File No: NA/897

November 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Escalol HP 610

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Director
Chemicals Notification and Assessment

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FULL PUBLIC REPORT

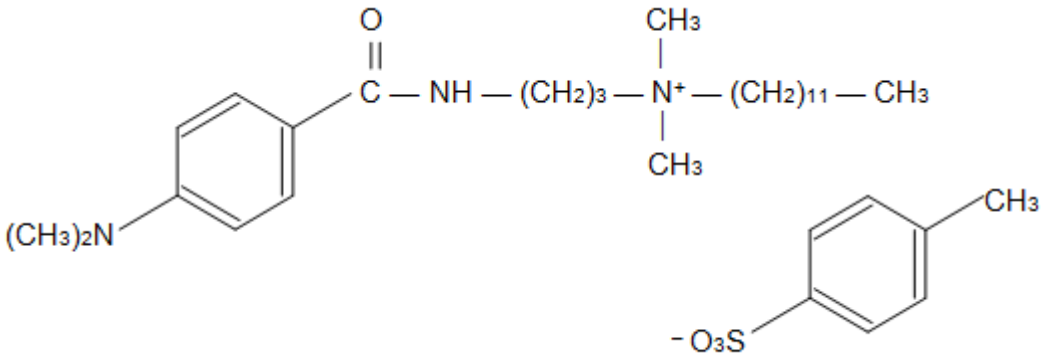
Escalol HP 610

1. APPLICANT

ISP (Australasia) Pty Ltd (ACN No.: 000 011 923) of 73 – 75 Derby St SILVERWATER NSW 2141 has submitted a standard notification statement in support of their application for an assessment certificate for Escalol HP 610 and has not applied for any information relating to Escalol HP 610 to be exempt from publication in the Full Public Report and Summary Report.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	1-dodecanaminium, N-[3-[[4-(dimethylamino) benzoyl]amino]propyl]-N,N-dimethyl-, salt with 4-methylbenzenesulfonic acid (1:1)
Chemical Abstracts Service (CAS) Registry No.:	156679-41-3
Other Name:	DDABDT
Marketing Name:	Escalol HP 610
Molecular Formula:	$C_{26}H_{48}N_3O^+.C_7H_7SO_3^-$
Structural Formula:	



Molecular Weight:	589 (typical)
Method of Detection and Determination:	Infrared (IR) spectroscopy, assay of cationic surfactants.
Spectral Data:	An IR spectrum was provided.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Light creamy waxy solid with intermittent crystals.
Boiling Point:	> 280°C
Specific Gravity:	1.14
Vapour Pressure:	< 4.5×10^{-6} kPa
Water Solubility:	164 mg/L at 20°C
Partition Co-efficient (n-octanol/water):	log P_{ow} approximately equal to 2
Hydrolysis as a Function of pH:	Determined – See comments below.
Adsorption/Desorption:	Not determined – See comments below.
Dissociation Constant:	Not determined – See comments below.
Flash Point:	Not determined.
Flammability Limits:	Not determined.
Autoignition Temperature:	Not determined.
Explosive Properties:	Not determined.
Reactivity/Stability:	Stable under normal conditions.

3.1 Comments on Physico-Chemical Properties

The water solubility was determined using a modified flask method described in OECD TG 105 (CHE, 1996a). Six samples were prepared by adding an excess of the notified chemical to double distilled water (25 mL). Pairs of closed flasks were stirred at 30°C for 24, 48 and 72 h, then equilibrated at 20°C for 24 h. An aliquot (1.5 mL) of each solution was removed and centrifuged and a sample was removed for analysis by HPLC. This method indicated that the solubility of the notified chemical is 164 mg/L.

