File No: NA/718

March 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

poly(oxy-1,2-ethanediyl), α-[2-[(2-hydroxyethyl)amino] -2-oxoethyl]-ω-hydroxy-, mono-C_{13-15}-alkyl ethers
(Aminol A15)

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Director
Chemicals Notification and Assessment

poly(oxy-1,2-ethanediyl), α-[2-[(2-hydroxyethyl)amino] -2-oxoethyl]-ω-hydroxy-, mono-C_{13-15}-alkyl ethers
(Aminol A15)

1. APPLICANT

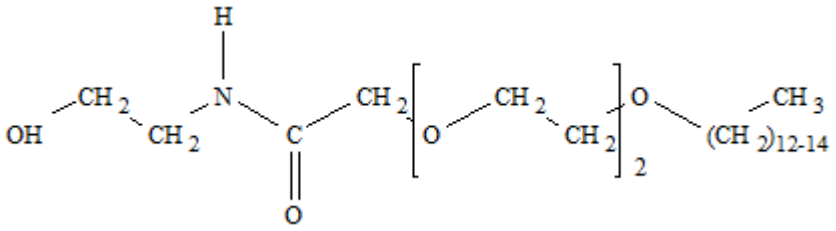
Asia Pacific Specialty Chemicals Limited of 15 Park Road SEVEN HILLS NSW 2147 has submitted a standard notification statement in support of their application for an assessment certificate for Aminol A15.

No claims were made for exempt information status.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	poly(oxy-1,2-ethanediyl), α-[2-[(2-hydroxyethyl)amino] -2-oxoethyl]-ω-hydroxy-, mono-C_{13-15}-alkyl ethers
Other Name:	Trideceth –2 carboxamide MEA
Chemical Abstracts Service (CAS) Registry No.:	107628-04-6
Marketing Names:	Aminol A15
Molecular Formula:	unspecified

Structural Formula:



Molecular Weight:	390-418
Method of Detection and Determination:	The notified chemical was separated by Gel Permeation Chromatography (GPC) and identified by infrared (IR) spectroscopy
Spectral Data:	Major characteristic IR absorbance peaks identified at: 1 115, 1 249, 1 347, 1 465, 1 542, 1 663, 2 854, 2 924 and 3 339 cm^{-1}

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Clear yellow liquid
Boiling Point:	No data provided (see comments below)
Specific Gravity:	0.9 g/m^3 at 20°C (see comments below)
Vapour Pressure:	No data provided (see comments below)
Water Solubility:	Completely miscible with water (see comments below)
Partition Co-efficient (n-octanol/water):	Not determined (see comments below)
Hydrolysis as a Function of pH:	Not determined (see comments below)
Adsorption/Desorption:	Not determined (see comments below)
Dissociation Constant:	Not determined (see comments below)
Flash Point:	Not determined (the product containing the notified chemical is not flammable
Flammability Limits:	Not flammable (the product)
Autoignition Temperature:	Not determined (the notified chemical is not expected to undergo auto ignition)
Explosive Properties:	Not explosive
Reactivity/Stability:	Not reactive

Comments on Physico-Chemical Properties

The notifier provided very little physico-chemical data appropriate to the new compound, and no test reports were submitted. However, the chemical structure is well defined, therefore it is possible to estimate the important physico-chemical properties using the ASTER USEPA (US EPA, 1999) database and Quantitative Structure Activity Relationships (QSARs). These are outlined below. While these data are estimated values from QSAR calculations, they appear reasonable for a substance with the given composition and structure of the notified chemical.

USEPA ASTER Ecotoxicity Database Calculated Physico-Chemical Profile

Boiling Point	423°C
Vapour Pressure	1.0×10^{-7} Pa.
Solubility in water	1.24 mg/L
Partition Coefficient	Log P = 5.11
Adsorption Coefficient	$LogK_{oc} = 4.12$
Hydrolysis Half Life	190 days.

The density of the chemical at 20ºC was determined using a PAAR density meter (Model DMA 48).

Vapour pressure was not provided by the notifier. QSAR suggests that the notified chemical has a vapour pressure of 1.0×10^{-7} Pa. This value, which seems a reasonable estimate based on the structure, is considered to be low and according to Mensink *et al.* (1995) the chemical is considered to be only very slightly volatile.

The notifier indicated that the notified chemical is completely miscible with water "forming an emulsion" when tested according to British Pharmacopoeia. The notified chemical is likely to have surfactant properties and it is a characteristic of such materials that they form micelles and other types of colloidal aggregates when mixed with water. While the QSAR estimate from the ASTER database of the US EPA estimates the solubility as 1.24 mg/L, this calculation would not have included the potential for colloidal aggregate formation. While the notifier claims that in the ecotoxicity studies (see further below) stock solutions of 1 000 mg/L were prepared without any undissolved material being observed, there is no apparent mention of this observation in any of the ecotoxicity reports. Nevertheless, this assessment accepts that the notified chemical would have high miscibility with water as a consequence of formation of micelles or other colloidal aggregates.

