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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Cinnamidopropyl trimonium chloride

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Director
Chemicals Notification and Assessment

TABLE OF CONTENTS

Cinnamidopropyl trimonium chloride

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Croda Singapore P/L (Trading as Croda Australia) of Suite A1, Ground Floor, 44-46 Mandarin St, Villawood, NSW, 2163.

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:

Chemical name
CAS number
Purity and nature of impurities

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:

Physico-chemical properties
Melting Point
Boiling Point
Density
Vapour Pressure
Water Solubility
Hydrolysis as a Function of pH
Partition Coefficient (n-octanol/water)
Adsorption/Desorption
Particle Size
Flash Point
Flammability Limits
Autoignition Temperature
Explosive Properties

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
LVC Permit (Permit no. 341)

NOTIFICATION IN OTHER COUNTRIES
No

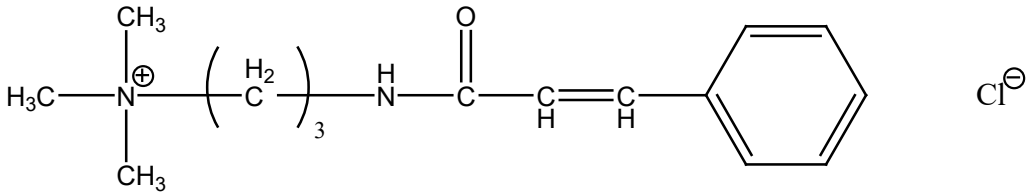
2. IDENTITY OF CHEMICAL

OTHER NAME(S)
Cinnamidopropyl trimonium chloride (INCI)

MARKETING NAME(S)
The notified chemical is imported as a 70% aqueous solution named Incroquat UV-283.

MOLECULAR FORMULA
$C_{15}H_{23}N_2O.Cl$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
282.8

SPECTRAL DATA

ANALYTICAL METHOD	Infrared Spectroscopy
Remarks	Peaks at 3400 (broad) 3080, 3960, 1660, 1620, 1555, 1480, 1330, 1225 and 990 cm^{-1}.

3. COMPOSITION

DEGREE OF PURITY
High

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical is imported into Australia as a 70% aqueous solution.

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

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

USE
Hair conditioning agent in cosmetic preparations.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
Croda Singapore P/L (Trading as Croda Australia), Villawood, NSW, 2163.

TRANSPORTATION AND PACKAGING
The notified chemical will be transported to formulators in 200 L steel drums. Final products containing the notified chemical will be packaged in plastic consumer sized containers. Typically container sizes will be 100 – 250 mL.

5.2. Operation description

Small samples will be removed from drums for analysis. The notified chemical is then pumped from the drums, weighed out and then pumped to a mixing vessel where other ingredients typical of hair conditioning products are added. Small samples of the formulated product are taken for quality control checking. The formulated product containing 1-4% of the notified chemical is then automatically filled into plastic containers and boxed for distribution to retail outlets.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Research & Development (R&D) Chemists	Up to 10	1 hour per day	Up to 50 days per year
Quality Control (Q&C) Chemists	Up to 10	2 hours per day	Up to 100 days per year
Production Personnel	Up to 50	Up to 8 hours per day	Up to 230 days per year
Warehouse and waste disposal personnel	Up to 10	2 – 3 hours per day	Up to 10 days per year

Exposure Details

R & D chemists may be exposed (mainly via the dermal route) to small quantities of an aqueous solution containing 70% notified chemical, when sampling the chemical from drums and testing various parameters. Exposure is controlled by the use of safety glasses, impervious gloves and laboratory coats.

Q & C chemists will be exposed to small quantities of products containing 1 – 4% of the notified chemical. The exposure is mainly expected to be dermal and they will wear safety glasses, impervious gloves and laboratory coats.

Production personnel are potentially exposed to 70% notified chemical when pumping quantities from the drum to weighing vessels and from these vessels to the mixing tank. Exposure is mainly likely to be dermal. Exposure during the filling process is not expected to occur except in the event of a machine malfunction. Overalls, safety boots, chemical goggles and impervious gloves will be employed to control exposure.

Warehouse and waste disposal personnel should not be exposed to high concentrations of the notified chemical and will typically wear overalls, safety boots and eye and hand protection if required.

Retail workers will only be exposed to up to 4% notified chemical in the event of a spill from damaged containers.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Since the notified chemical will not be manufactured locally, there will be no environmental exposure associated with this process in Australia. Environmental release of the notified chemical is unlikely during importation, storage and transportation, and an accidental spill/leak is the most likely reason for environmental release.

The notified chemical will be reformulated into hair conditioning products at a small number of sites in Australia. Release from the reformulation process is expected to be low. Up to 10 kg per annum of the imported chemical may remain in the empty containers. The empty import containers will be rinsed and the rinsate containing the notified chemical will be reused in subsequent batches.