The abiotic degradation of the notified chemical was investigated over five days at 50°C at pH 4, 7 and 9 using OECD TG 111 (CHE, 1996b). A quantity of the notified chemical was added to the each of the buffered solutions such that its final concentration was 82 microgram/mL. The resulting solutions were sampled at 0, 1, 2, 3, 4, 24, 48, 72, 96 and 120 hours. At these times an aliquot was removed for analysis by HPLC. The notifier indicates that there was no clear evidence of hydrolytic loss of the notified chemical observed over the five day period. The notified chemical contains an 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 based on the above.

The partition coefficient has not been determined due to the surface activity of the notified chemical. However, the notifier expects the notified chemical to have a partition coefficient of approximately log 2, which is indicative of a hydrophilic compound likely to partition mainly into the aqueous phase.

No adsorption/desorption tests were conducted presumably because the notified chemical is surface active. It is known that dissolved organic carbon from soils and sediment binds to cationic chemicals, neutralising the positive charge and removing it from the aquatic compartment making the substance less bioavailable and less toxic to aquatic organisms (Nabholz et al., 1993). Although the notified chemical is water soluble, as a consequence of its cationic nature, it is expected to associate with the soil and sediments.

Although no dissociation tests were conducted, the notified chemical will remain fully dissociated due to the quaternary ammonium group.

4. PURITY OF THE CHEMICAL

Degree of Purity: 65 - 75%

Hazardous Impurities: None.

Non-hazardous Impurities (> 1% by weight): Water (14 – 15%) in addition to the following:

Chemical Name	*CAS No.*	*Weight %*
propylene glycol stearate	142-75-6	8 –10%
dodecyl alcohol	121-53-8	3% (max.)
N-3-dimethylaminopropyl-p-dimethylaminobenzamide		6%

Additives/Adjuvants:

Chemical Name	*Weight %*
isopropylparaben	0.16%
isobutylparaben	0.12%
butylparaben	0.12%

5. USE, VOLUME AND FORMULATION

The notified chemical is a component in cosmetic formulations used at up to 2% in a range of products. Up to 1 tonne will be imported per year for the first five years in 22.7 kg polyethylene buckets. Two customers have been identified, one producing a reactive hair dye containing the notified chemical at 0.7% and the other a simple hair conditioner containing the notified chemical at a maximum of 1%.

6. OCCUPATIONAL EXPOSURE

At each premises where the notified chemical is to be formulated the number and category of workers and duration of exposure is as follows: 2 storemen, 2 QC personnel (2 hours/day, 12 times per year exposure to the raw material; 1 hour per day, 200 days per year to the finished cosmetics), 2 plant operators (2 hours per days, 200 days per year to the raw material), 10 packers (8 hours per day, 200 days per year to the finished cosmetics) and 2 product development personnel (2 hours per day, 12 days per year to the raw material).

Exposure of workers involved in transport and storage of the imported polyethylene containers is unlikely. Even in the event of rupture of the containers the notified chemical is unlikely to be released as it is a waxy solid and needs to be melted prior to addition to mixing vessels.

The notified chemical is melted prior to weighing manually into polypropylene containers prior to addition to 2000 kg mixing vessels in each of the two product manufacturers.

For the hair colourant, the notified chemical is weighed into a 100 kg polypropylene drum containing diluents and solubilisers which is then raised on a pallet to the rim of the mixing vessel and the contents added through an open stopcock for approximately 30 minutes. Worker exposure is expected to be mainly dermal and workers wear full personal protective equipment during these operations. For the hair protectant, the notified chemical is weighed into a polypropylene buckets which is raised on a pallet to the rim of the mixing vessel by a pallet jack. The contents of the bucket are then added to the mixing vessel manually. Worker exposure is controlled by the use of overalls, industrial safety shoes, facemask and gloves.

Quality control sampling is conducted for both the hair colourant and the hair conditioner from the mixing vessels. For the hair colourant a 30 cm sampling ladle is used deliver a sample to a screw top bottle. For the hair protectant a 1 m long sampling rod with a sampling cup is used to pour a sample to a screw top bottle. The notified chemical is contained in the formulations at a maximum concentration of 2% so that worker exposure to the small samples should be minimal.