The hydrolytic behaviour of the chemical has not been investigated. However, the polyethoxylate moieties are very stable and unlikely to hydrolyse in the usual environmental pH range of 4 to 9. The chemical also contains an amide functional group. This may be susceptible to hydrolysis, but it is likely to be slow within the environmental pH range. This is supported by the ASTER calculated value, which gives the half life of 190 days. According to (Mensink, 1995) this suggests that the notified chemical is slightly hydrolysing.

The notifier indicates that as the notified chemical is a non-ionic surfactant a reliable partition coefficient cannot be determined. This statement is accepted. However the QSAR calculated octanol/water partition coefficient (Log P_{ow}) is cited as 5.11 (based on CLogP programme (Syracuse Research Corporation, 1997)). The relatively high calculated value for Log P_{ow}

reflects the large hydrocarbon content in the molecule (ie. The $C_{13-15}H_{27-31}$ moiety) and indicates that the notified chemical will partition to the oil phase.

No adsorption/desorption data were provided for the notified chemical. However, the QSAR value (Log K_{oc} = 4.12) indicates that the notified chemical should sorb to soil and sediments. However, the relatively high water solubility may indicate that substance will be mobile in these phases.

The notified chemical contains no functional group, which could be protonated or deprotonated in the environmental pH range.

4. PURITY OF THE CHEMICAL

Degree of Purity: > 96%

Toxic or Hazardous Impurities:

Chemical name:	monoethanolamine
CAS No.:	141-43-5
Weight percentage:	0.5%
Toxic properties:	*List of Designated Hazardous Substances* (NOHSC, 1999b) R20 - Harmful by Inhalation; R36/37/38 - Irritating to Eyes, Respiratory System and Skin.

Other Impurities:

Chemical name:	water
Weight percentage:	3.5%

Additives/Adjuvants: none

5. USE, VOLUME AND FORMULATION

The notified chemical is a non ionic surfactant used as a thickener, at up to 10% in retail hair dye products.

The notified chemical will not be manufactured in Australia but will be imported in 140 kg plastic drums and stored at the notifiers warehouse. Reformulation of the notified chemical into hair dye products occurs at a single site in Victoria. Import volume for the notified chemical is expected to be 1 800 kg per annum over the next five years.

6. OCCUPATIONAL EXPOSURE

Waterside Transport and Storage
The notified chemical will be imported in 140 kg plastic drums. The total import volume will be transported by road to the notifiers warehouse for storage prior to transportation to the customers site.

For waterside, transport and warehouse workers, there is not expected to be any exposure to the notified chemical during storage and distribution, except in the event of a spill.

Reformulation

Category (Number of Workers)	*Nature of Work Done*	*Maximum Potential Exposure*	
		Hours/day	*Days/year*
Storeworker (1)	Storage of material.	0.5	12
Laboratory technicians (2)	Sampling & testing of raw ingredients and final products.	0.5	24
Compounders (3)	Dispensing raw ingredients; Manufacture of final product; Cleaning of vessels.	2	24
Linesetters (1)	Setting, monitoring and maintaining the filling line.	0.5	24

At the customer site, drums containing the notified chemical are stored prior to use and, after quality control analysis by laboratory technicians, are transferred via forklifts to the formulation area. The notified chemical is dispensed into a small plastic bucket, then manually added to the blender with other ingredients and mechanically mixed under local exhaust ventilation. The end product is pumped into a sealed tank, for subsequent filling into retail bottles. Mixing vessels are steam cleaned after each use.

Dermal and ocular exposure to the notified chemical is possible during manual dispensing, blending operations and in its diluted form during vessel cleaning. Exposure by inhalation is expected to be minimal given the expected low vapour pressure of the notified chemical. Exposure resulting from escape of aerosols containing the notified chemical during blending is minimised by good general and local exhaust ventilation in the mixing and dispensing areas. The storage, sampling and packaging areas are provided with general ventilation and laboratories are equipped with fume hoods. Linesetters who supervise the filling of the final product into retail bottles, may have contact with spills with end use product containing the notified chemical at up to 10%. Some skin contact may occur if spillage occurs during the filling process.

All workers at the formulation site wear safety glasses, protective clothing and gloves.

The final hair products will be transported to consumer outlets for sale to the public.

End-use
If professional hairdressers use the hair dye, some dermal exposure to the notified chemical may occur.

7. PUBLIC EXPOSURE

The notified chemical will enter the public domain as a hair dye product. The product may be applied every 4 to 6 weeks in bathrooms and hairdressing salons throughout Australia. Although public contact via skin and eyes will occur during use, exposure would be low because the concentration of the notified chemical in the product (<10%), intermittent use and washings of the excess dye from the hair following application. A small quantity of the volume (2%, approximately 200 kg/year) will remain in the bottle after emptying and will be disposed of to landfill via domestic garbage collection. The remaining notified chemical will be released to domestic sewer systems when excess dye is washed out of the hair. No significant public exposure to the notified chemical is anticipated during transport.