Release of the notified chemical from spills during reformulation and cleaning of equipment is expected to be up to 20 kg/annum. All the reformulation waste will be treated in an on-site treatment plant. The waste will be neutralised and the solids removed for landfill and the liquid effluent discharged to trade waste.

RELEASE OF CHEMICAL FROM USE

Since the notified chemical will be used as a hair-conditioning agent in cosmetics preparations, almost all of the notified chemical imported will enter the sewer when the products are washed off hair. Up to 10 kg of the notified chemical (1%) is expected to remain in emptied consumer product containers.

5.5. Disposal

Spilled or leaked material will be collected using absorbent material into containers and disposed of by a licensed waste disposal company. Rinsed empty import containers and solids removed from the wastewater treatment plant containing the notified chemical will be disposed of to landfill. Following use, emptied consumer product containers are expected to be collected through domestic garbage disposal and then disposed of to landfill.

5.6. Public exposure

The general public will come into contact with the notified chemical at a concentration of 1-4% during use of the hair conditioning products. Exposure routes include dermal, ocular and accidental ingestion.

6. PHYSICAL AND CHEMICAL PROPERTIES

The notified chemical is manufactured in water and never isolated or made available as neat substance. Physico-chemical property data has not been provided for the notified chemical itself.

Appearance at 20ºC and 101.3 kPa	Viscous yellow liquid (70% aqueous solution)
Melting Point	Not determined
Remarks	The aqueous solution of the notified chemical is liquid at room temperature.
Boiling Point	Not determined
Remarks	The aqueous solution of the notified chemical is expected to have a boiling point of approximately 100 ºC.
Density	Not determined
Remarks	The aqueous solution of the notified chemical is expected to have a density of approximately 1000kg/m^3.
Vapour Pressure	Not determined
Remarks	Based on the molecular structure of the notified chemical, the aqueous solution of the notified chemical is expected to have a vapour pressure corresponding to no more than that of water i.e. 3.17 kPa at 25 ºC.
Water Solubility	Not determined
Remarks	The notified chemical is a quaternary ammonium compound. Due to the presence of polar and non-polar ends it has surfactant/surface active properties. The notified chemical is imported as a 70% aqueous solution, indicative of high water solubility.
Hydrolysis as a Function of pH	Not determined
Remarks	The notified chemical contains one amide linkage that could be expected to undergo hydrolysis under extreme pH conditions. However, in the environmental pH range of 4 to 9, significant hydrolysis is unlikely to occur.
Partition Coefficient (n-octanol/water)	Not determined
Remarks	The notified chemical is potentially soluble in both water and octanol. The partition coefficient could not be determined due to its surface-active properties.
Adsorption/Desorption	Not determined
Remarks	The adsorption/desorption properties of the notified chemical could not be

determined due to its surface-active properties.

The notified chemical is potentially mobile in both aquatic and terrestrial compartments as it is water-soluble. However, based on its structure and the presence of a charged group it is expected to strongly adsorb to soil, particularly to silicates, similar to other quaternary ammonium compounds. Cationic surfactants with molecular weights of less than 1000 are known to bind with dissolved organic carbon (Nabholz *et al*. 1993). Therefore, the notified chemical can be expected to be immobile in soil.

Dissociation Constant Not determined

The notified chemical is expected to remain fully dissociated due to the quaternary ammonium group. The pH of a 70% aqueous solution of the notified chemical is 4 to 6.

Particle Size Not determined

Remarks The notified chemical imported as an aqueous solution.

Flash Point Not determined

Remarks The notified chemical is imported in aqueous form and therefore is unlikely to be combustible in this form.

Flammability Limits Not determined

Remarks The notified chemical is imported in aqueous form. The notified chemical does not react upon contact with water.

Autoignition Temperature Not determined

Remarks The notified chemical is imported in aqueous form and therefore is unlikely to self ignite in this form.

Explosive Properties Not determined

Remarks The notified chemical is imported in aqueous form and therefore is unlikely to be explosive in this form. There are no chemical groups that would imply explosive properties.

Reactivity

Remarks Expected to be stable under normal conditions of use.

7. TOXICOLOGICAL INVESTIGATIONS

The notified chemical is manufactured in water and never isolated or made available as neat substance The following toxicological studies were provided for aqueous solutions of notified chemical.

Endpoint and Result	*Assessment Conclusion*
Skin irritation – *in vitro*	moderately to mildly irritating
Eye irritation – *in vitro*	practically non irritating
Skin sensitisation – human repeat insult test.	no evidence of sensitisation.

7.1. Skin irritation –*In vitro*

TEST SUBSTANCE	Notified chemical at 70% in aqueous solution
METHOD	MatTek Co. EpiDerm™ Skin Model *in vitro* Toxicity Testing System.
Test system	Human epidermis skin model with human-derived epidermal keratinocytes.
Vehicle	None. Test Substance administered as supplied.
Exposure Period	1, 4.5 and 20 hours.
Remarks - Method	The viability and metabolising potential of cells in the skin layers were tested using MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl-tetrazolium bromide). Non-viable cells (i.e. damaged cells) inhibit the reduction of MTT. Two reference substances were also tested With some protocol deviations, the method is analogous to OECD TG 431 *In Vitro* Skin Corrosion: Human Skin Model Test.

