L (2700 ML).

Sewage outflow will be further diluted an average of 1:10 by the receiving waters, giving an environmental PEC of 0.45 μg/L. While this is only slightly below measured concentrations in fish, daphnia and algal tests (10-440 μg/L), there were no effects noted at these concentrations. Further, the substance may readily biodegrade and/or adsorb to sewage sludge where the likely concentration is expected to be <0.09 μg/L. However, there may be some effects on sewage micro-organisms, particularly if release occurs at relatively high concentrations from the formulation plant.

Wastes generated through product reformulation are estimated to be minimal, and will be disposed of to approved disposal facilities. Small amounts of residues in product containers will be disposed of with normal household garbage in a very diffuse manner to landfill.

The environmental hazard from the notified chemical is expected to be low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical was of very low acute oral and low acute dermal toxicity. It was a slight skin and eye irritant and not a skin sensitiser A repeat dose dietary study in rats established a NOEL of ≥1 000 mg/kg/day. The notified chemical was not mutagenic in Ames test and non clastogenic in chinese hamster V79 cells. The notified chemical is not classified as a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

Occupational health and safety
Exposure to the notified chemical is not expected during transport or storage except in the event of an accident. The risk of adverse health effects for transport and storage workers is considered to be low.

Dermal and ocular exposure can occur during weighing and transfer of the notified chemical into sealed mixing tanks. The presence of a vapour removal system and use of personal protective equipment should provide adequate protection against the notified chemical. During reformulation and packaging due to the enclosed nature of the processes exposure to the notified chemical is not expected to occur. Dermal exposure due to drips and spills might occur when connecting and disconnecting hoses and personal protection should provide adequate protection from the notified chemical. Dermal and ocular exposure which might occur during cleaning equipment should be curtailed by the use of safety glasses and protective gloves.

During quality control testing there could be ocular or dermal exposure to the notified chemical which could be adequately controlled by the use of fume hoods and personal protective equipment.

Given the low toxicity of the notified chemical and the use of engineering controls and personal protective equipment, health risk to workers is low during compounding, reformulation, packaging and quality control.

Public health

The notified chemical will be sold to the general public as a component of sun creams (up to 20%). According to the 'Technical Guidance Document in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No. 1488/94 on Risk Assessment for Existing Substances, Part I-IV', the typical application amount of sun cream is 8 g. If one assumes that sun cream is applied twice daily, then the daily exposure to the notified chemical is expected to be 20% of 16 g, or 3.2 g. Therefore, the level of exposure of a 70 kg adult, a 20 kg early school age child and a 10 kg toddler can be calculated. The dermal absorption of the sun cream is unknown, but for the purposes of this calculation it is assumed to be 10%. The total body exposure (100%) and the face, arms and legs exposure (30%) in a 70 kg adult would be 4.6 and 1.4 mg/kg bw/day of the notified chemical, respectively. For a 20 kg child, the total body and face, arms and legs exposure is expected to be 16 and 4.8 mg/kg bw/day of the notified chemical, respectively. Since it is likely that a 10 kg toddler would be clothed and not require a full body coverage of sun cream, even at the beach, only a 30% exposure has been calculated. In the 10 kg toddler, exposure to the notified chemical is expected to be 9.6 mg/kg bw/day.

Therefore, the highest exposure to the notified chemical was calculated to be 16 mg/kg bw/day in a 20 kg child, based on full body exposure twice daily. This is probably a very conservative calculation, and reflects a holiday situation, where the child is at the beach. This would not be expected to occur for more than 6 months of the year (covering the warm to hot months of spring and summer). During the remaining period of the year, a 30% application is more likely, especially during school time. Attributing 6 months to full body coverage and 6 months to 30% coverage, then a value of 9.2 mg/kg bw/day would be the exposure level of a 20 kg child to the notified chemical. The NOEL in the repeat dose toxicity study in rats was $\geq$1000 mg/kg bw/day. Using a 100 fold safety factor to take into account species differences and differences in sensitivity to the notified chemical, an acceptable dose for human use would be $\geq$10 mg/kg bw/day. This would safely cover the expected human exposure to the notified chemical in all of the above scenarios.

Although there was very slight skin and eye irritation caused by undiluted notified chemical in studies in rabbits, no dermal reactions were observed in the patch test in humans. Furthermore, it is normal practice to avoid putting sun creams in the eyes. Therefore, when sold to the public as a 20% component in sun creams, the risk of the general public to the notified chemical is considered to be low.

13. RECOMMENDATIONS

To minimise occupational exposure to Cetiol CC the following guidelines and precautions should be observed:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia 1987) and impermeable gloves should conform to AS/NZS

2161.2 (Standards Australia, 1992); all occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand,1994);

- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;

- A copy of the MSDS should be easily accessible to employees.

If products containing the notified chemical are hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999), workplace practices and control procedures consistent with State and Territory hazardous substances regulations must be in operation.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical may be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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Attachment 1

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

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

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

CORNEA

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

CONJUNCTIVAE

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

IRIS

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

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