8. ENVIRONMENTAL EXPOSURE

Release

The notified chemical may be released during formulation, dispensing, mixing, quality testing, packaging and equipment and drum cleaning. This release is expected to be up to 3% (a maximum of 300 kg) of a total Australia wide import volume of 10 000[1] kg per annum. All liquid waste and spills are contained and directed to the in-house effluent plant. The effluent treatment process is a batch process involving 10 000 litres per treatment cycle. During this process the alkaline effluent is adjusted to pH 6-10 using 32% (v/v) HCl. Ammonia stripping via aeration/evaporation is another feature of this process. The treated water is then released to the South Eastern Waste Water Treatment Plant.

The notifier states that the end use product (hair dye) containing the notified chemical is likely to be used by an individual once every 4 to 6 weeks. Application of the hair dye is expected to be carried out in bathrooms and other wet areas throughout Australia. The majority of release of the notified chemical is expected to occur at this time. Released product is expected to enter the sewers to be treated with the sewage before being released to the environment. The percentage of notified chemical which will be washed off the hair into the sewer is not known. The PEC estimation assumes that all of the notified chemical applied to the hair will be washed off (see Environmental Hazard section).

[1] A value of 10 000 kg per annum is used for this assessment and represents a conservative cumulative total as the notified chemical has been the subject of a previous NICNAS assessment.

The notifier estimates that up to 2% of the total import volume of the notified chemical may remain in the bottle after use. This equates to approximately 200 kg per annum, which will be consigned to landfill via domestic garbage.

Fate

The ready biodegradability of the notified chemical was undertaken using the Closed Bottle Test (301 D), the Modified Sturm Test (301 B), and the Modified OECD Screening Test (301 E) (OECD, 1995-1996).

In the Modified Sturm test (RCC NOTOX, 1987), after 29 days of incubation, the test substance was biodegraded by 36.5-52.5% depending on the starting concentration used. Since the level of 60% biodegradation was not reached, the notified chemical cannot be considered to be readily biodegradable.

Using the modified OECD screening test (OECD guideline 301E), the chemical was degraded by 79% over 19 days, as determined by a reduction in the BiAS (bismuth-active substance) level in the test medium. The BiAS level measures the amount of non-ionic surfactants containing polyethylene oxide. While this does not meet the OECD criteria for "readily biodegradable" as only the loss of the parent compound is measured and not mineralisation, degradation may be expected in the aquatic environment.

The Closed Bottle Test (Krachtwerktuigen, 1987) resulted in 73% of the notified chemical being degraded after 28 days suggesting that the notified chemical is readily biodegradable. According to OECD Guideline (301D), a test chemical giving a measured Biodegradation Oxygen Demand (BOD) greater than 60% of the Total Oxygen Demand (within 28 days), should be regarded as readily biodegradable. This level must be reached within 10 days of biodegradation exceeding 10%. Based on the data provided by the notifier it is not possible to ascertain whether this condition has been met, therefore the notified chemical cannot with certainty be regarded as readily biodegradable. Note, ASTER predicts the BOD half life to be 2-16 days.

The notified chemical will be used as a surfactant in a liquid hair dye and released to the environment via the sewer system after it has been rinsed from the hair. In the sewer, some is anticipated to adsorb to sewage sludge due to the expected surface active nature of the chemical. The sludge will either be sent to landfill or incinerated. Incineration products will include water and oxides of carbon and nitrogen. The remainder of chemical will stay in solution and is expected to be further diluted and degraded.

The Mackay Level 1 calculations from ASTER indicate that environmental partitioning will be mostly to soil (49.18%) and sediment (45.90) with 4.8% remaining in the aqueous phase. The relatively low molecular weight (390-418), the calculated Log K_{ow} (5.11) and the moderately low water solubility (calculated - 1.24 mg/L) of the notified chemical indicate that it has the potential to bioaccumulate (Connell, 1990). However, bioaccumulation potential should be moderated by the inherent biodegradability.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Aminol A15

Test	*Species*	*Outcome*	*Reference*
Acute oral toxicity	Rat	LD_{50} > 5 000 mg/kg	(Toxicol Laboratories Limited, 1986)
Skin irritation	Rabbit	Severe irritant	(RCC NOTOX, 1991b)
Eye irritation	Rabbit	Slight to moderate irritant	(RCC NOTOX, 1991a)
Skin sensitisation	Rabbit	Non sensitising	(LPT, 1997)

9.1.1 Oral Toxicity (Toxicol Laboratories Limited, 1986)

Test Substance:	Aminol A15
Species/strain:	Rat/Sprague Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	A single dose of 5 000 mg/kg (10 mL/kg) administered by gavage; vehicle was 0.25% aqueous solution of gum tragacanth
Clinical observations:	None
Mortality:	Nil
Morphological findings:	No abnormalities detected
Test method:	OECD TG 401 – limit test
LD_{50}:	> 5 000 mg/kg
Result:	The notified chemical was of very low acute toxicity when administered orally in a limit test in rats

9.1.2 Dermal Toxicity (Black, 1979)

An acute dermal toxicity study was not provided. The notifier submitted a published study containing analogue detergent data suggesting that dermal penetration data on alcohol sulphate and alcohol ether sulphate detergents would fill this data gap. Rats were treated with (^{14}C) labelled alcohol sulphates, alcohol ether sulphates and alcohol ethoxylates of varying chain length and degree of ethoxylation. Animals were monitored for 48 hours, then killed. Test substances were diluted in 1% LAS to improve solubility. A high percentage of topically applied radioactivity was removed in the rinse water, treated skin and skin patch for all tested chemicals except for dodecyl hexa ethoxylate, 48 hour after application. Ethoxylates had the highest skin penetration (maximum of 8.3 $\mu g/cm^2$), followed by maximum rates for alcohol sulphates of 0.26 $\mu g/cm^2$ and alcohol ether sulphates of 0.39 $\mu g/cm^2$.