RESULTS

Exposure Time	*% viability*	*% inhibition*
1 hour	83	17
4.5 hours	84	16
20 hours	12	88

Remarks - Results	ET-50 (time at which viability was reduced by 50%) was estimated to be approximately 8.6 hours. Based on test facility data, an ET-50 value of 4-12 is indicative of moderately to mildly irritating to skin. The ET-50 values for the two reference substances were consistent with the expected irritancy for these substances.
CONCLUSION	Under the conditions of this test, the notified chemical is predicted to be non-corrosive and moderately to mildly irritating to skin.
TEST FACILITY	Consumer Product Testing Co. (1998)

7.2. Eye Irritation – *in vitro*

TEST SUBSTANCE	Notified chemical at 0.7%, 1.75% and 3.5% in aqueous solution
METHOD	Hen's Egg Test (HET) - Chorionallantoic Membrane (CAM) Test (Modification of that described by Kemper and Luepke (1986)
Species	White Leghorn chicken egg
Number of Eggs	4
Observation Period	5 minutes
Treatment	After a 10-day incubation at 33°C, shell over the air section of each egg

	was removed and following hydration the inner membrane was removed to reveal the CAM. A 0.3 mL test solution was added to each CAM for a period of twenty seconds and effects of hyperemia, haemorrhage (including minimal haemorrhage) and coagulation were observed over a period of 5 minutes.
Remarks - Method	No details of test substance preparation was included. No positive control was included in the study.

RESULTS

Test solution	*Irritation Score*
Negative Control - Distilled Water (100%)	1.75
Notified Chemical (0.7%)	1.00
Notified Chemical (1.75%)	2.00
Notified Chemical (3.5%)	1.00

Remarks - Results	Individual scores of each test solution were not provided in the report. Numerical, time-dependent scoring was totaled for each CAM. Each reaction type was recorded only once yielding a maximum score of 32.
CONCLUSION	Under the conditions of this test, the notified chemical is predicted to be practically non-irritating to the eye at a concentration of 3.5% or less.
TEST FACILITY	Consumer Product Testing Co. (2004)

7.3. Skin sensitisation – human volunteers

TEST SUBSTANCE	Notified chemical at 7% in aqueous solution
METHOD	Patch test - repeated continuous induction exposure with rest periods (human repeat insult patch test)
Study Design	The study was conducted as single phase. No pilot phase was undertaken.
Study Group	56 human volunteers aged 19 to 75 years.
Vehicle	Distilled Water
Induction Procedure	Semi-occlusive application of 0.2 mL of a 10% dilution of the notified chemical as supplied (70% aqueous solution) for 24 hours, 3 times per week (Monday, Wednesday, Friday) for a total of 10 applications to the same skin area of the upper back. Inspection of the patch sites for irritation was conducted just prior to re-application.
Rest Period	Rest periods consisted of 24 hours following each Tuesday and Thursday removal and 48 hours following each Saturday removal.
Challenge Procedure	Approximately 14 days following the 10th application, a challenge patch was applied to the original and a virgin site and evaluated at 24 and 48 hours after application.
Remarks - Method	One subject did not complete the study. This was not related to the use of the test material.
RESULTS	
Remarks - Results	No signs of irritation were observed during induction or following the challenge exposure.
CONCLUSION	A repeat insult patch test was conducted using the notified chemical diluted with distilled water to 7% under a semi-occlusive dressing. The notified chemical was non-irritating and non-sensitising under the conditions of the test.

TEST FACILITY Consumer Product Testing co. (1997)

8. ENVIRONMENT

No environmental fate or ecotoxicity data were provided. The notifier provided a report titled "Environmental and Health Assessment of Substances in Household Detergents and Cosmetic Detergent Products" (CETOX 2001) published by the Danish Environmental Protection Agency to support the notification. This report reviews the available ecotoxicological data for cationic surfactants used as household detergent and cosmetic products.

Among the cationic surfactants reviewed in the report, the notifier claims the alkyltrimethylammonium chlorides (ATMAC) represent a group of compounds similar in structure to the notified chemical. There are certain structural differences, however, between the notified chemical and ATMAC. ATMAC normally comprise linear hydrophobic alkyl chains while the notified chemical (which incorporates the linear alkyl chain) also includes an aromatic ring, a double bond and an amide linkage. The notifier claims the alkyldimethylbenzylammonium chlorides (ADMBAC), which contain a benzyl ring at one end and a linear alkyl chain at the other, represent an additional group of cationic surfactants similar in structure to the notified chemical.