The hair colourant is automatically packed into 60 gm tubes and the hair conditioner into 125 mL bottles. Worker exposure is unlikely during these processes.

The notifier states that owing to the high cost of the notified chemical very little is left in the drums for removal by the waste contractor.

Cleaning and maintenance of equipment and lines should result in little worker exposure due to the low concentration of the notified chemical in the residues and in the wash solutions.

End use of the hair colourant is by the general public. End use of the hair conditioner is not specified but, if used in hair salons, worker exposure is expected to be minimal given the low concentration of the notified chemical.

7. PUBLIC EXPOSURE

Members of the public may be exposed to the notified chemical following transport accidents involving breakage of the containers carrying the undiluted solid or the finished hair care products. Such accidents are unlikely. It is also unlikely that public exposure to waste notified chemical will occur.

Consumers who purchase and use the finished hair care products containing the notified chemical will be exposed to it. The degree and type of exposure may vary depending on the frequency of application, the care taken with applications, the amount of hair care product applied on any occasion and the frequency of hair washing. However the low concentration of the notified chemical in the finished products indicates that public exposure is likely to be minimal.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

During formulation of the hair care products the notifier estimates that up to 0.65% per annum of notified chemical will be released into the environment as a result of spills and equipment cleaning. This equates up to 6.5 kg per annum.

Machinery and pumping equipment will be cleaned with alcohol and waste from this process will be incinerated by licensed hazardous waste contractors. Subsequent water washes will passed to bulk storage where the settled material will be collect and disposed of in landfill while wastewater will be released into the sewer.

It is expected that the plastic import drums containing residual polymer solution will be either incinerated or cleaned and the plastic recycled. The 60 g tubes and 125 mL bottles in which the hair product will be sold to consumers and the residues they contain (0.0035 g and 2 mL, respectively) will be disposed of in domestic landfill.

The majority of the notified chemical will be incorporated into hair products and as such will almost completely be released to the environment.

8.2 Fate

The notifier indicates that empty drums and their residues will be sent to licensed drum disposal contractors and either destroyed by high temperature incineration or cleaned and the plastic containers recycled. Incineration of the notified chemical will result in the formation of water vapour and oxides of carbon and nitrogen. Presumably, wastes resulting from the cleaning process will be released into the sewer.

The majority of the notified chemical will be released into the sewer following washing of hair. Here, despite its water solubility, the notified chemical is expected to adsorbed to sediments and be immobile due to its cationic nature. In landfill, the notified chemical is not expected to escape from the 60 g tubes and 125 mL bottles, however, if it did it would also adsorbed to soil and be immobile.

The notifier has provided the results of a ready biodegradation test in an aerobic aqueous media following OECD TG 301B (CHE, 1997a). The biodegradation was determined by the measurement of dissolved organic carbon produced after the medium was inoculated with a mixed population of aquatic microorganisms and stored in the dark at 22ºC for 28 days. Sodium benzoate was used as the standard material. The results indicated that 42% of the notified chemical had degraded over this time, while approximately 85% of the standard degraded in 28 days. The results indicate that notified substance is not readily biodegradable as less than 70% had degraded within 10 days of 10% having been reached. However, a reasonable degree of biodegradability may be predicted in water and soils from this stringent test.