The authors concluded that skin penetration was low for the alcohol sulphates and alcohol ether sulphates, but greater for alcohol ethoxylates; variation of the alcohol chain length and degree of ethoxylation affected penetration.

9.1.3 Inhalation Toxicity

Inhalation studies have been conducted on the basis that the notified chemical has low vapour pressure and is not used in a manner that would generate aerosols.

9.1.4 Skin Irritation (RCC NOTOX, 1991b)

Test Substance:	Aminol A15
Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	21 days
Method of administration:	0.5 mL of the notified chemical applied to intact skin for 4 hours
Test method:	OECD TG 404

Draize scores (see Attachment 1 for Draize scales):

	Number of Days After Treatment					
Animal #	***1***	***2***	***3***	***7***	***14***	***21***
Erythema						
1	2	4[A]	4[B]	1[C]	1[C]	1
2	1	3	4[B]	4[B]	1[D]	1
3	2	4	4[A]	4[B]	1[D]	1
Oedema						
1	3	4	4	1	1	1
2	3	4	4	3	1	0
3	3	4	4	3	1	1

A – the treated skin showed less elasticity.
B – Treated area showed fissuring of the skin and slight eschar formation.
C – The treated area showed new skin formation and was covered with scales.
D- Approximately 75% of the treated area showed new skin formation and approximately 25% showed scaliness.

Mean individual scores (24, 48 & 72 hour observation)	Erythema: 3.3, 2.7,3.3; Oedema: 3.3, 3.3, 3.3.
Comment:	Topical application resulted in slight eschar formation, fissuring of the skin and severe oedema in all three animals. The effects had not resolved within the study period and very slight oedema was noted in two animals and very slight erythema in all three animals on day 21. No signs of systemic toxicity were observed.
Result:	The notified chemical was a severe skin irritant to rabbit skin

9.1.3 Eye Irritation (RCC NOTOX, 1991a)

Test Substance:	Aminol A15
Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	7 days
Method of administration:	0.1 mL of the notified chemical was placed in the conjunctival sac of the left eye of each rabbit

Test method: OECD TG 405

Draize scores of unirrigated eyes:

	Time after instillation														
Animal	***1 hour***			***1 days***			***2 days***			***3 days***			***7 days***		
Cornea	*All scores were zero*														
Iris															
1		1			0			0			0			0	
2		1			0			0			0			0	
3		1			0			0			0			0	
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	2^S	2^N	1^L	2	1	1	2	1^N	1	1	0	0	0	0	0
2	1	2	1 ^{L}	2	1^N	1	2	1	1	2^S	0	0	0	0	0
3	2	2^S	1^L	2	1	1^L	2	1	2^L	2^S	1	1	0	0	0

[1] see Attachment 1 for Draize scales r=redness c=chemosis d=discharge.

L – lacrimation was observed. N – nictating membrane. S – scleral conjunctivae.

Mean individual scores (24, 48 & 72 hour observation) Corneal opacity: 0, 0, 0;
Iris lesion:0, 0, 0;
Conjunctivae redness: 1.7, 2, 2;
Conjunctivae chemosis: 0.7, 0.7, 1.

Comment: Injection of the iris had resolved by 24 hours and conjunctival irritation had resolved by day 7. No corneal effects were observed.

Result: The notified chemical was a slight to moderate eye irritant in rabbits

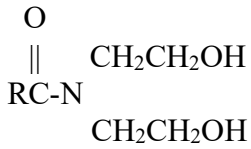
9.1.4 Skin Sensitisation (LPT, 1997)

Test Substance:	Aminol A15
Species/strain:	Guinea pig/Dunkin Hartley
Number of animals:	10 test males, 5 control males
Test method:	OECD TG 406 – Magnusson & Kligman Maximisation Test
Induction procedure:	Day 0 each animal received 2 intracutaneous injections (0.1 mL) in the scapular region: - Freund's Complete Adjuvant (FCA), 1:1 with 0.9% saline; - The test substance 1% in sesame oil; - The test substance in a 1:1 mixture of FCA. Day 7 The same region was treated with 2 mL of the test substance (8% in sesame oil) using the patch-test technique for 48 hours. One animal each from the test and control group died from stress associated with the shaving of the test site after induction. Control animals were treated similarly except that the test substance was substituted by sesame oil.
Challenge procedure:	Day 21 The left flank of each animal was treated with 2 mL of solution (0.8% aqueous hydroxypropylmethyl cellulose gel) containing the test substance (0.1% in sesame oil) under occlusive dressing for 24 hours.
Challenge outcome:	Erythema or oedema was not observed in test or control animals following challenge.
Result:	The notified chemical was non sensitising to the skin of guinea pigs.