The Danish report provides data on the toxicity of ATMAC and ADMBAC to selected aquatic organisms. Conclusions with respect to the notified chemical based on ATMAC and ADMAC data are not definitive due to the structural differences between the notified chemical and ATMAC as well as ADMAC. The notifier asserts that as the fate and ecotoxicity properties of the notified chemical are mainly driven by quaternary ammonium functionality and such functionality for the notified chemical is approximated by reading across the data for ATMAC and ADMBAC. This is considered an acceptable guide only with regard to the proposed import volume of the notified chemical of 1 tonne per annum.

8.1. Environmental fate

8.1.1. Ready biodegradability

According to CETOX (2001) the ultimate biodegradability of ATMAC has been examined by measuring oxygen uptake or the evolution of carbon dioxide. The biodegradability of various ATMAC during 10 days, reported as a percentage of Theoretical Oxygen Demand (ThOD) were 73%, 63%, 59%, 35% and 0% for C_8, C_{10}, C_{12}, C_{14} and C_{16} and C_{18} alkyl chain length ATMAC respectively. The report did not contain information on the inoculum and therefore it is not known if the tests conformed to OECD guidelines.

As part of the report, the Danish EPA conducted a ready biodegradability test on a C_{16} ATMAC at 10 mg/L (without acclimation of the inoculum) which showed 40% of ThOD was reached in 28 days.

The report indicated that due to bacterial toxicity and sorptive properties of cationic surfactants, results from screening tests may underestimate the biodegradation potential in the aquatic environment. Rapid and extensive mineralisation was observed when ^{14}C labelled C_{18} ATMAC was added to the Semicontinuous Activated Sludge (SCAS) system at 0.1 and 1.0 mg/L. One study showed that C_{18} ATMAC at 10 µg/L demonstrated extensive mineralisation in river water. This rapid transformation, which may occur in the environment, was confirmed by a half-life of C_{18} ATMAC of 2.2 days in acclimated river water. In another study it was concluded that no metabolites of C_{18} ATMAC with appreciable half-lives are formed.

The aerobic biodegradability of ADMBAC was examined in a number of standard screening tests, which were hampered by problems of toxicity and sorption as for ATMAC. The biodegradability in the MITI (Ministry of International Trace and Industry, Japan) Test of various ADMBAC was 79%, 95%, 89%, 83%, 5% and 0% of ThOD for C_8, C_{10}, C_{12}, C_{14}, C_{16} and C_{18} alkyl chain length ADMBAC respectively during 10 days of incubation. Information on the inoculum used in these tests was not reported. ADMBAC are generally less biodegradable with increasing chain length with little degradation of C_{16} and C_{18}. The report indicated that extensive ultimate biodegradation of C_8 to C_{14} ADMBAC may occur and may biodegrade as rapidly as ATMAC when present at environmentally realistic concentrations.

8.1.2. Bioaccumulation

Bioaccumulation studies using the fathead minnow suggest bioconcentration of ATMAC are hydrophobicity-dependent. However, the radiolabelling technique used does not allow a distinction between the parent compound and its metabolites formed therefore, the term Concentration Ratio (CR) was used instead of BCF.

The CR values were 2.4, 35 and 1962 for C_8, C_{12} and C_{16-18} alkyl chain length ATMAC respectively. Bioaccumulation data for ADMBAC was not reported.

8.2. Ecotoxicological investigations

The following acute aquatic toxicity data for ATMAC and ADMBAC were obtained from CETOX (2001).

8.2.1. Acute toxicity to fish

Some ATMAC were found to be toxic to fish with LC50 values (for golden orfe) for C_{12} to C_{20-22} ATMAC ranging from 0.36 to 8.6 mg/L. The LC50 of various ADMBAC to fish ranged from 0.5 to 3.5 mg/L.

8.2.2. Acute toxicity to aquatic invertebrates

ATMAC exhibit EC50 values below 1 mg/L for C_{16} (with the lowest EC50 of 0.1 mg/L for *Gammarus sp*.) towards various aquatic invertebrates. One study using ATMAC of C_{12}, C_{14}, C_{16}, C_{18} and C_{20-22} showed EC50 values ranging from 1.2 to 5.8 mg/L. Aquatic invertebrate toxicity data for ADMBAC or chronic toxicity data for both groups were not reported.

8.2.3. Algal growth inhibition test

Algae appear to be very sensitive to cationic surfactants. EC50 values are below 1 mg/L for a range of species and as low as 0.12 mg/L for a 96 hour test with C_{12} ATMAC with *Microcystis aeruginosa*. Low EC50 values are observed for C_{12-14} ADMBAC (0.67 for *Chlorella pyrenidosa* and 1.8 for *Dunaliella sp.)*.

