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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

FAT 74'002/A

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FULL PUBLIC REPORT

FAT 74'002/A

1. APPLICANT

Ciba Specialty Chemicals Pty Ltd of 235 Settlement Road THOMASTOWN VIC 3074 (ACN 97 005 061 469) has submitted a standard notification statement in support of their application for an assessment certificate for FAT 74'002/A.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data, details of the polymer composition and details of exact import volume and customers have been exempted from publication in the Full Public Report and the Summary Report. The marketing name is Tinosorb FR-conc.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Solid yellow powder
Boiling Point:	756 °C (calculated)
Melting Point:	No melting point up to 400 °C
Density:	1.46 g/ cm^3 at 20.3 °C
Vapour Pressure:	8.9×10^{-28} kPa at 25 °C
Water Solubility:	< 0.59 g/L (at 20 °C)
Partition Co-efficient (n-octanol/water):	log P_{ow} = -2.3 at 20 °C
Hydrolysis as a Function of pH:	$T_{1/2}$ at pH 4.0 unable to be determined $T_{1/2}$ at pH 7.0 > 1 year at 25°C $T_{1/2}$ at pH 9.0 > 1 year at 25°C
Adsorption/Desorption:	Not carried out.
Particle Size:	< 3.7 % < 10 μm ~ 50 % < 60 μm 10.4 % > 200 μm

Dissociation Constant:	Not carried out.
Flash Point:	Not relevant.
Flammability Limits:	Not highly flammable (EEC Directive 92/69 method A.10)
Autoignition Temperature:	Exotherm started at 247 °C Self-ignition at 313 °C.
Explosive Properties:	Combustible but not explosive.
Reactivity/Stability:	Not an oxidising substance.
Surface Tension:	69 mN/m at 90 % saturation (19.8 °C).

3.1 Comments on Physico-Chemical Properties

The physico-chemical parameters were determined via OECD Test Guidelines.

The melting point was determined to be greater than 400 °C via OECD TG 102 – Differential Thermal Calorimeter (Schmiedel, 1997a). In the study a sample of the chemical was heated from 30 °C to 400 °C at a rate of 200 K/min. This was done twice. In the first run an endothermic heat effect was observed between 228.3 and 242.7 ºC. After this the sample's mass had decreased by 32 %, and it appeared black and the volume had increased. In the second run this effect was observed at 166.6-209.8 ºC. A weight loss of 11.7 % was observed but the sample remained a yellow powder. The sample did not return to its original state, consequently the endothermic heat effect was not due to the melting of the sample.

Schmiedel (1997b) determined the density of the notified chemical following the OECD TG 109 – Gas Comparison Pycnometer.

Schmiedel (1998a) determined the vapour pressure of the notified chemical by calculation from the boiling point and using the modified Watson calculation.

The water solubility was determined by Schmiedel (1997c).

Using the method of Schmiedel (1998b, OECD TG 111), the hydrolysis of the notified chemical was examined at 50 ºC at different pH. It was determined that due to the chemical's low solubility (2 mg/L) at pH 4, the hydrolysis of the chemical could not be determined. However, at pH 7 and 9 after 5 days the degradation was found to be 10 %. The half-life of the chemical at pH 7 and 9 was estimated as 1 year under normal environmental conditions at 25 ºC. This indicates that the chemical is hydrolytically stable at pH 7 and 9.

Schmiedel (1997d) determined the partition coefficient of the notified chemical via a calculation method. In the preliminary test, it was found that the chemical had a low *n*-octanol solubility. Since this indicated a partition coefficient less than –2, neither the Flask Shaking Method (OECD TG 107) or the HPLC Method (OECD TG 117) could be used.

The adsorption/desorption and dissociation constant of the notified chemical were not determined. However, the low log P_{ow} and moderate water solubility indicate that the notified chemical will stay in solution, be mobile in soil and is unlikely to adsorb to soils and sediments. The molecule contains protonated nitrogens and sulphonate anions and is likely to remain amphoteric under environmental conditions (pH 4-9).

4. PURITY OF THE CHEMICAL

Degree of Purity: 71 %

Hazardous Impurities: The notified chemical contains 8 % unidentified organic by-products.

Non-hazardous Impurities (> 1% by weight): Exempt information.

Additives/Adjuvants: Exempt information.

5. USE, VOLUME AND FORMULATION

Use
FAT 74'002/A will be used as a component in laundry softener/conditioner liquid formulations for industrial and domestic use. The notified chemical functions as a UVA and UVB irradiation absorber after application to textiles, to which it is claimed to have a fixation rate of 48 %.

Volume
The notified chemical will be imported in commercial formulation in increasing amounts; 7.5 tonnes in year one, 11.25 tonnes in year two, 15 tonnes in year three and 22.5 tonnes in years four and five.

Formulation
The notified chemical will be imported in the product Tinosorb FR conc. at a concentration 11.2 % contained in 60 kg plastic drums designed for international transport. Tinosorb FR conc. will be sold at up to 13 commercial fabric softener manufacturers to use in formulating both commercial and domestic fabric softeners. Some repackaging of the plastic drums may occur at the notifier site. Blending operations will occur at the customer sites.