9.2 Repeated Dose Toxicity

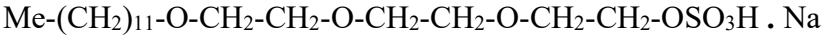
Repeat dose testing has not been performed on the notified chemical. However, in support of their application for a waiver to the Schedule requirements the notifier has submitted repeat dose studies on analogue substances:

- **Cocamide DEA** (CAS # 61791-31-9 & 68603-42-9) (9.2.1) a mixture of ethanolamides of coconut acid. Cocamide is offered as representation of the monoethanolamine moiety of the notified chemical and conforms generally to the formula:



RCO represents the fatty acids derived from coconut oil.

- **Sodium lauryl trioxyethylene sulfate** (CAS # 13150-00-0) (9.2.2) is offered as representing the ethoxylate portion of the notified chemical. Its structural formula is:



9.2.1 13 Week Dermal Repeat Dose Toxicity (Cosmetic Ingredient Review Expert Panel, 1996)

Study 1

Test substance:	Cocamide DEA
Species/strain:	Rats/Fischer 344
Number/sex of animals:	10/sex/dose group
Method of administration:	Topical application of 25, 50, 100, 200 and 400 mg/kg using 95% ethanol vehicle (dose volumes of 30, 61, 121, 243 or 485 mg/mL, respectively) for 13 weeks

Clinical observations:
There were no deaths in experimental or control groups at the end of the study. Group mean body weight depression of greater than 10% were noted in male rats from the 200 mg/kg dose group and male and female rats from the 400 mg/kg dose group. Skin irritation at the application site was observed in 8 females and 10 males from the 200 mg/kg group and all rats from the 400 mg/kg dose group. In the 100 mg/kg dose group, skin irritation was observed in one female and two male rats.

Clinical chemistry/Haematology
The results of haemotological evaluations in this study indicated a reduction in haemoglobin concentration in females from the 200 and 400 mg/kg dose groups and in males dosed with 400 mg/kg. A reduction in the haematocrit was noted in females of the three highest dose groups and in males of the 400 mg/kg dose group. Additionally, the red blood cell count was depressed in females of the 200 and 400 mg/kg dose groups. Perturbations in clinical chemistry values for serum albumin, cholesterol, and triglycerides were also observed in some of the dose groups, suggesting that Cocamide DEA may have an effect on the biochemical/metabolic functions of the liver.

Histopathology:
The principal microscopic skin changes were epidermal hyperplasia (≥25 mg/kg, both sexes), chronic-active inflammation (≥100 mg/kg, both sexes) parakeratosis and ulceration (≥200 mg/kg, both sexes; 100 mg/kg, males), and sebaceous gland hyperplasia (≥100 mg/kg, both sexes; 50 mg/kg, males). Parakeratosis was primarily responsible for the gross changes that were described as "skin crusts".

Renal tubular regeneration and renal mineralisation were noted in all female dose groups. The severity of renal tubule generation was greater in rats of the two highest dose groups (200 and 400 mg/kg), and the severity of renal mineralisation was greater in rats of the three highest dose groups (100, 200, and 400 mg/kg).

There seemed to be a correlation between dose-related increases (≥50 mg/kg) in absolute and relative kidney weights in females and Cocamide DEA-induced changes in the renal tubule.

Study 2

Test substance:	Cocamide DEA
Species/strain:	Mouse/B6C3F_1
Number/sex of animals:	10/sex/dose group
Method of administration:	Topical application of 50, 100, 200, 400, and 800 mg/kg using 95% ethanol vehicle (dose volumes of 20, 40, 80, 160 or 320 mg/mL, respectively) for 13 weeks

Clinical observations:
There were no deaths in experimental or control groups at any time during the study. Skin irritation at the application site was observed in all males and females of the 800 mg/kg dose group; gross skin lesions were noted in six of 10 males and five of 10 females.

Histopathology:
The principal microscopic changes in skin were epidermal and sebaceous gland hyperplasia (≥50 mg/kg, both sexes), chronic-active inflammation (≥200 mg/kg, males; ≥100 mg/kg, females), parakeratosis (≥200 mg/kg, males; ≥400 mg/kg, females), and ulceration (800 mg/kg, both sexes). Parakeratosis was primarily responsible for the gross changes that were described as "skin crusts" in males and females of the 800 mg/kg dose group. Weight increases in the liver, kidney, and lungs that were seen in experimental groups were considered to be treatment-related, but they occurred in the absence of pathological changes. Organ weight changes were present in ≥400 mg/kg dose groups (males) and in ≥200 mg/kg dose groups (females).