It should not bioaccumulate as the chemical is water soluble with a low log P value (Connell 1990).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Escalol HP 610

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	$LD_{50} > 5000$ mg/kg	MB Research (1994a)
acute dermal toxicity	rat	$LD_{50} > 2000$ mg/kg	MB Research (1994b)
skin irritation	rabbit	slight irritant	MB Research (1994c)
eye irritation	rabbit	severe irritant	MB Research (1994d)
skin sensitisation	human	not sensitising	Clinical Research Laboratories (1996)
phototoxicity/ photoallergy	human	not phototoxic, not photoallergenic	Clinical Research Laboratories (1995)

9.1.1 Oral Toxicity (MB Research, 1994a)

Species/strain:	rat/Wistar.
Number/sex of animals:	5/sex.
Observation period:	14 days.
Method of administration:	Oral (gavage) at 5000 mg/kg; vehicle: distilled water.
Test method:	TSCA 40 CFR 798.1175.
Mortality:	1 female on day 6.
Clinical observations:	Chromorhinorrhea (red nasal discharge), diarrhoea, chromodacryorrhea (red lacrimation) , emaciation, alopecia, brown staining of the body areas and soiling of the anogenital area in all animals.
Morphological findings:	Necropsy of the dead animal revealed abnormalities of the liver and gastrointestinal tract. Necropsy results of survivors were normal, except for alopecia in females.
LD_{50}:	> 5000 mg/kg.
Result:	The notified chemical was of very low acute oral toxicity in rats.

9.1.2 Dermal Toxicity (MB Research, 1994b)

Species/strain:	rabbit/New Zealand White (NZW).
Number/sex of animals:	5/sex.
Observation period:	14 days.
Method of administration:	Paste made with distilled water was applied under occlusive dressing for 24 hours; dose 2000 mg/kg.
Test method:	TSCA 40 CFR 798.1100.
Mortality:	1 female died on day 13.
Clinical observations:	Diarrhoea in the dead female. Signs in survivors were lethargy, diarrhoea, yellow nasal discharge, few faeces and soiling of the anogenital area.
Morphological findings:	Necropsy of the dead animal revealed abnormalities of the lungs, liver, kidneys and gastrointestinal tract. Surviving animals demonstrated abnormalities of treated skin, kidneys and G I tract. One survivor was normal.

Draize scores:

Time after treatment (days)	***animal 1***	***2***	***3***	***4***	***5***
Erythema					
1 (males)	[a]2	2	2	3	2
1 (females)	2	2	1	2	1
7 (males)	2f	2f	1f	2f	2f
7 (females)	3	0	0	2	0
14 (males)	0f	0f	0	0	1f
14 (females)	1	0	0	1	dead
Oedema					
1 (males)	2	1	2	2	2
1 (females)	2	1	0	2	1
7 (males)	0	0	0	1	1
7 (females)	0f	0	0	0f	0
14 (males)	0	0	0	0	0
14 (females)	0f	0	0f	0f	dead

[a] see Attachment 1 for Draize scales; f = flaky skin

LD_{50}: > 2000 mg/kg.

Comment: The notified chemical appears to be a slight to moderate skin irritant in rabbits.

Result: The notified chemical was of low acute dermal toxicity in rabbits.

9.1.3 Inhalation Toxicity

Data not provided.

9.1.4 Skin Irritation (MB Research, 1994c)

Species/strain: rabbit/NZW.

Number/sex of animals: 1 male, 5 females.

Observation period: 72 hours.

Method of administration: 0.5 g of the test substance was applied under a semi-occlusive gauze dressing for 4 hours.

Test method: TSCA 40 CFR 798.4470

Comment: Draize scores were zero for erythema or oedema at 1, 24, 48 and 72 hours post-treatment except for slight erythema (grade 1) in one female at 24 hours and 2 females at 1 hour.

Result: The notified chemical was slightly irritating to the skin of rabbits.

9.1.5 Eye Irritation (MB Research, 1994d)

Species/strain: rabbit/NZW.

Number/sex of animals: 1 male animal tested with undiluted substance; 6 females treated with a 3% suspension of the test substance in propylene glycol (only the data for 3 of the females were included in the report).

Observation period: 72 hours.

Method of administration: 0.1 mL of the test substance into 1 eye with the other eye serving as control.