6. OCCUPATIONAL EXPOSURE

There is potential worker exposure in the event of spillage during transport or handling incidents. However, due to the robust nature of the packaging, exposure is unlikely.

Formulation
The incorporation of Tinosorb FR conc. in liquid formulations destined for use in commercial laundries and in domestic washes is expected to occur in up to 13 customer sites. The

batching operation consists of weighing out Tinosorb FR conc. which is either manually added to a blending vessel or transferred via a closed system. Either process is under the control of local exhaust ventilation. The maximum concentration of the notified chemical in Tinosorb FR conc. is 11.2 %. During the blending procedure, the mixer is enclosed and exposure is unlikely to occur. Packing lines are almost exclusively closed systems and are automated. There is potential for skin exposure during quality control sampling, product changeover and equipment maintenance. The maximum concentration of the notified chemical in end-use softeners is 0.5 – 0.7 %. Workers handling connections or equipment are required to use long PVC or impervious gloves, overalls and goggles. An estimated up to 20 workers are potentially exposed per fabric softener manufacturer. Of these, 8 workers would be handling the notified chemical in either open vats or closed systems.

Product Repackaging
Any repacking of the Tinosorb FR conc. that is required will be carried out at the notifier's site, where facilities enable the safe handling of hazardous substances and air flow is monitored. A maximum of 2 workers would be involved in repackaging up to 100 kg, or 10 days/year for 15-20 minutes/day.

End Use
Fabric softener containing the notified chemical at 0.5 to 0.7 % will be added to washing machines during the rinse cycle. Skin contact may occur during the addition, or if contact with rinse water and treated fabric.

7. PUBLIC EXPOSURE

The notified chemical will be used as an ingredient in the manufacture of fabric softeners/conditioners that will be available for sale to commercial users and the public. Members of the public are likely to make dermal contact with both the products containing the notified chemical and clothes treated using these products. The potential for public exposure to the notified chemical during transport, reformulation or disposal is assessed as low.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Softener Formulation Plants
Formulation plants will rinse the process equipment with water and use the rinseate as the base for the next batch of the product. Thus, there will be no loss of the notified chemical due to process equipment cleaning.

Any notified chemical lost from to spills would likely be contained by bunding and sealed flooring. Spills are likely to be less than 2 L, which equates to approximately 3 kg from a 60 kg drum, *ie* 5 %. Any clean-up material will be disposed of to landfill. Thus, a maximum of 1.5 tonnes of the notified chemical may go to landfill in spilt material.

There will be some residual product left in the empty import containers. The notifier has estimated this to be less than 10 g per container, *ie* 0.02 %. The containers will be rinsed and

the rinseate used in the formulation process. If the drums are not rinsed on site but are disposed of to landfill, then up to 50 kg of the notified chemical may be disposed of to landfill in the empty drums.

End User Site
There will be some loss due to spillage but volumes will be very small at low concentration (0.5 –0.7 %) and in a very dispersed manner.

There will be some softener left in the end-use container, which will likely be disposed of to landfill via domestic garbage. This is estimated at less than 1%, accounting for *ca.* 300 kg per annum maximum of notified chemical disposed of to landfill.

8.2 Fate

Up to 1550 kg of the notified chemical may annually be disposed of to landfill due from spills and in empty drums. Due to the chemical's low log P_{ow} and water solubility, it is likely to leach out in a diffuse and dispersed manner.

The notifier stated that the chemical has a 48 % fixation rate. Thus, approximately 46 % of the notified chemical will be washed to the sewer and treated in an on-site wastewater treatment plant or sewage treatment plant (STP). In either case some of the notified chemical may associate with the sludge and some will pass out in the effluent.

Two biodegradation tests were submitted by the notifier in order to determine the potential biodegradation of the notified chemical in the environment.

The ready biodegradability of the chemical was determined in a Manometric Respirometry test (OECD TG 301 F) by Hertl (1998a). The test was duplicated, with 26 and 24 mg of the test substance (purity 63.9 %) added to two 500 mL Erlenmyer Flasks at concentrations of 104 and 96 mg/L. Activated sludge obtained from a domestic wastewater treatment plant was added to the test flasks to obtain a final sludge concentration of 30 mg suspended solid/L. A mineral medium was added to make up a volume of 250 mL. A control containing 25.1 mg of the reference substance aniline and activated sludge was prepared.

The test flasks were incubated in the dark for 28 days at 22 °C. After correction for the mean Biochemical Oxygen Demand (BOD) the mean degradation rate of the notified chemical was determined to be 2.9 %. Therefore the chemical is considered to be not readily biodegradable. By contrast aniline degraded by 73 % by day 14 indicating the test was viable.