Comment –Study 1 and Study 2:
The National Toxicology Program Working Group for Cocamide DEA concluded that the dermal application of the test substance was associated with microscopic lesions in the skin of male and female F334 rats and in the kidneys of female rats. Treatment-related microscopic lesions were observed in the skin of $B6C3F_1$ mice. In rats and mice, the skin lesions tended to have a dose response with regard to the incidence and severity of the changes. Renal tubule regeneration was particularly increased in female rats of the 200 and 400 mg/kg groups.

Based on the above findings, an NTP 2 year chronic study was initiated in 1993 testing doses of ≤100 mg/kg/day in rats and ≤ 400 mg/kg/day in mice. No information in the open literature is available on the status of the 2 year study.

9.2.2.1 Two-Year Repeat Dose Oral toxicity Study Including Two Generation Reproduction Investigation (Tusing, 1962)

Test substance:	Sodium lauryl trioxyethylene sulphate
Species/strain:	Rat/*Carworth Farm 'E'*
Number/sex of animals:	30/sex/group

Study design:
Main Study:
Each group received 0, 0.1% or 0.5% of the test substance daily in the diet for a period of 105 weeks. 10 animals of each group were sacrificed at 52 weeks and the rest at 105 weeks for pathology.

Reproduction Study:
This commenced 14 weeks into the main study using rats from the control and 0.1% treatment group. 10 male and 10 female rats from each group were paired (P_1), then returned to the original study. The 1st generation offspring (F_1) were maintained on the diets assigned to their parents. At approximately 100 days of age the F_1 rats were mated to produce the F_2 generation. The F_2 rats were maintained on the appropriate diet for 5 weeks after weaning at which time they were sacrificed.

Findings:
Main Study:
No adverse effects with respect to survival, growth, food consumption or clinical pathology. Scattered differences were found in organ:weight body ratios. Microscopic evaluation of tissues revealed no pathogenic changes related to treatment.

Reproduction Study:
No adverse effect on fertility, litter size, lactation or survival of offspring. No treatment related changes in blood indices or urine analyses or microscopy in the F_1 and F_2 generations.

9.2.2.2 Skin Tumourigenicity (Tusing, 1962)

Test substance:	Sodium lauryl trioxyethylene sulphate
Species/strain:	Mouse/Swiss
Number/sex of animals:	30 females, control and test groups

Study design:
The test substance was applied twice weekly, in 5% aqueous solution to the clipped skin of the intrascapular region. Two drops (about 0.1mL) were used or each application; this dose represented about 5 mg of chemical. The experiment was conducted for 105 weeks, so that the total quantity of test material was about one gram.

Findings:
No papillomas or other skin tumours were observed in any of the treated animals during the course of the study. Mortality in the experimental groups did not differ substantially from that for control animals.

9.2 Genotoxicity

9.2.1 *Salmonella typhimurium* Reverse Mutation Assay (Toxicol Laboratories Limited, 1987)

Test Substance:	Aminol A15
Strains:	*Salmonella typhimurium* TA 1537, TA 1535, TA 100 & TA 98
Concentration range:	the assay was performed in two independent experiments with or without metabolic activation provided by rat liver S9; the test substance and controls were tested in triplicate at the following concentrations: 0, 8, 40, 200, 1 000 and 5 000 μg/plate
Test method:	Similar to OECD TG 474
Comment:	The test substance was not toxic towards the tester strains at 5 000 μg/plate.

	There were no significant increases in revertant colony numbers at any dose level, either in the presence or absence of metabolic activation.
Result:	The notified chemical was no mutagenic under the conditions of the test.

9.4 Overall Assessment of Toxicological Data

The notified chemical exhibited very low acute oral toxicity (LD_{50} > 5 000 mg/kg) in rats. The notified chemical was a severe skin irritant and a slight to moderate eye irritant in rabbits. It was non sensitising to rabbit skin. No acute inhalation or dermal toxicity studies were provided. Analogue data suggests it would not be readily absorbed into the systemic circulation by the dermal route.

Repeat dose toxicity testing for the notified chemical has not been conducted. However, surrogate data on Cocamide DEA (representing the monoethanolamine moiety of the notified chemical) and sodium lauryl trioxyethylene sulphate (representing the ethoxylate surfactant portion of the notified chemical) was provided.

In 13 week repeat dermal toxicity studies, Cocamide DEA caused dose related microscopic lesions in the skin of mice and rats and in the kidneys of female rats. Given the non ionic surfactant nature of the notified chemical, it is expected that it would also cause severe skin lesions as observed with Cocamide DEA following repeated exposure. The findings from the acute skin irritation studies on the notified chemical support this.

In a 2-year chronic oral (diet) study using sodium lauryl trioxyethylene sulphate, no adverse effects were observed in rats with respect to survival, growth, reproduction, food consumption, or clinical pathology. No treatment related microscopic lesions were observed. Scattered differences were found in organ:body weight ratios. No effects of the substance were observed in first or second generation offspring of the original animals. By analogy the notified chemical would share the same metabolic fate as that of sodium lauryl trioxyethylene sulphate, and therefore share the same low toxicity following oral administration. Twice weekly topical application of 5% aqueous solutions of sodium lauryl trioxyethylene sulphate to skin of female Swiss mice did not lead to the development of skin tumours in any animals.

