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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

FC-1100 Fluorad Mist Control Agent

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Street Address:	334 - 336 Illawarra Road MARRICKVILLE NSW 2204, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
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FC-1100 Fluorad Mist Control Agent

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
3M Australia Pty Ltd, of 2-74 Dunheved Circuit ST MARYS NSW 2760.

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formula, spectral data, and volumes of importation.

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)
A similar chemical was notified in Australia as NA/240 in 1996.

NOTIFICATION IN OTHER COUNTRIES
USA, 1998 (PMN 973111).

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
FC-1100 Fluorad Mist Control Agent.

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD UV/VIS, NMR, and IR.

3. COMPOSITION

DEGREE OF PURITY
>95%.

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
None

ADDITIVES/ADJUVANTS

Chemical Name	Water		
CAS No.	7732-18-5	*Weight %*	50

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Import.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	<10	<10	<10	<10	<10

USE
The notified chemical will be used as a surfactant, incorporated at a concentration of 45-55%, in an imported mist control agent (Fluorad™ Mist Control Agent FC-1100). It will be used as a sulphuric acid mist suppressant at the concentration of 10-20 ppm in the surface of electrowinning baths for metal recovery.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Not stated.

IDENTITY OF MANUFACTURER/RECIPIENTS
3M Australia Pty Ltd

TRANSPORTATION AND PACKAGING
FC-1100 Fluorad Mist Control Agent containing the notified chemical will be packaged in 200 L polyethylene drums when imported. These drums will be transported to the users without repackage or reformulation.

5.2. Operation Description

At the electrowinning sites, FC-1100 Fluorad Mist Control Agent will be diluted with water via a drop mechanism to a concentration of 25-100 ppm. This diluted surfactant is added into the incoming electrolyte and then to the electrowinning tanks. The final concentration of the notified chemical in electrolyte solution will be 10-20 ppm. Approximately 200 mL per hour of the finished product will be used in the workshop. The notified chemical will produce a stable foam blanket to reduce tank house acid mist levels.

5.3. Occupational exposure

Exposure Details
Workers who could be exposed to the notified chemical include warehouse personnel, forklift drivers, churn operators, foremen, quality assurance personnel, processing engineers and maintenance workers.

During its application as a mist control agent, approximately 20-30 process workers and technical staff will handle the product containing the notified chemical. The main route of exposure is dermal contact, and eye contamination is also possible. Workers in the preparation room will handle product containing 45-55% notified chemical and could be exposed to the notified chemical when manually diluting the notified chemical with water and coupling drums to pumps to add the notified chemical mixture to the electrolyte. Workers in the electrowinning room only handle 10-20 ppm notified chemical solution and they may be exposed to the notified chemical when adding/removing cathodes and carrying out maintenance.

Workers will wear protective equipment consisting of overalls, gloves and eyewear in the preparation and electrowinning rooms.

During transport and storage, workers are unlikely to be exposed to the notified chemical except when packaging is accidentally breached.

Occupational exposure during weighing and charging is also estimated by the EASE (Estimation and Assessment of Substance Exposure) program developed by the Health and Safety Executive, UK (1997). In the calculation of occupational exposure, the surface area of occupational exposure is selected to be 1000 cm^2 (NICNAS, 1996).

	EASE Prediction
Physical state	Liquid
Temperature	25°C

Dermal exposure	
Use-pattern	- Non-dispersive use - Direct handling
Contact-level	Intermittent
Predicted dermal exposure	0.1-1 mg/cm^2/day
Surface area of occupational exposure	1000 cm^2
Concentration of the chemical in product	45-55%
Occupational exposure (dermal)	45-550 mg/day

5.4. Release

RELEASE OF CHEMICAL AT SITE

Release of the notified chemical following import and transport to the user site will be minimal and confined to accidental spills. The MSDS has adequate instructions to contain and recover spills.

RELEASE OF CHEMICAL FROM USE

Release of the chemical when used as a mist-control agent will be limited, as it is used in a closed system to maximise metal recovery.

After metal recovery, the spent electrolyte is recycled with replenishment of the chemical. The notifier indicates that the chemical needs to be renewed because of its sorption to particulate matter and other surfaces in the system, and small losses (<<1 ppm) associated with drag-out (product adhering to the metal sheets when removed from the electrolyte bath). It is also claimed that it is non-foaming when used as a mist-control agent, and would not be subject to dispersal by wind.

5.5. Disposal

Empty totes will be rinsed with water, which will be disposed of to a waste water treatment system. This is expected to comprise about 1% of the imported mixture. As these totes are made of polyethylene, they may be landfilled or returned to a polyethylene reclamation site. Steel drums will be disposed of "according to local regulations". However, it is not clear what happens when the electrolyte is contaminated to the extent that it can no longer be recycled/replenished, for example when the water is evaporated from the strong sulphuric acid solution and the solids disposed of to landfill, or the solution is released to the sewer, presumably with proper dilution.

5.6. Public exposure

The product FC-1100 will only be used in manufacturing processes, and therefore, the general public will not be exposed to the notified chemical at this source.

Minor public exposure may result from accidental spillage of the notified chemical during transport, storage, and during end use, but any such events are expected to be rare.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa	Amber solid (notified chemical) Dark brown liquid (FC-1100 Fluorad Mist Control Agent)
Melting Point/Freezing Point	>150°C (Decomposes)
Remarks	92-130°C in US PMN.
Density	1220 kg/m^3 (FC-1100 Fluorad Mist Control Agent)
Remarks	1640 kg/m^3 (estimated value in US PMN)

Vapour Pressure $8x10^{-4}$ kPa at 25ºC (estimated value)

Remarks This is the value included in the assessment of NA/240. A value of 0.74 Pa at 25ºC is contained in the US PMN submission, but again this appears to refer to the substance assessed as NA/240.

Water Solubility Completely miscible in water

Remarks A sample of freeze-dried material was used to prepare a 45% solution, which was then evaporated in steps. As the water was removed, the remaining material became very viscous and then solid-like. However, at no stage did it separate into two phases.

TEST FACILITY 3M Specialty Materials Manufacturing Division Analytical Laboratory (2003)

Hydrolysis as a Function of pH Not determined

Remarks The notifier has indicated that FC-1100 is stable for weeks under acidic conditions when it is used to mist suppress 20% sulphuric acid solutions of pH <<1. Hydrolysis under alkaline conditions is possible, but very unlikely as sulfonamides are expected to be stable under ambient environmental conditions.