The second test (Ohshima 2000) studied the biodegradation of the notified chemical by microorganisms using a method equivalent to OECD TG 301C. Six test vessels were prepared, three containing activated sludge and the test substance. In each of these, 30 mg of the chemical were added to the basal culture medium so that the concentration of the organic substance reached 100 mg/L. The vessels were inoculated with activated sludge so that the concentration of the suspended reached 30 mg/L. In one test vessel the test substance aniline was added to the culture medium and inoculated with activated sludge as described previously. The test vessels were incubated for 28 days at 25 ± 1°C. After 28 days the percentage degradation by BOD and HPLC was determined:

- BOD - 0%, 0%, 0%

- HPLC – 1%, 2%, 1% Average 1%

The percentage degradation of the aniline after 28 days was 70 %. Therefore it was concluded that the test substance was not biodegraded by microorganisms under the test conditions.

A bioaccumulation test was performed by a method equivalent to OECD TG 305 (Yakata 2000). The study consisted of an acute toxicity test and a bioaccumulation test.

In the acute toxicity test, ten orange-red killifish (*Oryzias latipes*) were exposed to each test concentration (not stated) for 96 hours in a semi static system, with water renewal every 8-16 hours in light exclusion conditions. The result gave a 96 h LC_{50} value of >350 mg/L.

In the bioaccumulation test, *Cyprinus carpio* were exposed to the test substance over a period of 28 days in a continuous flow system. The flow rate to the test water through a 100 L tank was 2 mL/min for the stock solution and 1600 mL/min for dilution water. Test concentrations selected from preliminary results for the 96 h LC_{50} and analytical detection limits, were Level 1, 1.58 mg/L and Level 2, 0.158 mg/L. The number of fish in the test were 24 for Levels 1 and 2 and 8 for a control.

Analysis of fish in each tank was performed 5 times over the duration of the test. Four fish were removed and divided into two groups. An aliquot of test water was taken from each test once before the first analysis of test fish and at the same time as analysis of the test fish. These water and fish samples were analysed by HPLC to determine the Bioconcentration Factor at steady state (BCFss). The measured concentration of the test substance in test fish after 15, 21 and 28 days was less than the minimum determination limit of the test substance, therefore the minimum determination limit was used as the mean concentration of the test substance in test fish in a steady state.

The calculated BFCss were determined as: Level 1 ≤ 1.4
Level 2 ≤ 14

Therefore it can be concluded that the bioaccumulation potential is low.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of FAT 74'002/A

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 5000 mg/kg	Project No. 1050/024, Safepharm Laboratories Ltd, UK, 1997
acute dermal toxicity	rat	LD_{50} > 2000 mg/kg	Project No. 1050/025 Safepharm

			Laboratories Ltd, UK, 1997
skin irritation	rabbit	Non-irritating	Project No. 1050/026 Safepharm Laboratories Ltd, UK, 1997
eye irritation	rabbit	Slightly to moderately irritating	Project No. 1050/027 Safepharm Laboratories Ltd, UK, 1997
skin sensitisation	guinea pig	Non-sensitiser	Project No. 1050/028 Safepharm Laboratories Ltd, UK, 1997

9.1.1 Oral Toxicity (FAT 74'002: Acute Oral Toxicity in the Rat, SPL Project No. 1050/024, Safepharm Laboratories Ltd, UK, 1997)

Species/strain:	Sprague-Dawley (Crl: CD)
Number/sex of animals:	5 each
Observation period:	14 days
Method of administration:	Single oral dose; 5000 mg/kg suspended in arachis oil BP.
Test method:	OECD TG 401
Mortality:	There were no deaths during the study.
Clinical observations:	No signs of clinical toxicity were observed during the study**.**
Morphological findings:	No abnormalities were noted at necropsy.
Comment:	A range finding study was performed using 10, 500 and 5000 mg/kg. No clinical signs were observed as a result of the notified chemical treatment; 5000 mg/kg was consequently used for the main study. Body weight gain for males in week 1 were 62, 50, 79, 72 and 44 g. In week 2, gains were 80, 79, 46, 57 and 48 g. Body weight gain in week 1 (females) were 14, 25, 11, 12 and 17 g. In week 2, gains were 26, 23, 19, 23, 21 g.
LD_{50}*:*	> 5000 mg/kg

Result:	the notified chemical was of very low acute oral toxicity in rats.

9.1.2 Dermal Toxicity (FAT 74'002: Acute Dermal Toxicity in the Rat, SPL Project No. 1050/025, Safepharm Laboratories Ltd, UK, 1997)

Species/strain:	Sprague-Dawley (Crl: CD)
Number/sex of animals:	5 each
Observation period:	14 days
Method of administration:	Single 24-hour semi-occluded dermal application to intact skin at a dose level of 2000 mg/kg.
Test method:	OECD TG 402; Limit test
Mortality:	There were no deaths during the study.
Clinical observations:	No signs of clinical toxicity or skin irritation were observed during the study**.** All animals showed expected weight gain during the experiment, except for 1 female, which showed a weight loss in week 1, followed by a weight gain in week 2.
Morphological findings:	No abnormalities were noted at necropsy.
Comment:	Actual body weights were not provided.
LD_{50}*:*	> 2000 mg/kg
Result:	the notified chemical was of low dermal toxicity in rats

9.1.4 Skin Irritation (FAT 74'002: Acute Dermal Irritation Test in the Rabbit, SPL Project No. 1050/026, Safepharm Laboratories Ltd, UK.)