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

Up to 20 kg per annum of the notified chemical is expected to be released to the environment during the formulation process (from spills and rinsed residue in empty import containers). Nearly all of the imported notified chemical will eventually be released into the aquatic environment via the sewerage systems through formulation and use (washing off the hair) of the cosmetic products. A small amount of the chemical is also expected to be disposed of to landfill in solids removed from the onsite treatment plant and as residue in empty consumer containers (up to 10 kg per annum) via domestic garbage.

The notified chemical is not expected to be volatile, therefore, it should not dissipate into air from the surfaces to which the products containing it is applied. It is readily soluble in water but not expected to readily hydrolyse in natural waters at environmental pH values.

The notified chemical is potentially mobile in soils and water. However, it is expected to adsorb strongly to soil and sediments due to its cationic nature. Based on the study results reviewed (Section 8.1.1) for similar surfactants with longer alkyl chain lengths, the notified chemical may be ultimately biodegradable. Therefore, when disposed in landfill the chemical can be expected to become associated with soil and sediment and slowly degrade through biological and abiotic processes.

Based on maximum annual imports of 1000 kg per annum, and assuming a worst-case scenario that all of this is eventually released to sewer and not removed during sewage treatment processes, the daily release on a nationwide basis to receiving waters is estimated to be 2.74 kg/day. Assuming a national population of 20 million and that each person contributes an average 200 L/day to overall sewage flows, the worst-case predicted environmental concentration (PEC) in sewage effluent on a nationwide basis is estimated as 0.6849 µg/L (Environment Australia 2003). Based on the respective dilution factors of 0 and 10 for inland and ocean discharges of effluents, the PECs of the notified chemical in freshwater and marine water may approximate 0.6849 µg/L and 0.0685 µg/L, respectively.

It is not possible to use the SIMPLETREAT 3.0 model to model the fate of the chemical in sewage treatment plants (STP) as the vapour pressure and the log Kow are not determined. Therefore, the following risk assessment is based on the above worst-case PEC values (assuming no portioning to sludge).

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 0.1 m of soil (density 1000 kg/m^3). Using these assumptions, irrigation with a concentration of 0.6849 µg/L may potentially result in a soil concentration of approximately 0.0068 mg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 0.034 mg/kg and 0.068 mg/kg, respectively.

The notified chemical has the potential to bioaccumulate due to its low molecular weight. This will be limited due to the predicted high water solubility, the low volume imported and diffuse release to the sewer Australia wide.

9.1.2. Environment – effects assessment

In general, algae appeared to be the most sensitive species to the cationic surfactants. However, of the data provided the most sensitive species were aquatic invertebrates with a 48-hour EC50 value of 0.1 mg/L for C_{16} ATMAC (for the crustacean *Gammarus sp*.). As no ecotoxicity data are available for the notified chemical, a greater uncertainty has to be incorporated in extrapolating the available toxicity data on other surfactants to assess the toxicity of the notified chemical. Therefore, using the lowest datum of 0.1 mg/L, a predicted no effect concentration (PNEC for aquatic ecosystems) of 0.1 µg/L has been derived by dividing the EC50 value by an

uncertainty (safety) factor of 1000 (instead of a safety factor of 100 used when toxicity data is available for three trophic levels).

9.1.3. Environment – risk characterisation

The resulting risk quotient (PEC/PNEC) values are 6.8 for fresh water and 0.68 for marine water. The value for freshwater is above 1, indicating a potential concern to the aquatic compartment.

Cationic surfactants with molecular weights of less than 1000 such as the notified chemical are known to bind with dissolved organic carbon (Nabholz *et al*. 1993). Based on its structure and the presence of a charged group, the notified chemical is expected to strongly adsorb to soil, particularly to silicates similar to other quaternary ammonium compounds. Similarly, a part of the notified chemical can also be expected to be removed due to adsorption to sludge in STP or to sediments in aquatic environment.

Therefore, the risk quotients are recalculated assuming that 50% of the notified chemical is adsorbed to sludge in STPs throughout Australia and are presented below:

Location	PEC µg/L	PNEC µg/L	Risk Quotient (RQ)
Australia-wide STPs			
Ocean outfall	0.0685*	0.1	0.68*
	0.0342#		0.34#
Inland River	0.6849*	0.1	6.8*
	0.3425#		3.4#

* PEC and RQ values calculated assuming no removal in STP

\# PEC and the RQ values calculated assuming 50% of the notified chemical partitioned into biosolids during the STP process.

The risk quotients, however, are based on a worst-case PNEC value for the notified chemical calculated using a safety factor of 1000 (due to the high level of uncertainty involved in using aquatic toxicity data on similar chemicals). If aquatic toxicity data on the notified chemical were available, a safety factor of 100 could have been applied reducing this quotient to below 1.