Partition Coefficient (n-octanol/water) Not determined

Remarks The test is not applicable for a surface active agent. The higher homologue material assessed as NA/240 had a partition co-efficient range of log Pow of -0.6 to 0.3, based on an estimation of the ratios of the solubilities in water and octanol. Given that the water solubility of the notified mixture is higher, the log Pow might be expected to be even lower than this estimate.

Adsorption/Desorption Not determined

Remarks Due to its high water solubility and expected low partition co-efficient, FC-1100 is not expected to adsorb to soils/sediment to any great extent, except by nature of its surface activity.

Dissociation Constant pKa = 3-5 (estimated)

Remarks The principal components of the notified chemical are expected to have typical basicity/acidity.

Particle Size Not determined (Not applicable to 50% aqueous solution)

Remarks	> 450 µm	16% w/w
	250-425 µm	15% w/w
	53-250 µm	39% w/w
	< 53 µm	30% w/w (data from NA/240)

Flash Point Not determined (Not applicable to 50% aqueous solution)

Remarks >100°C (product information sheet)

Flammability Limits Not flammable

Remarks Not applicable to 50% aqueous solution.

Autoignition Temperature Not auto-flammable.

Explosive Properties Not explosive under influence of flame.

Remarks Combustion products include oxides of carbon, nitrogen and sulphur, and HF from

incineration of product.

Reactivity	Not expected to be reactive
Viscosity	70 cps (from product information sheet)
Fat Solubility	<210 mg/L at 37°C (from US PMN and NA/240 report)
Surface Tension	19.5 mN/L/m at 20ºC (from US PMN and NA/240 report)
pH	5.3 (FC-1100 Fluorad Mist Control Agent)

7. TOXICOLOGICAL INVESTIGATIONS

Four study reports including acute oral toxicity, dermal irritation, eye irritation and in vitro mutagenicity studies were provided by the notifier for this notification. The toxicological data submitted for Amphoteric Fluoroalkylamide Derivative (5965P), which was assessed in NICNAS report NA/240, were used to support this notification.

The toxicological assessment part of NICNAS report NA/240 for Amphoteric Fluoroalkylamide Derivative (5965P) is attached to this report. Amphoteric Fluoroalkylamide Derivative (5965P) has the same structure as the notified chemical except it has 4-8 carbon atoms in the fluorinated carbon chain.

The following table lists all the study results from the previous and current assessments. Test materials T-5951 and T-2816CoC are the other names for the notified chemical in this notification, and T-2816, T-5679, T-5680 and T-5681, for the chemical in NA/240.

Toxicity study (year)	*Test material*	*Assessment Conclusion*
Rat, acute oral (1991)*	T-2816	LD50 >5000 mg/kg bw, low toxicity
Rat, acute oral (1994)	T-5951	LD50 >5000 mg/kg bw, low toxicity
Rat, acute dermal (1991)*	T-2816	LD50 >2000 mg/kg bw, low toxicity
Rat, acute inhalation		Not provided
Rabbit, skin irritation (1991)*	T-2816	slightly irritating
Rabbit, skin irritation (1994)	T-5951	slightly irritating
Rabbit, eye irritation (1991)*	T-2816	slightly irritating
Rabbit, eye irritation (1994)	T-5951	Slight to moderately irritating
Guinea pig, skin sensitisation - adjuvant test (1991)*	T-2816	evidence of sensitisation.
Guinea pig, skin sensitisation - adjuvant test (1993)*	T-5679	limited evidence of sensitisation
Guinea pig, skin sensitisation - adjuvant test (1993)*	T-5680	no evidence of sensitisation.
Guinea pig, skin sensitisation - adjuvant test (1993)*	T-5681	no evidence of sensitisation.
Guinea pig, skin sensitisation - adjuvant test (1995)*	T-2816	limited evidence of sensitisation
Rat, oral repeat dose toxicity-28 days. (1991)*	T-2816	No NOEL or NOAEL was established
Rat, oral repeat dose toxicity-28 days. (1991)*	T-2816	NOAEL=10 mg/kg/day and NOEL=1 mg/kg/day based on the effects on liver and kidney

Genotoxicity - bacterial & yeast reverse mutation (1980)	T-2816CoC	non mutagenic
Genotoxicity - bacterial reverse mutation (1991)*	T-2816	non mutagenic
Genotoxicity - bacterial reverse mutation (1991)*	T-2816	non mutagenic
Genotoxicity - bacterial reverse mutation (1991)*	T-2816	non mutagenic
Genotoxicity – in vitro chromosome aberration (1991)*	T-2816	non clastogenic
Genotoxicity – in vivo		Not provided

* Test reports were assessed in NICNAS notification NA/240.

7.1. Acute toxicity – oral

TEST SUBSTANCE T-5951

METHOD OECD TG 401 Acute Oral Toxicity – Limit Test.
Species/Strain Rat/Cr1:CD(SD)BR
Vehicle None
Remarks - Method

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	5000	None

LD50 >5000 mg/kg bw
Signs of Toxicity Red stained face, yellow stained or wet urogenital area and soft stool were observed. All animals returned to a normal appearance by day 5 after treatment.
Effects in Organs None.
Remarks - Results None.

CONCLUSION T-5951 is of low toxicity via the oral route.

TEST FACILITY Hazleton Wisconsin (1994a).

7.2. Irritation – skin

TEST SUBSTANCE T-5951

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3
Vehicle None.
Observation Period 72 hours
Type of Dressing Semi-occlusive.
Remarks - Method

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			

Erythema/Eschar	0	0	0	1	4 hour	0
Oedema	0	0	0	0	-	0

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

Remarks - Results

CONCLUSION T-5951 is slightly irritating to skin.

TEST FACILITY Hazleton Wisconsin (1994b).

7.3. Irritation - eye

TEST SUBSTANCE T-5951

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3
Observation Period 7 days
Remarks - Method

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	2	1.7	1.7	2	96 hours	0
Conjunctiva: chemosis	1.3	0.7	0.7	2	72 hours	0
Conjunctiva: discharge	1.3	0	0	2	48 hours	0
Corneal opacity	0	0	0	1	1 hour	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results Results of sodium fluorescein examinations in all animals were zero.

CONCLUSION T-5951 is slight to moderately irritating to the eye.

TEST FACILITY Hazleton Wisconsin (1994c).

7.4. Genotoxicity - bacteria

TEST SUBSTANCE T-2816CoC

METHOD Similar to OECD TG 471 Bacterial Reverse Mutation Test.
Species/Strain *S. typhimurium*: TA1538, TA1535, TA1537, TA98, TA100.
Saccharomyces cerevisiae D3
Metabolic Activation System Aroclor 1254-stimulated metabolic activation system
Concentration Range in Main Test *S. typhimurium tests*
a) With metabolic activation: 5-1000 µg/plate.
b) Without metabolic activation: 5-1000 µg/plate.