Species/strain:	Rabbits/New Zealand White
Number/sex of animals:	6 male
Observation period:	Animals were examined for dermal reactions 1, 24 and 48 hrs after test substance application.
Method of administration:	0.5 g of the test material, as supplied, moistened in 0.5 mL water was applied by a closed patch method to intact and shorn skin for 4 hrs.
Test method:	OECD TG 404

Comment: The primary irritation index (PII) was 0. No corrosive effects were observed.

Result: the notified chemical was non-irritating to the skin of rabbits.

9.1.5 Eye Irritation (FAT 74'002: Acute Eye Irritation Test in the Rabbit, SPL Project No. 1050/027, Safepharm Laboratories Ltd, UK.)

Species/strain: **Rabbit/ New Zealand White**

Number/sex of animals: 6/1 female and 5 males

Observation period: Animals were examined for eye lesions 1, 24, 48 and 72 hrs after test substance application.

Method of administration: 0.1 mL of the test material (70 mg) was applied as supplied on the cornea the right eye of each animal; the left eye served as the control; the treated eyes remained unwashed for 24 hrs. To minimise pain on chemical application, the local anaesthetic "Ophthaine" (proxymetacaine hydrochloride) was instilled into both eyes.

Test method: OECD TG 405

Draize scores of unirrigated eyes:

Animal	***1 day***		***2 days***		***3 days***	
Cornea	***o***	***a***	***o***	***a***	***o***	***a***
1	[1]0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
Iris						
1	0		0		0	
2	0		0		0	
3	0		0		0	
4	0		0		0	
5	0		0		0	
6	0		0		0	

Conjunctiva	*r*	*c*	*d*	*r*	*c*	*d*	*r*	*c*	*d*
1	2	2	1	1	1	0	0	0	0
2	1	0	0	0	0	0	0	0	0
3	1	0	0 Re	0	0	0	0	0	0
4	2	1	0	2	1	0	1	0	0
5	1	0	0	0	0	0	0	0	0
6	1	0	0	1	0	0	0	0	0

[1] see Attachment 1 for Draize scales Re = residual material around treated eye
o = opacity a = area r = redness c = chemosis d = discharge

Irrigated eyes:

Comment: Residual test material was noted around the treated eye of 5/6 animals during the study. Staining of the fur around the treated eye was noted in 1/6 animals at 1 hour post treatment. No corneal effects were noted, however iridial inflammation was observed in 1/6 at 1 hour post treatment.

Moderate conjunctival irritation was noted in 6/6 treated eyes at 1 hour post treatment. Minimal irritation was noted in 3/6 animals at 48 hours post treatment, and 1/6 at 72 hours post treatment. The mean conjunctival scores for redness and chemosis were 0.7 and 0.3. The mean scores for ocular irritation were 4.3, 2.0 and 0.3 for 1 day, 2 days and 3 days respectively.

All rabbits showed positive effects as a result of the notified chemical.

Result: the notified chemical was slightly to moderately irritating to the eyes of rabbits.

9.1.6 Skin Sensitisation (FAT 74'002: Magnusson & Kligman Maximisation Study in the Guinea Pig, SRL project No. 1050/028, Safepharm Laboratories, 1997, UK)

Species/strain: Guinea pig/ albino, Dunkin Hartley

Number of animals: 20 males used for the study, 10 used as a control

Induction procedure: Intradermal: 10 w/v % in distilled water

test group: One day before induction exposure, the fur was shaved on the left flank. On the day of exposure, a row of three injections (0.1 mL each) was made on each side of the mid-

line. The injections were:

Day 1

1. Freund's Complete Adjuvant and water (1:1)
2. A 10 % w/v formulation of the notified chemical in distilled water (1:1)
3. A 10 % w/v formulation of the notified chemical in Freund's Complete Adjuvant (1:1)

control group: The same administrative procedure for the intradermal injections was used as for the test group, utilising

Day 1

1. Freund's Complete Adjuvant and water (1:1)
2. distilled water
3. A 50 % w/v distilled water and Freund's Complete Adjuvant (1:1)

Topical: 50 w/v % in distilled water

Day 7

Applications were made topically using Whatmans filter paper following the same procedure as for the test group. The dressing is kept in place for 48 hours.

Challenge procedure:

Day 21

Topical: 50 w/v % of the notified chemical in distilled water was loaded on a Whatmans (No. 4) filter paper and held in place on the short right flank of each animal. A 25 w/v % solution of notified chemical in distilled water was equally applied to the short left flank of each animal. After 24 hours, the occluded patches were removed, and challenge sites swabbed with distilled water. The sites were evaluated for erythema and oedema, or any observable reaction.