The risk quotient for freshwater is reduced but is still above 1. However, given that only about 25% of effluent is released into fresh water in Australia, the risk quotient is 3.4/4 = 0.85 and is acceptable. This is expected to be further reduced due to adsorption of the notified chemical in the aquatic environment. Most natural waters contain colloidal humic material, which is negatively charged as a consequence of its high content of carboxylate groups. The notified chemical released to the water compartment would become associated with colloidal material and eventually assimilated into bottom sediments and would be unlikely to be re-mobilised. Therefore, when the sewer water is discharged into aquatic environment, the resulting risk quotients can be expected to be further reduced. Based on the above risk assessment, the use of the notified chemical is unlikely to pose an unacceptable risk to the aquatic life at import levels less than 1 tonne per annum.

Bioaccumulation is not expected due to the diffuse use pattern, low import volume and the predicted high water solubility. Based on the proposed import volumes and use pattern the notified chemical is not expected to pose an unacceptable risk to the health of aquatic life. However, it is noted that the safety margin for freshwater is narrow and is based on surrogate data for different structures. Therefore, a Standard notification containing physico-chemical properties, environmental fate data, particularly with respect to adsorption characteristics of the notified chemical and a full suite of aquatic toxicity data on the notified chemical should be submitted if the import volume is increased above the currently assessed level of one tonne per annum.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Workers that have the potential for exposure to the notified chemical at a concentration of 70% include warehouse and waste disposal personnel, R&D chemists and production personnel. For all these workers dermal exposure is the most likely route, however there is also the potential for ocular exposure from splashes.

Warehouse personnel
Exposure to the notified chemical is expected to be negligible except in the case of an accidental spill.

R&D chemists
Exposure to the notified chemical is expected to be low due to the small samples involved and the limited exposure time and would be limited by the use of PPE.

Production personnel
Incidental exposure to drips and spills of the notified chemical could occur during the transfer of the notified chemical to the weighing vessel or mixing tank. Exposure would be limited by the use of PPE.

Waste disposal personnel
Incidental skin contact is also identified for workers involved with drum disposal. However, personal protective equipment would minimise any dermal exposure.

Following formulation of the hair conditioner the workers that have the potential for exposure to up to 4% notified chemical include Q&C Chemists, production personnel and retail workers. Again, dermal exposure is the most likely route, however there is also the potential for ocular exposure from splashes.

Q&C chemists
Exposure to the notified chemical is expected to be low due to low concentration, the small samples involved and the limited exposure time. Exposure would be limited by the use of PPE.

Production personnel
Due to the automated nature of the filling process, exposure to the notified chemical is expected to be negligible except in the case of a machine malfunction.

Retail workers
Exposure to the notified chemical is expected to be negligible except in the case of an accidental spill. However, even in the event of an accident, exposure to the notified chemical is expected to be low due to the low concentration and the small pack size.

9.2.2. Public health – exposure assessment

Dermal and ocular exposure to up to 4% notified chemical will occur during use of the hair conditioning products. The exposure is expected to be widespread and repeated. The notified chemical can be used in conventional and leave-in conditioners. An estimate of exposure is as follows:

Product	*Application Quantity (g/application)**	*Application Frequency per Day**	*Retention Factor (%)**	*% Notified Chemical in Product*	*Exposure to Notified Chemical (mg/kg bw/day)****
Rinse out conditioner	14.0	0.28	1	4	0.03
Leave in conditioner**	5.0	2	10	4	0.7

*data from EU SCCNFP (Scientific Committee on Cosmetic Products and Non-food products intended for Consumers) (SNCNFP, 2003)
** no data in EU SCCNFP for leave in conditioners. Data for hair styling products used.
*** assuming 60kg body weight

There is also a slight chance of ingestion of the notified chemical. A 10 kg child ingesting 5 mL of a 4% solution would receive a dose of approximately 20 mg/kg bw.

9.2.3. Human health - effects assessment

The following toxicological data for the notified chemical were submitted: an *in vitro* skin irritancy test, an *in vitro* eye irritancy test and a human repeat insult patch test.

In addition, the notifier provided a detailed review of the toxicity of other alkyltrimethylammonium (ATMA) salts and alkyldimethylbenzylammonium chlorides (ADMBAC) (CETOX, 2001). This data has been used to indicate the likely human health effects of the notified chemical. No study reports have been evaluated.

Toxicokinetics, metabolism and distribution.
Percutaneous absorption of a radiolabelled C_{12} ATMA salt in 3% aqueous solution was low and corresponded to 0.6 of the applied ^{14}C activity in 72 hours. Approximately 60% of the absorbed surfactant was excreted in the urine within the first 24 hours, with 13.2% remaining on the skin after rinsing. Cutaneous application of the surfactant without rinsing resulted in a greater level of percutaneous absorption (3.15%) in 48 hours.

Following oral administration of a radiolabelled C_{16} ATMA salt, 80% of the ^{14}C activity was found in the gastrointestinal tract after 8 hours. Within 3 days of ingestion, 92% of the administered radioactivity had been excreted in the faeces and 1% in the urine indicating poor intestinal absorption.