Saccharomyces cerevisiae tests
a) With metabolic activation: 0.05-5%.
b) Without metabolic activation: 0.05-5%.
Vehicle Ethanol
Remarks - Method

RESULTS

S. typhimurium tests

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	5000			
Test 1		Not observed	Not observed	Not observed
Test 2		Not observed	Not observed	Not observed
Present	5000			
Test 1		Not observed	Not observed	Not observed
Test 2		Not observed	Not observed	Not observed

Saccharomyces cerevisiae tests

Metabolic Activation	*Test Substance Concentration (%) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1		Not observed	Not observed	Not observed
Test 2		Not observed	Not observed	Not observed
Present				
Test 1		Not observed	Not observed	Not observed
Test 2		Not observed	Not observed	Not observed

Remarks - Results

CONCLUSION T-2816CoC was not mutagenic to bacteria or yeast under the conditions of the test.

TEST FACILITY SRI International (1980).

8. ENVIRONMENT

8.1. Environmental fate

A biological oxygen demand (BOD) test indicates that the drop in BOD over the test period was low compared with the chemical oxygen demand (see details below). This is consistent with the higher homologue material assessed as NA/240, which was not readily biodegradable (3-6% measured by CO_2 evolution in a modified Sturm test after 28 days).

Bioaccumulation is not likely due to the high water solubility, and the expected low partition co-efficient and fat solubility.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE Notified chemical

METHOD OECD TG 203 Fish, Acute Toxicity Test static.
Species Fathead minnow (*Pimephales promelas*)
Exposure Period 96 hours
Auxiliary Solvent Nil
Water Hardness 44-52 mg $CaCO_3$/L
Analytical Monitoring Nil
Remarks – Method Juvenile fish of mean length 21.3 ± 2.8 mm, and mean wet weight 80 ± 40 mg were tested in 4 L glass jars containing 3 L of test solution (loading rate 267 mg of fish per L of test solution) and were not fed for

24 hours before test initiation. There were 10 fish per replicate, with two replicates per test concentration, and a 16 h light: 8 h dark daily photoperiod.

Test solutions were prepared by mass addition of the test substance to dechlorinated City of Duluth tap water, followed by vigorous stirring. The temperature remained within 19.9-20.7ºC, the pH within 6.7 to 7.9 and the dissolved oxygen content between 4.8 and 8.9 mg/L. The lone deviation from the minimum 60% saturation occurred at 72 h for the highest test concentration, and may have been due to decaying fish. The LC50s were determined by the Trimmed Spearman-Karber method, and the NOEC using Fisher's Exact test.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*1 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	-	20	-	0	0	0	0
78	-	20	-	0	0	1	1
130	-	20	-	0	0	0	2
216	-	20	-	0	0	0	0
360	-	20	-	0	0	0	0
600	-	20	-	0	0	0	0
1000	-	20	-	0	0	15	17

LC50 >1000 mg/L at 24 hours.
>1000 mg/L at 48 hours.
841 mg/L at 72 hours.
804 mg/L (95% CL 757-854) at 96 hours.

NOEC 600 mg/L at 96 hours.

Remarks – Results After 72 and 96 hours all replicates containing the test substance had one or two fish resting at the bottom, as well as one or two fish inverted. There were no other sub-lethal observations. Deaths at the two lowest concentrations are unlikely to have been related to the presence of the test substance, since these were not concentration responsive. The delayed onset of death at the highest concentration is also noted.

CONCLUSION The test substance is practically non-toxic to the fathead minnow.

TEST FACILITY AScI Corporation (1997a)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test – static test.

Species *Daphnia magna*

Exposure Period 48 hours

Auxiliary Solvent Nil

Water Hardness 52 mg $CaCO_3$/L

Analytical Monitoring Nil

Remarks - Method Healthy less than 24 h old neonate daphnids were tested in 250 mL borosilicate glass beakers containing 200 mL of test solution. There were 5 daphnids per replicate, with 4 replicates per test concentration, and a 16 h light: 8 h dark daily photoperiod. Organisms were not fed during the test.

Test solutions were prepared by mass addition of the test substance to dechlorinated City of Duluth tap water, followed by vigorous stirring.

The temperature remained within 20.2-20.3ºC, the pH within 6.9 to 8.1 and the dissolved oxygen content between 8.2 and 8.8 mg/L. Immobilised organisms were those that did not swim within 15 seconds after exposure chambers were gently agitated. The LC50 was determined by the EPA Probit method, and the NOEC using Fisher's Exact test.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	-	20	0	2
130	-	20	0	3
216	-	20	0	1
360	-	20	1	5
600	-	20	1	9
1000	-	20	8	16

LC50	>1000 mg/L at 24 hours 675 mg/L (95% CL 481-883) at 48 hours
NOEC	360 mg/L at 48 hours
Remarks - Results	The remaining live daphnids were noted as normal throughout, except at the two highest test concentrations after 48 hours where they were noted as pale. Again immobilisation/deaths at the two lowest concentrations were not considered related to the presence of the test substance, since they were not concentration responsive. The delayed onset of immobilisation/death at all concentrations is again noted.

CONCLUSION The test substance is practically non-toxic to *Daphnia magna*.

TEST FACILITY AScI Corporation (1997b)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test.

Species	Green alga (*Selenastrum capricornutum*)
Exposure Period	96 hours
Concentration Range	
Nominal	38.9, 64.8, 108, 180 and 300 mg/L
Actual	Not tested
Auxiliary Solvent	Nil
Water Hardness	Not provided
Analytical Monitoring	Nil
Remarks - Method	Algae were tested in 250 mL borosilicate glass beakers (sterilised via autoclaving) containing 100 mL of algal medium (OECD recommended)/ test solution. The initial cell density was $1.2x10^4$ cells per mL. These beakers were continuously illuminated using cool-white fluorescent lamps at 740 ft-candles on a shaker table set at 100 rpm. Six control replicates and four replicates per test concentration were employed. Test solutions were prepared by mass addition of 300 mg the test substance to 500 mL of algal medium (sterilised by 0.22 µm filtration) followed by mechanical stirring. Each test concentration was made up by volume addition of the stock to the algal medium. The temperature remained within 24.6-26.4ºC, while the pH range was 7.2 to 8.1 initially but 7.8-10.0 after 96 hours. The rise in pH occurred particularly at the lower concentrations. Daily cell counts were made by direct microscopic enumeration using an Improved Neubauer hemacytometer. Immobilised

organisms were those that did not swim within 15 seconds after exposure chambers were gently agitated. The LC50s were determined by the Trimmed Spearman-Karber method, and the NOEC using TOXSTAT software.