Test method: OECD TG 406

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
25%	0/30	0/30	0/30	0/30
50%	0/30	0/30	0/30	0/30

*time after patch removal :

Comment: Observations during induction included yellow coloured staining, erythema, which ranged from slight to well-defined and very slight oedema. Some bleeding from the intradermal induction sites were noted in five test group animals at 1-hour.

No skin reactions were noted at the challenge sites of the notified chemical in 50 or 25 % w/v (distilled water) in the test or control group animals at the 24-hour or 48-hour observations. Body weight gains in the test group, between

day 0 and 24, were comparable to those observed in the control group for the same period.

The notified chemical produced a 0 % sensitisation rate (0/20).

Result: the notified chemical was non-sensitising to the skin of guinea pigs under the stated conditions.

9.2 Repeated Dose Oral Toxicity (FAT 74'002: Twenty-eight Day Repeated Dose Oral (Gavage) Toxicity Study in the Rat SRL Project No. 1050/029, Safepharm Laboratories, 1997, UK)

Species/strain: Sprague-Dawley Crl:CD BR rats

Number/sex of animals: 5/sex/dose

Method of administration: Gavage

Dose/Study duration: Dose levels of 150, 400 and 1000 mg/kg/day over 28 days. A control group of 5 each males and females used 1 % carboxymethylcellulose vehicle. Two additional recovery groups, each of five males and five females were treated with 1000 mg/kg/day or vehicle alone for up to 28 days and maintained without treatment for a further 14 days.

Test method: OECD TG 407

Clinical observations:
One 1000 mg/kg/day female showed increased salivation immediately after dosing on day 21. This was attributed to either an unpleasant taste or locally irritant formulation. One control female and one treated at 1000 mg/kg/day showed fur loss and swelling of the right forepaw, respectively. Recovery 1000 mg/kg/day males showed a statistically significant increase in bodyweight gain during the second ½ of the treatment-free period. This gain was not seen to represent an adverse effect on health.

In a battery of tests observing behavioural changes, functional performance and sensory reactivity, no treatment-related changes were observed.

Clinical chemistry/Haematology
Recovery males at 1000 mg/kg/day showed a statistically significant reduction in reticulocyte count *cf*. to recovery controls, but not *cf*. non-recovery individuals. These same males also showed a statistically significant increase in plasma sodium concentration *cf*. to controls. As there was no other evidence of renal dysfunction (*eg*. other electrolyte imbalance or histopathological changes). These increases were not considered toxicologically important.

Pathology

No treatment-related changes in organ weight were observed. One male at 1000 mg/kg/day assigned to the recovery group was killed on day 10 following an injury to its snout and jaw. Autopsy showed a number of macroscopic changes including pale liver, dark patches on the lungs, congestion and distension of the small intestine and dark red-coloured contents in the stomach. These findings were not seen as related to the notified chemical.

Histopathology
No treatment-related microscopic abnormalities were detected.

Result
No toxicologically significant changes were observed when 1000 mg/kg/day was administered by gavage. The NOAEL was 1000 mg/kg/day.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (FAT 74'002: Reverse Mutation Assay "Ames Test" Using *Salmonella typhimurium* and *E coli*, SRL Project No. 1050/030, Safepharm Laboratories, 1997, UK)

Strains:	*S. typhimurium* TA1535, TA1537, TA98, TA100 and *E coli* WP2*uvr*A$^-$
Metabolic activation:	liver microsomal fraction (S9) from rats pretreated with Arochlor 1254
Concentration range:	*S. typhimurium* and *E coli* treated with 0, 50, 150, 500, 1 500, 5 000 microgram/plate evaluated with or without S9 The controls used were: • vehicle control: dimethyl sulphoxide • positive control without metabolic activation for TA100, TA135 and WP2*urv*A: *N*-ethyl-*N*'-nitro-*N*-nitrosoguanidine • positive control with metabolic activation: 2-aminoanthracene • TA98: 4-nitroquinoline-1-oxide • TA1537: 9-aminoacridine
Test method:	OECD TG 471 and 472
Comment:	Vehicle control plates produced revertant colonies within the normal range. The positive controls, with or without metabolic activation, produced marked increases in the number of revertant colonies. The notified chemical did not exhibit any increases in numbers of revertant colonies on plates containing the notified chemical compared to negative control plates for any of the bacterial strains at any dose, +/- S9. There was precipitation observed at 5 000 microgram/plate.

Result: The notified chemical was non mutagenic under the conditions of the test.