The notified chemical was found not to be mutagenic by bacterial reverse mutation. No data on clastogenic potential was provided.

According to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999a), the notified chemical meets the criteria for classification as a skin irritant. The overall hazard classification is Irritant (Xi) with risk phrase R38 – Irritating to Skin, assigned.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies have been supplied by the notifier. The tests were carried out according to OECD Test Guidelines (TG).

Test	*Species*	*Concentrations[a] (mg/L)*	*Results (Nominal) mg/L*
96 h Static Acute Toxicity	*Leuciscus idus melanotus* (Golden Ide)	2, 3, 4	$2 < LC_{50} < 4$ NOEC $\leq$ 1
48 h Acute Immobilisation	*Daphnia magna*	0, 0.125, 0.25, 0.5, 1, 2, 4, 8, 16	$0.5 < EC_{50} < 2$ NOEC $\leq$ 0.5
Inhibition of Algal Growth	*Scenedesmus subspicatus*	0, 0.125, 0.25, 0.5, 1.0, 2.0	E_bC_{50}(72 h) = 2.0 E_rC_{50}(72 h) > 2.0

[a] Nominal concentrations.

10.1 Acute Toxicity – Fish (Institut Fresenius, 1991b)

This test was undertaken according to OECD TG 203. After 96 hours, 20% mortality was observed at both 2 and 3 mg/L test level and 100% mortality was observed at the highest test level (4 mg/L) after 24 h. Hence the LC_{50} is likely to be between 2 and 4 mg/L. The test laboratory indicated that the LC_{50} value (3 mg/L) was determined by probit analysis. However, because of an absence of control data (0.0 mg/L) and a "no effect" concentration (i.e. 20% mortality at the lowest concentration of 2 mg/L), confirmation by probit analysis is precluded.

10.2 Acute Toxicity – Invertebrates (Institut Fresenius, 1991a)

The test for Acute Toxicity on daphnia was undertaken according to OECD TG 202 I (Acute Immobilisation). At a concentration of 4 mg/L and above, 100% immobilisation was observed after 24 h in the daphnia test. No immobilisation was observed at 0.5 mg/L and below. After 24 h, 50% immobilisation was observed at 2 mg/L, increasing to 100% by 48 h. At 1 mg/L, 40% immobilisation was observed after 48 h. Hence, the EC_{50} is between 0.5 and 2 mg/L. A more accurate estimate such as by use of probit analysis is precluded as immobilisation between 0 and 100% was only observed at one concentration.

Daphnia chronic toxicity data was not provided by the notifier on the basis that the notified chemical is readily biodegradable. The notified chemical does not meet the criteria for ready biodegradation as required by OECD TG 301E. However, this assessment accepts that the notified chemical should be extensively biodegraded over time.

10.3 Chronic Toxicity – Alga (Institut Fresenius, 1998)

This test was conducted according to OECD TG 201. The toxic effect was investigated by determination of the inhibition of the biomass production and the growth rate of the algae after an exposure period of 72 hours. Under the conditions being tested a NOEC and 100% inhibition could not be determined. The algal inhibition of growth rate to 50% (E_rC_{50}) was estimated by extrapolation of the concentration/response compared to the control. A single Guideline variation occurred whereby the concentration of $NaHCO_3$ used in the nutrient medium was doubled from that indicated in the Guideline.

10.4 Conclusion

The ecotoxicity data for the notified chemical indicate that chemical is moderately toxic to fish and algae and moderately to highly toxic to daphnids. This is supported by calculated acute ecotoxicity data (LC_{50}) sourced from the USEPA ASTER Database (see below). The reported LC_{50} for the most sensitive species (rainbow trout) was 1.09 mg/L indicating that the notified chemical is moderately toxic to fish.

Calculated acute ecotoxicity data (LC_{50}) sourced from the USEPA ASTER Database

Water Flea (*Daphnia magna*)	1.87 mg/L
Blue gill (*Lepomis macrochirus*)	2.45 mg/L
Fathead minnow (*Pimephales promelas*)	2.93 mg/L
Channel catfish (*Ictalurus punctatus*)	1.27 mg/L
Rainbow trout (*Oncorhynchus mykiss*)	1.09 mg/L
Calculated chronic data are only available for Fathead minnow (*Pimephales promelas*)	85 µg/L

The ecotoxicity predictions for fish and daphnids above are within the range reported by the notifier.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The vast majority of notified chemical will be discharged to sewer through product use. The notifier has provided a predicted environmental concentration (PEC) based on likely levels of use.

As the product will be used throughout the country and sent to sewage treatment plants in both city and country locations, this assessment has calculated a PEC based on continental use at the maximum projected level of use:

Maximum Import Volume per annum:	10 000 kg
Amount discharged to sewer:	100%
Volume discharged per day:	27 kg
Sewer output per day*:	2 700 ML
Concentration in Sewage Treatment Plant:	10.15 µg/L
Concentration in sewage after 20 % (estimated) adsorption to sewage sludge:	8.12
Further diluted (1:10) in receiving waters:	0.81 µg/L
Safety Factor (Daphnia EC_{50}(48 h) = 0.5 mg/L):	616

*Sewer output based on an Australian population of 18 million, each using 150 L water per day.