RESULTS

Biomass		*Growth*	
EbC50 *mg/L at 96 h*	*NOEC* *mg/L at 96 h*	*ErC50* *mg/L at 96 h*	*NOEC* *mg/L at 96 h*
78 (CL 72-84)	38.9	149 (CL 138-160)	38.9

Remarks - Results: After 24 h the EbC50 and ErC50 were 205 mg/L and not calculable respectively, but were close to the 96 h values after 48 h, with some recovery of growth rate thereafter. The effect was said to be algistatic based on the production of cells previously exposed to the 300 mg/L concentration during the definitive test.

CONCLUSION: The test substance is harmful to the green alga (*Selenastrum capricornutum*).

TEST FACILITY: AScI Corporation (1997c)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 209 Activated Sludge, Respiration Inhibition Test.
- Inoculum: Activated sludge from the western Lake Superior Sanitary District, Duluth
- Exposure Period: 3 hours
- Concentration Range Nominal: 1000 mg/L
- Remarks – Method: The required amount of carbon-treated water was added to 16 mL synthetic sewage in a 1 L borosilicate glass beaker, followed by the required amount of test substance and then 200 mL of the sludge, making a final test solution volume of 500 mL. There were two inoculum controls and 1 test concentration. The sludge was determined to have a total suspended solids (TSS) concentration of 5.4 g/L at test time, making the TSS concentration in the test solutions equal to 3.1 g/L.

  Incubation was between 20.2 to 21.8ºC with vigorous aeration. A reference test using between 7 and 30 mg/L 3,5-dichlorophenol was performed concurrently. The EC50 was determined by Trimmed Spearman-Karber analysis.

RESULTS
- IC50: >1000 mg/L
- NOEC: 1000 mg/L
- Remarks – Results: For each exposure dissolved oxygen (DO) depletion and time interval was correlated and the slope of the regression line was calculated as the respiration rate. There was 4-11% inhibition after 3 hours. As respiration rates of the two inoculum controls (6-9%) did not vary by more than 15% and the 3-h EC50 of the reference substance (16.2 mg/L) indicated the sludge had normal sensitivity, the test was considered as valid.

CONCLUSION: The test substance in not inhibitory to sewage micro-organisms.

TEST FACILITY ASciI Corporation (1997d)

8.3. Biochemical/chemical oxygen demand (BOD/COD)

TEST SUBSTANCE Notified chemical

METHOD Not stated
Inoculum Not stated
Exposure Period 28 days
Auxiliary Solvent Nil
Analytical Monitoring Nil
Remarks - Method Samples of 10.5, 17.5, 26.2 and 52.4 mg/L were incubated at 19.4-19.8ºC for up to 28 days. There is no indication as to how these were prepared.

RESULTS

BOD (28 days) mg/kg	*COD mg O_2/kg*	*BOD/COD*
<38,200	161,300	<0.24

Remarks - Results

CONCLUSION The low drop in BOD over the test period compared with the chemical oxygen demand indicates the notified mixture is not easily biodegradable.

TEST FACILITY ASciI Corporation (1997e).

8.4 Microtox Testing

Brief details have been provided (AScI Corporation 1997f). Duplicate solutions of 125, 250, 500 and 1000 mg/L were subjected to this test (no details given), and the results measured at 5, 15 and 30 minutes. The 30 minute EC50 was 571 (95% CL 531-614) mg/L, again indicating low toxicity.

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

As it is used in a closed system to maximise metal recovery, release of the notified chemical during use as a mist-control agent will be limited. After metal recovery, the spent electrolyte needs to be replenished with the chemical because of its sorption to particulate matter and other surfaces in the system, and small losses (<<1 ppm) associated with drag-out (product adhering to the metal sheets when removed from the electrolyte bath). The material will presumably remain with the sheets, or be removed on cleaning. Any chemical trapped by filters during use as a mist control agent will be disposed of to landfill with the filters.

About 1% of the imported mixture is expected to be disposed of to a waste water treatment system after empty totes are rinsed with water. However, it is not clear what happens when the electrolyte is contaminated to the extent that it can no longer be recycled, for example whether the water is evaporated from the strong sulphuric acid solution and the solids disposed of to landfill, or is the solution released to the sewer, presumably after adequate dilution.

Limited data confirm that the notified chemical is unlikely to degrade through hydrolysis or biodegradation in either landfills or the sewer. Potential mobility in a landfill situation is unclear and in water it is also not clear whether it would remain in the aqueous phase (as suggested by its high water solubility), or partition to soils/sediments (suggested by its surface activity). However, the chemical may be expected to degrade slowly to its perfluorinated

component, which will be stable.

The predicted environmental concentration (PEC) in the aquatic environment is estimated using a worst-case scenario assuming all the notified chemical is evenly released over the period of one year from a single user to sewer, which has a daily capacity of 20 ML, and where there is no removal:

Amount released to sewer per day	10000/365 kg
Capacity	20 ML
PEC_{sewer}	10 000 365 x 20,000 000 = 1.37 mg/L
PEC_{inland} (dilution factor 1)	1.37 mg/L
PEC_{ocean} (dilution factor 10)	0.137 mg/L

9.1.2. Environment – effects assessment

Data provided indicate the notified chemical is practically non-toxic to fish, daphnids, sewage micro-organisms and microtox bacteria, but is harmful to green algae.

Using the lowest EC50 actual datum (EbC50 to green algae = 78 mg/L) and a safety factor of 100 (OECD), as there are data for three trophic levels, a predicted no effect concentration (PNEC) for aquatic ecosystems of 0.78 mg/L has been determined (EC50/100).

9.1.3. Environment – risk characterisation

While the notified chemical will be used in closed systems, there will be some release to the aquatic environment from the disposal of rinsings containing drum residues to the sewer. A small amount may also be landfilled through disposal of filters etc. Losses associated with chemical adhering to metal sheets are most likely to eventually deposit on soil.

However, the extent of environmental release through the disposal of spent electrolyte, either to landfill or to the sewer, as well as cleaning the baths, is not clear. Assuming a worst case that all is disposed of to the sewer from a single user over the period of one year the PEC/PNEC for an inland situation is 1.37/0.78 = 1.76. Since the risk quotient (RQ) is greater than 1, it will be important that spent electrolyte is not discharged to the sewer.

While the more diffuse releases in the aquatic environment should not pose a potential risk to aquatic organisms, due to the relatively low aquatic toxicity, the main concern with environmental release of the notified chemical either to land or water is the eventual degradation to its perfluorinated component perfluorobutane sulfonate (PFBS). This persistent molecule is currently being assessed by NICNAS since it is being used as a replacement for former perfluorooctane sulfonate (PFOS) containing compounds and polymers.