9.3.2 Chromosomal Aberration Assay in Chinese Hamster Lung (CHL) Cells (FAT 74'002: Chromosomal Aberration Assay in CHL Cells *In Vitro,* SRL Project No. 1050/031, Safepharm Laboratories, 1997, UK)

Cells: CHL

Metabolic activation system: liver microsomal fraction (S9) from rats pretreated with Aroclor 1254

Metabolic Activation	Experiment Number	Test concentration (μg/mL)	Controls
	experiment 1:		
-S9	treatment time =	(a) 12-hour continuous exposure to the notified chemical prior to cell harvest	**Control groups:** *vehicle control:* DMSO is used for all experiments
	dose	312.5, 625 and 1250 microgram/mL for metaphase analysis	
+S9	treatment time =	(b) 4-hour exposure to the notified chemical and S9-mix followed by a treatment-free incubation period of 8 hours before harvest	*positive control:* mitomycin C (0.075 microgram/mL)
	dose	312.5, 625 and 1250 microgram/mL for metaphase analysis	*positive control:* CP (10 microgram/mL)
-S9	**experiment 2** treatment time =	(a) (i) 24 hours exposure to the notified chemical prior to cell harvest	*positive controls:* mitomycin C (0.025 microgram/mL) for (a)(i, ii) and CP (10 microgram/mL) for (a) (iii) and (b)(ii)
	dose:	312.5, 625 and 1250 microgram/mL for metaphase analysis	
	treatment time =	(ii) 48 continuous hours exposure to the notified chemical	Colcemid (demecolcine) (0.1 microgram/mL) was used in harvesting for each experiment
	dose:	312.5, 625 and 1250 microgram/mL for metaphase analysis	
	treatment time =	(iii) 6 hours exposure to the notified chemical prior to cell harvest, phosphate buffered saline wash, followed by a further 18 hours in the absence of notified chemical media	

		prior to harvest. This group acts as a control group for b(i)
	dose:	312.5, 625 and 1250 microgram/mL for metaphase analysis
	treatment time =	(iv) 12 continuous hours exposure to the notified chemical
	dose:	312.5, 625 and 1250 microgram/mL for metaphase analysis
-S9	treatment time =	(b) (i) 6 hours exposure to the notified chemical and S9-mix, then a phosphate buffered saline wash, followed by a further 8 hours in the absence of notified chemical media prior to harvest.
		312.5, 625 and 1250 microgram/mL for metaphase analysis
		(ii) 4 hours exposure to the notified chemical and S9-mix, then a phosphate buffered saline wash, followed by a further 8 hours in the absence of notified chemical media prior to harvest.

CP - cyclophosphamide
DMSO – dimethylsulphoxide

Test method:	OECD TG 474
Comment:	The mitotic index data do not show a dose-related toxic response in any treatment group. The notified chemical did not induce any statistically significant increases in the frequency of cells with aberrations at any dose level in any treatment group. The notified chemical did not induce any significant increase in the numbers of polyploid cells at any one dose level in either treatment group.
Result:	The notified chemical was non toxic and non clastogenic under the conditions of the test.

9.4 Overall Assessment of Toxicological Data

Toxicological data were provided for the notified chemical FAT 74’002/A.

The notified chemical is of very low acute oral toxicity (LD_{50}>5000 mg/kg bw) and low dermal acute toxicity (LD_{50}>2000 mg/kg bw) in rats. It is a slight to moderate eye irritant in rabbits, but not a skin irritant in rabbits or a skin sensitiser in guinea pigs

In a twenty-eight day repeated dose oral toxicity study, no toxicologically significant changes were observed when 150-1000 mg/kg/day was administered by gavage. The NOAEL was 1000 mg/kg/day. In genotoxicity studies, FAT 74'002/A tested negative in an Ames test (up to 5000 µg/plate) and was neither toxic nor clastogenic in the chromosomal aberration assay using Chinese Hamster Lung cells (up to 1250 µg/mL).

Based on the studies provided, FAT 74'002/A is not classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1994).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies were supplied by the notifier. The tests were carried out according to OECD Test Methods.

Test	*Species*	*Results (mg/L)*
96 h acute semi-static OECD TG 203	Rainbow trout *(Oncorhynchus mykiss)*	LC_{50} > 120 NOEC ≥ 120
48 h acute immobilisation OECD TG 202	Water Flea (*Daphnia magna*)	EC_{50} > 120 NOEC ≥ 120
72 h growth OECD 201	Algae (*Selenastrum capricornutum*)	E_RC_{50} > 120 E_BC_{50} > 120 NOEC = 120
Respiration Inhibition OECD 209	Activated Sludge Test	EC_{50} > 1000 mg/L

* NOEC - no observable effect concentration

Fish (Rainbow trout)

Hertl (1998 b) conducted a 96 h acute toxicity study of the notified chemical on rainbow trout following OECD TG 203. The limit test found that the chemical was not toxic on fish up to a concentration of 120 mg/L, so the only concentration studied was 120 mg/L and a control. Seven fish were added to each test vessel. The temperature was maintained at 14-15ºC and the fish were not fed. The test medium was replaced daily. Observations of mortality, condition and behaviour were made daily. No abnormal behaviour or mortality was observed, and no observable effect concentration was determined to be ≥ 120 mg/L, and the LC_{50} > 120 mg/mL.