Acute toxicity.
Acute oral toxicity LD50 values in rats have been reported for various ATMA salts (C_{12}-C_{18}) in the range 250 – 1000 mg/kg bw and for various ADMBAC (unspecified chain length – C_{18}) in the range 280-525 mg/kg bw. A dermal acute LD50 value for a $C_{14\text{-}18}$ ADMBAC was reported as 1420 mg/kg bw. Dermal and inhalation acute toxicity data for ATMA salts were not available.

Based on this information, the notified chemical is likely to be harmful if swallowed and may be harmful in contact with skin.

Irritation and Sensitisation.
The notified chemical was a moderate to mild skin irritant *in vitro*. A 7% aqueous solution of the notified chemical was found to be non-irritating and non-sensitising in a human repeat insult patch test. In an *in vitro* eye irritation study, the notified chemical was predicted to be practically non-irritating to the eye at a concentration of 3.5% or less.

A number of ATMA salts (C_{10}-C_{16}) tested in concentrations between 0.1 and 1% in water were found to be significantly irritating or injurious to the rabbit eye. A 5% solution of a C_{18} ATMA salt was very irritating to guinea pig eyes. A non-specified ADMBAC caused minor to moderate eye irritation at 0.625 and 1.25% concentrations. Longer chain (chain length unspecified) ATMA salts are reported as less irritating to the rabbit eye than the shorter alkyl chain homologue. Based on this information, the notified chemical is likely to be irritating or severely irritating to the eye.

Repeated Dose Toxicity.
A C_{16} ATMA salt was administered to rats in the drinking water for 1 year at 10, 20 and 45 mg/kg/day and the only effect was reduced body weight gain (unspecified value) in the high dose group.

Mutagenicity.
A C_{16} ATMA salt was not mutagenic in *Salmonella typhimurium* and did not induce transformation in Syrian golden hamster embryo cells. No mutagenicity or genetic damage was detected in 9 short-term genotoxicity tests with C_{16} and C_{18} ATMA salts in a separate study. C_{16} ADMBAC was not mutagenic in *Salmonella typhimurium* and did not induce transformation in Syrian golden hamster embryo cells. In other short-term genotoxicity assay

(Salmonella/microsome assay) and rec-assay (bacterial DNA repair test) no mutagenic effects were indicated.

Toxicity for reproduction.
No embryo toxic effects were seen when a C_{18} salt was applied dermally at 0.9, 1.5 and 2.5% to pregnant rats during days 6 – 15 of gestation. There was no increase in the incidence of foetal malformations. A C_{16} ATMA salt was not teratogenic at oral dosages of 50 mg/kg/day and below. Mild embryonic effects were observed with 50 mg/kg/day, but these effects were attributed to maternal toxicity rather than to a primary embryonic effect. The lower doses showed no embryo toxic effects. No embryotoxic activity was detected when C_{18} ADMBAC was applied topically to pregnant rats during the period of major organogenesis at doses up to 6.6%, which was sufficient to cause adverse maternal reactions.

Overseas regulation
The notified chemical appears to be used in a number of hair conditioning products overseas, however, no information on the concentration of the notified chemical in these products was available.

Alkyl (C_{12}-C_{22}) trimethyl ammonium, bromide and chloride (a quaternary ammonium compound which is similar to the notified chemical) are listed in Annex VI (List Of Preservatives Allowed) of the EU Cosmetic Directive (Cosmetic Directive 2000). The maximum authorised concentration is 0.1%. However, the Directive also states these chemicals may also be added to cosmetic products in concentration other than those laid down in this Annex for other specific purposes apparent from the presentation of the products. The notified chemical will not be used as a preservative. It will be used as a hair conditioning agent in rinse-off cosmetic preparations. Thus, the concentration restriction of 0.1% does not apply to the notified chemical with regards to this notification.

Hazard classification for health effects.
Most undiluted cationic surfactants satisfy the criteria for classification as Harmful (Xn) with R22 and as Irritant (Xi) for skin and eyes with R38 and R41. (CETOX, 2001)

Based on the limited toxicological data for the notified chemical, it is not possible to classify the notified chemical as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004). However, based on the *in vitro* skin irritation study, the analogue data provided and classification of similar chemicals, the following classification and labelling details should apply:

R22 Harmful if swallowed
R38 Irritating to skin
R41 Risk of serious damage to eyes

The HET-CAM test method is not yet validated. The EU national regulatory authorities accept positive outcomes from this test method for classifying and labelling severe irritants (R41). Where a negative result is obtained, an *in vivo* test is subsequently required, as the HET-CAM test method has not been shown to adequately discriminate between eye irritants and non-irritants. For the detection of ocular corrosives and severe irritants it is recommended that all test substances should be evaluated undiluted unless dilution is justified. (ICCVAM, 2004). Although the notified chemical was considered to be practically non-irritating in the HET-CAM study provided, the R41 classification for the notified chemical (based on analogue data) is still considered appropriate as only a dilute form of the notified chemical was tested.