Unlike PFOS and related higher homologues, PFBS has not been widely detected in the environment. In a recent publication (Taniyasu *et al,* 2003) PFBS was tested for in water, fish, birds and humans obtained from a number of locations in Japan, but not detected. This may be due to insensitive detection limits compared with those for perfluorohexane sulfonate (PFHxS), which was detected in about 33% of fish blood samples, where there were much lower detection limits.

Earlier Moody *et al* (2002) detected PFBS only in two samples (at concentrations close to the detection limit, which was more sensitive than above) of fish livers taken from two sites (of the six tested) in a creek running beside an airport. PFBS was not detectable either upstream or downstream of the site where an aqueous film forming foam (AFFF) had been spilt at this airport. By contrast PFHxS was detected in six of eight samples and perfluoropentanesulfonate (PFPeS) was also detected at four of the six sites, though again levels for the latter were relatively low.

It is unclear whether this reflects a much lower use level of PFBS in the past (it may not have been present to any great extent in the mix of homologues previously used) or its greater mobility due to its much higher water solubility, and consequent much wider dispersion at

lower levels.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Workers involved in the manual operations in the preparation and electrowinning rooms. are potentially exposed to the notified chemical. Intermittent dermal and ocular exposure may occur during certain processes, for example, dilution of the imported mixture and addition to the electrolyte tanks. However, exposure to the notified chemical in the electrowinning room is limited because of the low concentration of notified chemical (10-20 ppm) in the electrolyte solution.

During transport and storage, workers are unlikely to be exposed to the notified chemical except when packaging is accidentally breached.

9.2.2. Public health – exposure assessment

Excluding accidental spillage during transport, storage and reformulation, the public will not be exposed to the notified chemical.

9.2.3. Human health - effects assessment

A small number of studies was submitted for the notified chemical. However, in the earlier NICNAS assessment of the C4-8 analogue of the chemical, a large number of studies was submitted; these were considered suitable for use in this toxicological assessment.

Based on the available data, the notified chemical is of low acute oral and dermal toxicity in rats. It is very slight skin irritant in rabbits, however, it is a slight to moderate irritant in rabbit eye.

A number of Magnusson and Kligman skin sensitisation studies were submitted in the assessment of the C4-8 analogue. Although one study indicated that the analogue was a skin sensitiser in guinea-pigs, the other four studies, conducted to international recognised standards, indicated limited or no evidence of sensitisation. On weight of evidence, it was concluded that the analogue chemical was most likely not a skin sensitiser. By analogy, the notified chemical in this assessment is likely to have similar sensitising potential.

In two 28-day oral repeat dose rat studies submitted in the assessment of the C4-8 analogue, the target organs were the liver and kidney. Alterations in liver structure were detected at, and above, doses of 25 mg/kg/day. Lesions observed in the liver and kidney were not reversible when a dose of 800 mg/kg/day was administered for 28 days. The NOEL is established as 1 mg/kg/day with the NOAEL 10 mg/kg/day, both based on the effects in liver and kidney.

The notified chemical and its C4-8 analogue, when assessed in *in vitro* assays, was not mutagenic or clastogenic. No *in vivo* study was provided.

The notified chemical contains perfluorobutanesulfonate (PFBS) as a portion of its structure. PFBS is indicated to highly bind to serum albumin but is not considered to be bioaccumulative (NICNAS, 2005).

Based on the available data for the notified chemical and the C4-8 analogue, the notified chemical is not classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is a surfactant which will be incorporated into a mist control agent to be used only by the process workers in the electrowinning baths for metal recovery. As intermittent skin contact may occur during dilution of the 50% imported solution and addition to the electrolyte baths, there is a risk of skin and eye irritation so personal protection is required. Repeated dose studies in

rats indicated effects on the liver and kidney, so repeated exposure to the notified chemical should be avoided. The risk of adverse effects is low for workers in the electrowinning room as the concentration of notified chemical in electrolyte is very low (10–20 ppm) and workers will be protected by PPE against the electrolyte solution hazards.

Based on the assessment of health effects, the NOAEL of 10 mg/kg/day is used in the risk characterisation. The absorption rate from dermal exposure is assumed to be 10% and a bodyweight of 70 kg is used for estimation.

From the exposure estimates, the following margin of exposure (MOEs) is calculated for the exposure scenario (MOE = NOAEL/internal dose).

Occupational exposure (dermal) from the EASE estimation	45-550 mg/day
Absorbed dose (10% dermal)	4.5-55 mg/day
Margin of Exposure (MOE) (NOAEL*70 kg/absorbed dose)	12.7-155.6

The EASE program did not include the scenario of occupational exposure with personal protective equipment (PPE). If workers wear overalls, gloves and eye protection, the MOE is expected to be well over 100 with the industrial controls. Taking into account that exposure estimate was the worst-case, the risk of adverse health effects in workers exposed to the notified chemical is considered to be low particularly when industrial control is in place and PPE is worn.

9.2.5. Public health – risk characterisation

As there will be no exposure of the public to the notified chemical, the health risk to the public from exposure to the notified chemical is considered negligible.

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.

	Hazard category	***Hazard statement***
Chronic hazards to the aquatic environment	3	Harmful to aquatic life with long lasting effects

10.2. Environmental risk assessment

As long as spent electrolytes are not released to the sewer, 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 based on its reported use pattern.

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, 1994a). 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, 1994b). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - Local exhaust ventilation

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Do not eat, drink or smoke when using this product
  - Wash hands thoroughly with soap and water after use and before eating or smoking.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Safety goggles
  - Gloves
  - Industrial clothing

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Environment

Disposal

- The notified chemical should be disposed of in a licensed industrial or commercial incineration facility capable of handling halogenated materials and with proper controls for HF.
- Do not dispose of spent electrolyte solutions into the sewer.

Emergency procedures

- Spills/release of the notified chemical should be contained and covered with commercially available inorganic absorbent material, working from around the edges of

the spill inwards, until it appears dry. As much of the spill should be collected as possible, and the residue cleaned up with water.

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 Subsection 64(1) of the Act; if
- use is proposed in situations where greater release/dispersal to the environment is likely, such as in fire-fighting foams,

or

(2) Under Subsection 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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ATTACHMENT

The following part is from the NICNAS assessment report (NA/240) on Amphoteric Fluoroalkylamide Derivative (5965P). Amphoteric Fluoroalkylamide Derivative (5965P) has similar structure to the notified chemical except it has 4-8 carbon atoms in the radical chain.