Aquatic Invertebrates (Daphnia)

The acute immobilisation of the notified chemical to daphnia was determined by Hertl (1998 c) according to OECD TG 202. A limit test found that the chemical was not toxic to daphnia up to a nominal concentration of 120 mg/L, so the only concentration studied was 120 mg/L and a control. Twenty daphnia were divided between 2 test vessels (100 ml/L glass beakers) in 50 mL test medium. The test was performed over 48 hours at 19-20 °C in the dark.

No immobilised or dead test animals were observed over the 48 hour test period in the control or 120 mg/mL test concentration. Therefore the NOEC and 48 h EC_{50} were determined to be greater than 120 mg/L.

Algae

The growth inhibition of the notified chemical to algae (*Selenastrum capricornutum)* was determined by Hertl (1998d) in a 72 hour static test according to OECD TG 201. A limit test found that the chemical had no effect on the growth of algae up to a nominal concentration of 120 mg/mL. Due to the photosensitivity of the test substance, the test was conducted in two parts. In the first part, the test medium of nominal concentration 120 mg/L was incubated for 24 hours and illuminated at about 8400 Lux, reducing the parent compound to degradation products. It was found to contain 8-9 % of the initial nominal concentration.

In the second part, the test medium was freshly prepared immediately before the start of the test. Three replicated were produced per test concentration and six control replicates. The test was started by inoculation of a biomass of 10000 algal cells per mL test medium (50 mL) and incubated at 23 °C at 7600-8800 Lux for 72 hours. Inhibition of algal growth was determined from mean values of counted algal cell densities at 24, 48 and 72 hours.

In the freshly prepared test media, the concentration of the test substance was determined to be 94 and 96 % of nominal. The concentration decreased rapidly over 24 hours of illumination to 8-9 %. Therefore at the commencement of the second part of the test the algae were exposed mainly to the parent compound but from day 1 onwards, the portion of parent compound was only 9 % of the nominal value.

Results of the test showed that the notified chemical and its degradation products have no inhibitory effect on the growth of algae up to a nominal concentration of 120 mg/L. Therefore the NOEC and 72 h EC50 for algal growth rate and biomass were determined to be greater than 120 mg/L.

Microorganisms

The inhibitory effect of the test substance on the respiration of aerobic wastewater microorganisms was tested by Hertl (1997), according to OECD TG 209. The sludge was obtained from a wastewater treatment plant treating mainly domestic sewage. Nominal test concentrations of 10, 32, 100, 320 and 1000 mg/L of the notified chemical were prepared by dissolving measured amounts of the substance into 1000 mL test flasks. To this was added 284 mL of deionised water, which was then stirred for 24 hours to dissolve the test substance. Synthetic sewage (16 mL) and 200 mL of sludge inoculum made up the test volumes to 500 mL. The preparation of the test solutions was done in the dark due to the photosensitivity of the test substance.

Two controls without the test substance, and three nominal concentrations of the reference substance, 3,5-dichlorophenol, were tested under the same conditions. The test was performed in the dark over an incubation period of 3 hours at 19-21 °C in parallel, during which time the test media were continuously aerated. After 3 hours the respiration rate of samples of each test medium were determined. It was found that the test substance had no inhibitiory effect on the respiration rate of sewage sludge microorganisms up to and including a nominal concentration of 1000 mg/L. Therefore the 3 h EC50 was determined to be greater than 1000 mg/L.

Conclusion

The ecotoxicity data for the notified chemical indicate that it is practically non toxic to fish, daphnia, algae and sewage sludge microorganisms.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The two main pathways of exposure of the environment to the notified chemical are by disposal of import drums and waste chemical to landfill, and in particular in effluent from water treatment plants. Due to the moderate water solubility and low log P_{ow} a significant portion of the chemical released to sewers in wash water is expected to remain in the effluent. If it is presumed that the softener containing the notified chemical is used in the domestic market, at 48% fixation, up to 15 tonnes will be washed into the municipal sewer per year. The resultant Predicted Environmental Concentration (PEC) can then be calculated as follows.

Amount entering released annually	15000 kg
Volume of effluent produced per person	150 L
Population	18 million
Amount of effluent produce nationally annually	9.8×10^5 ML
Dilution when discharged into the environment after treatment in STP	10
PEC	1.4 μg/L (1.4 ppb)

Ecotoxicity tests supplied for assessment indicated that the notified chemical is practically non toxic to aquatic species, therefore the risk to the aquatic environment is low. If the NOEC level is taken as 120 mg/L for aquatic organisms tested, there is a safety factor of four orders of magnitude, indicating that the notified chemical presents a low hazard to the aquatic environment. The chemical may leach from landfill due to its moderate water solubility, however, leaching is expected to be diffuse and widespread.

Biodegradability tests demonstrated that the chemical is not readily biodegradable. However, a bioaccumulation test determined that the bioaccumulation potential of the notified chemical is low. Other factors which support this conclusion include the moderate water solubility, low lipid solubility and low log P_{ow}. In addition, although the chemical is not biodegradable it appears to be very photosensitive, therefore extensive degradation by photolysis is expected when the notified chemical is released into the aquatic environment.