Quaternary ammonium compounds have been considered by the National Drugs and Poisons Schedule Committee (NDPSC) for inclusion into the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). Preparations containing quaternary ammonium compounds (except those separately specified) above 5% (but not above 20%) are Schedule 5 entries in the SUSDP.

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is likely to be acutely toxic and has the potential to cause irritation to the

skin and serious damage to the eyes.

Workers that have the potential for exposure to the notified chemical at a concentration of 70% include warehouse and waste disposal personnel, R&D chemists and production personnel. Exposure and hence the risk of irritation is most likely for production personnel during the transfer of the 70% aqueous solution to the weighing and mixing vessels. Due to the possible risk of skin irritation and damage to the eyes the following personal protective equipment should be worn: Protective eyewear, chemical resistant industrial clothing (coveralls) and impermeable gloves.

The risk to warehouse and waste disposal personnel and R&D chemists is expected to be low due to the limited predicted exposure. However, in order minimise the risk of adverse irritancy effects, similar PPE to that described above should be worn.

Following formulation of the hair conditioner, there is the potential for exposure to up to 4% notified chemical. At this concentration, the notified chemical is below the cut off for classification as a skin and eye irritant according to NOHSC *Approved Criteria for Classifying Hazardous Substances.* Therefore, the risk of an adverse irritant response from exposure to the notified chemical at this concentration is considered to be low. This is supported by the results from the human repeat insult patch test and the *in vitro* eye irritation study. Overall, the risk to workers following formulation is expected to be low due to the negligible to low exposure predicted. However, as a precaution workers should avoid contact with the eyes.

9.2.5. Public health – risk characterisation

Dermal and ocular exposure to up to 4% notified chemical will occur during use. As discussed in section 9.2.4, the risk of an adverse irritant response from exposure to the notified chemical at this concentration is considered to be low, however, eye irritation effects cannot be fully discounted.

The estimated exposure to the notified chemical following accidental ingestion was 20 mg/kg bw. This is over 100 times less than the lowest acute oral LD50 provided in the analogue data (250 mg/kg bw). Therefore, the risk of lethal effects as a result of accidental ingestion is low.

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

10.1. Hazard classification

Based on the limited toxicological data for the notified chemical, it is not possible to classify the notified chemical as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004). However, based on the *in vitro* skin irritation study, the analogue data provided and classification of similar chemicals, the following classification and labelling details should apply:

R22 Harmful if swallowed
R38 Irritating to skin
R41 Risk of serious damage to eyes

and

As a comparison only, the classification for skin irritation of the 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: Irritant Category 2
Signal word: Warning

Hazard statement: Causes skin irritation

There is insufficient data to classify the other toxicological end points including the toxicity to aquatic organisms under this system.

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratios the notified chemical is not considered to pose an unacceptable risk to the environment based on its proposed import volumes and reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

Production Personnel

There is Moderate Concern to occupational health and safety under the conditions of the occupational settings described due to the potential for ocular exposure.

All other workers

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is No Significant Concern to public health when used at a concentration of 1-4% in formulated hair conditioner products.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of Incroquat UV-283 provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for Incroquat UV-283 provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS

Hazard Classification and Labelling

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - conc≥25%: R22; R38; R41
  - 20%≤conc<25%: R38; R41
  - 10%≤conc<20%: R41
  - 5%≤conc<10%: R36

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced:
  - Avoid contact with skin and eyes

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as diluted for use:
  - Avoid contact with eyes

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - Protective eyewear, chemical resistant industrial clothing (coveralls) and impermeable gloves;

  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.

Public Health

- The following measures should be taken to minimise public exposure to the notified chemical:
  - The notified chemical should not be used in the consumer products at 5% or above.

Disposal

- The notified chemical should be disposed of by a licensed contractor to be disposed of according to approved method of chemical waste disposal.

Emergency procedures

- Spills should be contained and collected with an appropriate absorbent and put into containers for disposal. Flush the spill area with warm soapy water.
- Spilled material should not be allowed to enter waterways.

AICS

- When the notified chemical is added to the Australian Inventory of Chemical Substances (AICS), it should be annotated with the following conditions of use:
  - 'for use in consumer products at a maximum concentration of <5%'
  - 'introduced in quantities not exceeding one tonne per annum'
- For all other types of introduction the notified chemical will be regarded under the Act as a new chemical, and therefore subject to notification and assessment.

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
  - the importation volume exceeds one tonne per annum notified chemical; or
  - the notified chemical is included in consumer products at a concentration of 5% or above

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. For the two conditions described under subsection 64 (1) the following information will need to be submitted if a secondary notification is required:
  - physico-chemical properties, environmental fate data (particularly with respect to

adsorption characteristics of the notified chemical), and a full suite of aquatic toxicity data (increase in volume).

– evidence that the notified chemical is unlikely to cause an adverse eye irritancy response at that concentration (increase in concentration).

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