FULL PUBLIC REPORT FOR AMPHOTERIC FLUOROALKYLAMIDE DERIVATIVE (5965P)

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Table 1 Summary of the acute toxicity of Amphoteric Fluoroalkylamide Derivative (5965P)

Test	Species	Outcome	Reference
Acute oral toxicity	Rat	LD_{50} > 5000 mg/kg	(4)
Acute dermal toxicity	Rat	LD_{50} > 2000 mg/kg	(5)
Skin irritation	Rabbit	slight irritant	(6)
Eye irritation	Rabbit	slight irritant	(7)
Skin Sensitisation	Guinea pig	non sensitiser	(8,9,10,11,12)

9.1.1 Oral Toxicity (4)

Wistar rats (5 per sex; 7 weeks old) were administered a single gavage dose of 5000 mg /kg of the notified chemical . The animals were maintained for 14 days. Mortality and clinical signs of toxicity were assessed several times on the day of test compound administration, and twice daily (for mortalities) and daily (for clinical signs of toxicity) thereafter. Body weight was determined on days 1, 8 and 15. An autopsy was performed on all animals at the completion of the study.

No deaths were seen during the 14 day study. On the day of chemical administration, respiratory rates, lethargy, piloerection and/or hunched posture were noted in the majority of animals.

The acute oral LD_{50} of the notified chemical was greater than 5000 mg/kg in male and female rats.

9.1.2 Dermal Toxicity (5)

A dose of 2000 mg/kg of the notified chemical was applied to shaved, intact skin of Wistar rats (5 per sex, 7 weeks old). The area was occluded for 24 hours, after which, the residual chemical was removed using a water moistened tissue. The study was terminated after 14 days. Mortality and clinical signs of toxicity were assessed several times on the day of test compound application, and twice daily (for mortalities) and daily (for clinical signs of toxicity) thereafter. Body weight was determined on days 1, 8 and 15. An autopsy was performed on all animals at the completion of the study.

No deaths, abnormal clinical signs or evidence of skin irritation was noted during the study.

The acute dermal LD_{50} of the notified chemical was greater than 2000 mg/kg in male and female rats.

9.1.3 Skin Irritation (6)

The fur was removed from the back of 3 female New Zealand White rabbits, and 500 mg of the notified chemical was applied to the intact skin for 4 hours. Residual chemical was then removed. Animals were examined daily for clinical signs of toxicity. Body weight was determined the day of chemical application. Skin reactions were assessed approximately 55 minutes, 24, 48 and 72 hours after chemical removal. The severity of the reactions was determined by the degree of erythema and oedema, as described by Draize.

Very slight erythema (grade 1) which resolved within 24 hours was noted in 2 of 3 animals 55 minutes after chemical application.

The notified chemical was a slight dermal irritant in rabbits.

9.1.4 Eye Irritation (7)

A dose of approximately 94 mg of the notified chemical was instilled into the left conjunctival sac of 3 female New Zealand White rabbits. The study was terminated after 7 days. Clinical signs of toxicity were assessed on a daily basis. Body weight was determined on the day of application. The eyes were examined 1, 24, 48 and 72 hours, and 7 days, after chemical instillation, and the degree of irritation assessed using the Draize method. To assess the presence, and severity, of corneal damage, a 2% fluorescein solution was instilled into the eyes 24 hours after chemical instillation.

Mild conjunctival hyperaemia and chemosis was noted in all animals for a period of 72 hours following chemical installation. Mean total Draize score was 6 after 1 hour, and 2 after 72 hours.

The notified chemical was a slight ocular irritant in rabbits.

9.1.5 Skin Sensitisation (8,9,10,11,12)

Study 1 (8) Five female Himalayan albino guinea-pigs (approximately 11 weeks old) were used in a preliminary induction dose finding study. Subsequently, thirty female Himalayan albino guinea-pigs were divided into a control (n = 10) and a treatment group (n = 20). The hair was removed from a region behind the right shoulder. An induction dose of 0.2 mL of a 50% w/w suspension of the notified chemical in distilled water was applied to the exposed skin of the treatment group on days 1, 3, 5 and 8. In addition, intradermal injections of 0.1 mL of Freunds Complete Adjuvant were administered either side of the application area to the control and treatment groups, on day 5. Excess test material was removed, and the site assessed for evidence of erythema, on day 10. The control and treatment groups were challenged 2 weeks after the last induction dose. The challenge dose for each animal consisted of 0.05 mL of a 0, 1%, 2% and 5% solution of the notified chemical in distilled water, and was applied to a clipped region of the left flank at four separate sites. The residual test material was removed after 24 hours. The application sites were assessed for redness and swelling 24 and 48 hours after removal of the test material. In addition, animals were examined for clinical signs of toxicity on a daily basis, and body weights were determined at the beginning and end of the study.

A total of 14 of 20 treated animals showed cutaneous red spots (grade 1) 24 hours after removal of the 5% challenge dose. Similarly, 3 of 20 animals and 2 of 20 animals showed grade 1 cutaneous reactions 24 hours after removal of the 2% and 1% challenge dose respectively. Forty eight hours after removal of the 5%, 2% and 1% challenge doses, 9 of 20, 3 of 20 and 2 of 20 animals showed evidence of grade 1 cutaneous reactions respectively. After 48 hours, 2 of 10 animals in the 5% challenge dose control group showed grade 1 reactions. The remainder of the control animals did not react.

The notified chemical caused skin sensitisation in the guinea-pig.

Study 2 (9) Thirty male albino Dunkin/Hartley guinea pigs (4-5 weeks old) were divided into groups of 10 control animals, and 20 treated animals. In the test animals, an area of hair was removed from the scapular region of each animal, and paired intradermal injections containing Freund's Complete Adjuvant (FCA) diluted equally with water, 0.5% Amphoteric Fluoroalkylamide Derivative (5965P) in water or 0.5% Amphoteric Fluoroalkylamide Derivative (5965P) in FCA were given in the area. Six days after injections, the areas were pre-treated with sodium lauryl sulfate, and 0.4 mL of 70% Amphoteric Fluoroalkylamide Derivative (5965P) in water on a patch, was applied and covered with an occlusive dressing. The dressing and patch were removed after 24 hours. Control animals were similarly treated, however, the test compound was deleted. Two weeks after the topical application, hair was removed from the left flank of each animal (control and test), and 0.2 mL of 35% or 70% Amphoteric Fluoroalkylamide Derivative (5965P) in water was applied to two separate sites. The application site was occluded for 24 hours. Clinical signs of toxicity were assessed daily, and body weight was determined at the beginning and conclusion of study. Dermal eschar, erythema and oedema formation were assessed after the induction phase, and 24, 48 and 72 hours after the challenge phase.