The overall hazard to the environment of the notified chemical is considered to be low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment
Toxicological data were provided for the notified chemical FAT 74'002/A.

FAT 74'002/A was found to have very low acute oral toxicity (LD_{50} > 5000 mg/kg) and low acute dermal toxicity in rats (LD_{50} > 2000 mg/kg). A skin irritation study in the rabbit found FAT 74'002/A non-irritating, however, the notified chemical was found slightly to moderately irritating to the eyes of rabbits and all rabbits showed positive effects. A skin sensitisation study utilising the guinea pig found the notified chemical a non-sensitiser.

In a twenty-eight day repeated dose oral toxicity study, the NOAEL was 1000 mg/kg/day, the highest dose tested. In genotoxicity studies, FAT 74'002/A tested negative in an Ames test and was neither toxic nor clastogenic in the chromosomal aberration assay using Chinese Hamster Lung (CHL) cells.

Based on the studies provided, FAT 74'002/A is not classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1994).

Occupational Health and Safety
The notified chemical FAT 74'002/A exists as a powder but is introduced to Australia in a liquid formulation as Tinosorb FR conc. Workers maybe exposed to the notified chemical at 11.2 % if spillage occurs during the transport and blending procedures. There is potential for skin exposure during quality control sampling, product changeover and equipment maintenance. The maximum concentrations of the notified chemical to both commercial and domestic fabric softeners is low (<1 %). Workers handling connections or equipment are required to use long PVC or impervious gloves, overalls and goggles.

If repackaging is conducted, eye protection should be worn to prevent irritation. The risk of eye irritation during formulation is low due to the automated process. However eye protection is recommended in case spillage occurs. The risk during use of end-use products is very low due to the low concentration of notified chemical in the products.

The notified chemical is of low concern to the health and safety of workers handling the chemical.

Public Health
Members of the public are likely to make dermal contact with both the fabric softeners/conditioner containing the notified chemical and clothes treated using these products. However, the risk to public health from the notified chemical is likely to be low because it presents a low hazard, is present at low concentrations and is unlikely to be readily bioavailable.

13. RECOMMENDATIONS

To minimise occupational exposure to FAT 74'002/A, the following guidelines and precautions should be observed:

- Eye protection should be worn when handling the concentrate containing the notified chemical;
- Guidance in selection of goggles may be obtained from Australian Standard (AS) 1336 (Standards Australia, 1994) and Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); for industrial clothing guidance may be found in AS 3765.2 (Standards Australia, 1990); for impermeable gloves or mittens in AS/NZS 2161.2 (Standards Australia/Standards New Zealand, 1998); for occupational footwear in AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994a and other internationally accepted standards);
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the MSDS should be easily accessible to employees.

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:2011(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, the director must be informed if any of the circumstances stipulated under subsection 64(2) of the Act arise, and secondary notification of the notified chemical may be required. No other specific conditions are prescribed.

16. REFERENCES

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Ohshima, Y (2000): Biodegradation Test of FAT 74'002/A by Microorganisms. Test Number 13554: RCC Umweltchemie AG, Switzerland, on behalf of CIBA Specialty Chemicals Pty Ltd.

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Schmiedel, U. (1997d): Determination of the Partition Coefficient (N-Octanol/Water) of FAT 74'002/A. Study Project Number 666101: RCC Umweltchemie AG, Switzerland, on behalf of CIBA Specialty Chemicals Pty Ltd.

Schmiedel, U. (1998a): Calculation of the Vapour Pressure of FAT 74'002/A. Study Project Number 666077: RCC Umweltchemie AG, Switzerland, on behalf of CIBA Specialty Chemicals Pty Ltd.

Schmiedel, U. (1998b): Hydrolysis Determination of FAT 74'002/A at Different pH Values. Study Project Number 673481: RCC Umweltchemie AG, Switzerland, on behalf of CIBA Specialty Chemicals Pty Ltd.

Standards Australia/Standards New Zealand (1994a) Australian/New Zealand Standard 2210-1994, Occupational Protective Footwear. Standards Association of Australia/Standards Association of New Zealand.

Standards Australia (1990) Australian Standard 3765.2-1990, Clothing for Protection against Hazardous Chemicals Part 2 Limited protection against specific chemicals. Standards Association of Australia.

Standards Australia (1994) Australian Standard 1336-1994, Eye protection in the Industrial Environment. Standards Association of Australia.

Standards Australia/Standards New Zealand (1992) Australian/New Zealand Standard 1337-1992, Eye Protectors for Industrial Applications. Standards Association of Australia/ Standards Association of New Zealand.

Standards Australia/Standards New Zealand (1998) Australian/New Zealand Standard 2161.2-1998, Occupational protective gloves, Part 2: General requirements. Standards Association of Australia/Standards Association of New Zealand.

Yakata, N (2000): Bioaccumulation Test of FAT 74'002/A in Carp. Test Number 43555. RCC Umweltchemie AG, Switzerland, on behalf of CIBA Specialty Chemicals Pty Ltd.

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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