The Safety Factor for this chemical, using the lowest estimate for the most sensitive species (*Daphnia magna)* and the PEC is considered narrow and indicates that the notified chemical poses a potential environmental hazard. However, the percentage of the notified chemical adsorbing to sewage sludge may be higher than the 20% estimated in the PEC. This, together with the conservative estimate of household sewage output and the inherently biodegradable nature of the notified chemical may considerably diminish the risk associated with its use up to the maximum levels proposed.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical is of very low acute oral toxicity in rats, a slight to moderate eye irritant and a severe skin irritant in rabbits, but not a skin sensitiser in rabbits. No acute dermal or inhalation toxicity studies were provided. Repeat dose toxicity testing for the notified chemical was not conducted. However, surrogate data on Cocamide DEA and sodium lauryl trioxyethylene sulphate was provided. Cocamide DEA caused dose-related microscopic lesions in the skin of mice and rats and in the kidneys of female rats in a 13 week repeat dermal toxicity study. In a 2-year chronic oral study (which included a 2-generation reproduction component) using sodium lauryl trioxyethylene sulphate, no adverse effects were observed. Twice weekly topical application of sodium lauryl trioxyethylene sulphate did not induce skin tumours in female mice. The notified chemical was not mutagenic in bacteria. Investigations into clastogenicity have not been conducted.

Based on the data supplied, and in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999a), the notified chemical meets the criteria for classification as a skin irritant. The overall hazard classification is Irritant (Xi) with risk phrase R38 – Irritating to Skin, assigned.

Occupational Health and Safety

During importation and transportation of the notified chemical, there is unlikely to be any worker exposure, except in the event of a spill. Exposure after a spill can be minimised by the use of the recommended practices for spillage clean up given in the Material Safety Data Sheet (MSDS) supplied by the notifier.

Worker exposure may occur to the notified chemical during blending operations. There is potential for ocular and dermal contact and to a lesser extent inhalation exposure during manual dispensing of the product containing the notified chemical to the blender and mixing. Should dermal or ocular contact occur, the notified chemical is unlikely to cause systemic toxicity, however there is a risk of eye irritation and possibly slight skin irritation. Workers will need to be protected by personal protective equipment (goggles, gloves and overalls), and the presence of effective engineering controls, for example, closed mixer and local exhaust ventilation. In addition, the notifier stated that the workers involved will receive education and training on safe use of the notified chemical and preventive controls.

General ventilation in the storage, sampling and packaging areas, local exhaust ventilation over the dispensing and mixing areas and a fume hood in the laboratories are employed to control exposure to the notified chemical and therefore minimise the risk of irritant effects.

Should the end-use products containing the notified chemical be used by professional hairdressers, the risk of skin irritation arising from exposure to the notified chemical is low due to the low concentration (10%) in finished products. However, it cannot be excluded, particularly as hairdressers by occupation are likely to have a compromised skin barrier function. Professional hairdressers may experience occasional eye splashes. They may suffer transient eye irritation but at less than 10% concentration in the products or mixtures, the risk of severe eye irritation is low.

Public Health
As the notified chemical will be used in hair dye products, there will be widespread public exposure. The notified chemical is a severe skin irritant and a slight to moderate eye irritant. Consequently, Aminol A15 is to be proposed for scheduling by the National Drugs and Poisoning Scheduling Committee (NDPSC).

13. RECOMMENDATIONS

Occupational Health and Safety

To minimise occupational exposure to Aminol A15 the following guidelines and precautions should be observed:

Formulators:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);
- Industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.1 (Standards Australia, 1990);
- Impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia, 1998);
- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994);
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;

Hairdressers:

Hairdressers are encouraged to consult guidance documents for identifying and managing health risks in hairdressing that have been published by some state occupational health and safety authorities (Division of Workplace Health and Safety, 1994), (WorkCover Corporation, 1996), (WorkCover NSW, 1997). The notifier should advise the hairdressing industry of the availability of state government publications in addition to any current industry codes;

All workers:

- Good occupational hygiene should be practised to minimise the potential for skin and eye contact and ingestion. In addition, there should be prompt removal of skin and eye contaminants; and

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

Public Health

If the conditions of use are varied with greater exposure to the public further information will be required to assess the hazards to public health.

The public health assessment has recommended that Aminol A15 be considered for scheduling by the NDPSC.

14. MATERIAL SAFETY DATA SHEET

The MSDS for Aminol A15 was provided in accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994).

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

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise.

Under Section 64(1) of the Act, should the notified chemical be introduced or likely to be introduced at a volume greater than 10 000 kg per annum, the Director is to be advised within 28 days and both a water solubility test and a *Daphnia* sp reproduction test need to be submitted for assessment.

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Attachment 1

The Draize Scale for evaluation of skin reactions is as follows:

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

The Draize scale for evaluation of eye reactions is as follows:

CORNEA

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

CONJUNCTIVAE

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

IRIS

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