No signs of toxicity, or body weight changes were noted during the study. Slight irritation was noted following the induction Amphoteric Fluoroalkylamide Derivative (5965P) intradermal injection. Slight erythema was seen in both control and treated groups following the removal of the induction patches. Slight erythema (grade 1) was noted in 1 of 20 treated animals 24 hours after challenge.

The notified chemical (Amphoteric Fluoroalkylamide Derivative (5965P)) did not cause sensitisation in the guinea pig.

Study 3 (10) Thirty young adult albino Haz:(DH)fBR guinea pigs were divided into groups of 10 control animals, and 20 treated animals. In the test animals, an area of hair was removed from the scapular region of each animal, and paired intradermal injections containing FCA diluted equally with water, 0.1 mL of a 5% w/w T-5679 (45% Amphoteric Fluoroalkylamide Derivative (5965P); 40% water; 15% diethylene glycol butyl ether) in water or 0.1 mL of 5% T-5679 in FCA were given in the area. Six days after injections, the areas were pre-treated with 10% sodium lauryl sulfate in petroleum. After 24 hours, undiluted test material or water (controls) was applied to a patch and placed over the injection sites and occluded for 48 hours. Two weeks after the topical application, hair was removed from the left flank of each animal (control and test), and undiluted test material or water (controls) was applied to the exposed sites. The application site was occluded for 24 hours. Clinical signs of toxicity were assessed daily, and body weight was determined at the beginning and conclusion of study. Dermal eschar, erythema and oedema formation were assessed after the induction phase, and 24, 48 hours after the challenge phase.

No signs of toxicity, or body weight changes were noted during the study. Scattered mild redness (grade 1) was noted in 1 of 20 tested animals 24 hours after challenge.

The test formulation, 45% Amphoteric Fluoroalkylamide Derivative (5965P), 40% water and 15% diethylene glycol butyl ether (T-5679), did not cause skin sensitisation in the guinea pig.

Study 4 (11) Thirty young adult albino Haz:(DH)fBR guinea pigs were divided into groups of 10 control animals, and 20 treated animals. In the test animals, an area of hair was removed from the scapular region of each animal, and paired intradermal injections containing 0.1 mL of FCA diluted equally with water, 0.1 mL of a 5% w/w T-5680 (12% Amphoteric Fluoroalkylamide Derivative (5965P); 84% water; 4% diethylene glycol butyl ether) in water or 0.1 mL of 5% T-5680 in FCA were given in the area. Six days after injections, the areas were pre-treated with 10% sodium lauryl sulfate in petroleum. After 24 hours, undiluted test material or water (controls) was applied to a patch and placed over the injection sites and occluded for 48 hours. Two weeks after the topical application, hair was removed from the left flank of each animal (control and test), and undiluted test material or water (controls) was applied to the exposed sites. The application site was occluded for 24 hours. Clinical signs of toxicity were assessed daily, and body weight was determined at the beginning and conclusion of study. Dermal eschar, erythema and oedema formation were assessed after the induction phase, and 24 and 48 hours after the challenge phase.

No signs of toxicity, body weight changes, or dermal reactions were noted during the study.

The test formulation, 12% Amphoteric Fluoroalkylamide Derivative (5965P); 84% water; 4% diethylene glycol butyl ether (T-5680), did not cause skin sensitisation in the guinea pig.

Study 5 (12) Thirty young adult albino Haz:(DH)fBR guinea pigs were divided into groups of 10 control animals, and 20 treated animals. In the test animals, an area of hair was removed from the scapular region of each animal, and paired intradermal injections containing 0.1 mL of FCA diluted equally with water, 0.1 mL of a 5% w/w T-5681 (2.75% Amphoteric Fluoroalkylamide Derivative (5965P); 96.25% water; 1% diethylene glycol butyl ether) in water or 0.1 mL of 5% T-5681 in FCA were given in the area. Six days after injections, the areas were pre-treated with 10% sodium lauryl sulfate in petroleum. After 24 hours, undiluted test material or water (controls) was applied to a patch and placed over the injection sites and occluded for 48 hours. Two weeks after the topical application, hair was removed from the left flank of each animal (control and test), and undiluted test material or water (controls) was applied to the exposed sites. The application site was occluded for 24 hours. Clinical signs of toxicity were assessed daily, and body weight was determined at the beginning and conclusion of study. Dermal eschar, erythema and oedema formation were assessed after the induction phase, and 24 and 48 hours after the challenge phase.

No signs of toxicity, body weight changes or dermal reactions were noted during the study.

The test formulation, 2.75% Amphoteric Fluoroalkylamide Derivative (5965P); 96.25% water; 1% diethylene glycol butyl ether (T-5681), did not cause skin sensitisation in the guinea pig.

9.2 Repeated Dose Toxicity (13,14)

Study 1 (13). Groups of 5 Wistar rats per sex (approximately 6 weeks old) were administered 0, 50 mg (LD), 200 mg (MD) or 800 mg (HD) of the notified chemical (Amphoteric Fluoroalkylamide Derivative (5965P)); > 95% purity, in distilled water)/kg/day, by gavage, for 28 days. Separate groups (n = 5 per sex) of rats which had been untreated, or had received 800 mg/kg/day for 28 days, were maintained and not treated for an additional 14 day recovery period. Clinical signs of toxicity were assessed daily, animal mortality was determined twice daily, food consumption and body weight was determined weekly, and an ophthalmic examination was carried out prior to study commencement, during the final week of treatment and recovery period. Blood to determine haematological and clinical biochemical parameters were collected at the completion of the study. Autopsies, which included selected organ histopathology, and organ weight determinations, were carried out at study termination.

General lethargy was noted in HD males whilst being treated, and during the recovery phase. Focal areas of alopecia, chromodacryorrhoea, and a foamy appearance to the urine were noted in HD males and females during the treatment and recovery phase. Excess salivation was seen in MD and HD animals, and respiratory rales was noted in HD females, during the treatment period. Body weight gain was reduced in HD and MD animals at the conclusion of the treatment period, and remained marginally depressed in HD animals during the recovery phase.

Red blood cell numbers and haematocrit were increased in HD animals. Red blood cell haemoglobin content and platelet numbers were marginally decreased in all treatment groups. The decrease in platelets was statistically significant in all male dose groups and repeated dosing lower doses. At the end of the recovery period, the haemoglobin concentration remained low in HD males and females. In addition, red blood cell numbers and haematocrit were significantly reduced at the conclusion of the recovery period in HD females. White blood cell numbers were increased in all treated groups, and were statistically increased in HD males and MD and HD females.

Serum phosphorous was elevated in MD and HD males and females, and urea was increased in MD and HD males, and in HD females. An elevation in creatinine and ALP levels, and a reduction in serum glucose, were noted in HD males and females. At the end of the recovery period ALP remained elevated in HD females. An increase in ALP levels was also noted in MD females following treatment. AST was increased in HD females along with ALT elevations in MD and HD females. Serum cholesterol and triglycerides were reduced, and ALT was elevated, in LD, MD and HD males at the conclusion of the treatment period, and triglycerides remained decreased in HD females after the recovery period. Cholesterol was also reduced in all treated female groups. Serum sodium levels where elevated in LD and HD female groups.

Liver, adrenals and spleen relative weights were increased in MD and HD females, and liver, kidney and adrenals relative weights were increased in MD and HD males. Relative liver weight in HD males and females, and relative kidney and spleen weight in HD females remained elevated at the conclusion of the recovery period. Hepatocyte hypertrophy was noted in all treated males, and in 3 of 5 HD females. Similar pathology was noted at the completion of the recovery period in 2 of 5 HD males and 1 of 5 HD females. Diffuse adrenal cortical vacuolation was noted in all treated males, and in MD and HD females. These changes persisted in HD animals and were present at the end of the recovery period. Slight renal cortical cellular hypertrophy was noted in 4 of 5 HD males at the conclusion of the treatment phase.

Study 2 (14). Because effects considered to be treatment related were noted in the 50 mg/day dose groups, the study was repeated in female medium and high dose groups. Groups of 5 Wistar rats per sex (approximately 6 weeks old) were administered 0, 1 mg (LD), 10 mg (MD) or 25 mg (HD) of the notified chemical (Amphoteric Fluoroalkylamide Derivative (5965P); > 95% purity, in distilled water)/kg/day, by gavage, for 28 days. Separate groups of rats (n = 5 per sex) which had been untreated, or had received 25 mg/kg/day for 28 days, were maintained and not treated for an additional 14 days recovery period. Clinical signs of toxicity were assessed daily, animal mortality was determined twice daily, food consumption and body weight was determined weekly, and an ophthalmic examination was carried out prior to study commencement, and during the final week of the treatment and recovery period. Blood to determine haematological and clinical biochemical parameters was collected at the completion of the study. Autopsies, which included selected organ histopathology, and organ weight determinations, were carried out at study termination.

A statistically significant decrease in the platelet number, and an increase in the prothrombin time, was noted at the completion of the recovery period in the HD male group. Cholesterol was decreased in MD and HD males, and in HD females at the completion of the treatment period, and remained low at the end of the recovery period in HD males. Serum ALT was increased in HD females. Relative liver weight was increased in MD and HD males, and kidney and adrenal weights were marginally increased in HD males. Relative weights of the ovaries

were increased in the HD female group at the end of the recovery period. No histological abnormalities were noted. There were no treatment related effects at the lowest dose of 1 mg/kg/day.

9.3 Genotoxicity

9.3.1. *Salmonella typhimurium* Reverse Mutation Assay (15,16)

Study 1 (15). In the Ames test using *Salmonella typhimurium*, strains TA1535, TA1537, TA98 and TA100 at concentrations of 100 - 3330 µg/plate, and in the presence or absence of metabolic activation, the notified chemical (Amphoteric Fluoroalkylamide Derivative (5965P)), failed to induce a dose-related increase in the number of reverse mutations. The positive controls used without metabolic activation were sodium azide in saline (TA1535), 9-aminoacridine in saline (TA1537), daunomycine in saline (TA98) and methylmethane-sulfonate in DMSO (TA100), and, with metabolic activation, 2-aminoanthracene in DMSO (all strains). The positive controls significantly increased the number of revertants and indicated that the assay functioned correctly.

Study 2 (16). This test was conducted as a duplicate to (15). In the Ames test using *Salmonella typhimurium*, strains TA1535, TA1537, TA98 and TA100, the notified chemical (Amphoteric Fluoroalkylamide Derivative (5965P)), at concentrations of 100 - 5000 µg/plate, and in the presence or absence of metabolic activation, failed to induce reverse mutations. The positive controls used without metabolic activation were sodium azide in saline (TA1535), 9-aminoacridine in saline (TA1537), daunomycine in saline (TA98) and methylmethanesulfonate in DMSO (TA100), and, with metabolic activation, 2-aminoanthracene in DMSO (all strains). The positive controls significantly increased the number of revertants and indicated that the assay functioned correctly.

9.3.2. *Escherichia coli* Reverse Mutation Assay (17)

In the Ames test using *Escherichia coli* bacteria, strain WP_2*uvrA*, the notified chemical (Amphoteric Fluoroalkylamide Derivative (5965P)), at concentrations of 100 - 5000 µg/plate, and in the presence or absence of metabolic activation, failed to induce reverse mutations. The positive controls used without metabolic activation was 4-Nitroquinoline N-oxide in DMSO, and, with metabolic activation was 2-aminoanthracene in DMSO. The positive controls significantly increased the number of revertants and indicated that the assay functioned correctly.

9.3.3. Chromosomal Aberration Assay (18)

The notified chemical (Amphoteric Fluoroalkylamide Derivative (5965P)), when examined at concentrations ranging from 3 to 5000 µg/mL, with or without metabolic activation, did not induce clastogenicity in cultured human lymphocytes after 24 and 48 hours treatment (18). The positive control chemicals, mitomycin C and cyclophosphamide, produced a significant increase in the incidence of cells with chromosomal aberrations.

The notified chemical when examined at concentrations ranging from 10 to 1000 µg/mL (for 24 hours) or 10 to 500 µg/mL (for 48 hours), with or without metabolic activation, did not induce clastogenicity in cultured human lymphocytes (19). The positive control chemical mitomycin C produced a significant increase in the incidence of cells with chromosomal aberrations.

9.4 Overall Assessment of Toxicological Data

The studies demonstrated that the notified chemical has low acute oral, and low acute dermal toxicity in rats, is a slight dermal and ocular irritant in rabbits. Although one sensitisation study indicated that the chemical is a dermal sensitiser, four studies conducted to international recognised standards, indicated that the notified chemical was not a sensitiser. Therefore, on the weight of evidence, it may be concluded that the notified chemical is most probably not a dermal sensitiser. Twenty eight day repeat dose studies indicated that the target organs are the liver, kidney, spleen and adrenals. Alterations in liver structure were detected at, and above, doses of 25 mg/kg/day. The pathology induced in the liver and kidney was not reversible when a dose of 800 mg/kg/day was administered for 28 days. The compound, when assessed in *in vitro* assays, was not mutagenic or clastogenic.

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