Test method: TSCA 40 CFR 798.4500

Draize scores:

Animal	***1 hour***			***1 day***			***2 days***			***3 days***		
Cornea	no corneal effects											
Iris	no iridal effects											
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	1	2	2	2	2	2	0	0	0	0	0	0
2	1	2	2	1	1	1	1	0	0	0	0	0
3	1	2	2	2	2	2	1	0	0	0	0	0

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

Individual Mean Scores: redness: 0.67 : 0.67 : 1
chemosis: 0.67 : 0.34 : 0.67
discharge: 0.67 : 0.34 : 0.67

Comment: Corneal opacity, iritis and severe conjunctival irritation were observed in the male animal treated with undiluted test substance and the study was terminated after 1 day because of the severity of the reactions. At 1 hour post-instillation mild corneal opacity (grade 2), slight iritis (grade 1) and

	moderate conjunctival effects (redness, grade 2; chemosis, grade 3; discharge, grade 2) were observed; at 1 day swelling precluded corneal and iridal observations but conjunctival redness and discharge were moderate (grade 2). As a result observations were not continued.
Result:	The notified chemical was severely irritating to the eyes of rabbits. A 3% solution of the notified chemical was a slight to moderate irritant to the eyes of rabbits.

9.1.6 Repeat Insult Patch Test (Clinical Research Laboratories, 1996)

Species/strain:	human.
Number of humans:	102 panellists completed the study.
Induction procedure:	A 10% solution of the test substance in mineral oil was applied under a semi-occlusive patch to the upper back for 24 hours. Patches were applied to the same site on Monday, Wednesday and Friday for a 3-week induction period. Sites were graded for irritation/sensitisation 24 & 48 hours after patch removal.
Challenge procedure:	Following a 2-week rest period, challenge patches were applied to previously untreated sites on the back for 24 hours. Test sites were evaluated on patch removal and 48 and 72 hours later.
Test method:	Not specifically stated in the report.
Comment:	No dermal reactions were noted in the challenge phase of the study.
Result:	The notified chemical was not sensitising to the skin of humans and no clinically significant irritation was observed.

9.1.6 Phototoxicity and Photoallergy Test (Clinical Research Laboratories, 1995)

Species/strain:	human.
Number of humans:	29 panellists completed the photoallergy study and a subgroup of 10 panellists completed the phototoxicity study.
Photoallergy test induction procedure:	0.2 mL of a 10% solution of the notified chemical in mineral oil was applied to duplicate test sites on the back for 24 hours under semi-occlusive dressing. One site was irradiated with twice the panellists minimal erythemal dose of short wave UV (UVB). The remaining site served as control. The procedure was carried out twice weekly for a total of six applications. Test and control sites were evaluated 24 hours after irradiation.

Challenge procedure:	Approximately 2 weeks following the last application, identical patches were applied to sites previously unexposed to the test substance. Twenty-four hours later the patches were removed and one test site was irradiated with a non-erythrogenic dose of UVA radiation equivalent to approximately 10 J/cm^2. An additional untreated site was also irradiated. The challenge sites were graded 24, 48 and 72 hours after irradiation.
Phototoxicity:	0.2 mL of a 10% solution of the notified chemical in mineral oil was applied to a site on the back for 24 hours under semi-occlusive dressing. This site and an untreated site were irradiated with long wave UV at a dosage of approximately 10 J/cm^2. Treated and control sites were graded 24 and 48 hours later.
Test method:	Not specifically stated in the report.
Comment:	No visible skin reactions were observed in either test.
Result:	The notified chemical was neither photoallergic nor phototoxic to human skin.

9.2 Repeated Dose Toxicity (Safepharm Laboratories, 1997)

Species/strain:	rat/Sprague-Dawley.
Number/sex of animals:	5/sex/dose group.
Method of administration:	Oral (gavage) for 28 consecutive days; vehicle: 1% carboxy methylcellulose.
Dose/Study duration:	Doses of 0, 15, 150 and 1000 mg/kg/day for 28 days.
Test method:	67/548/EEC (method B7)

Clinical observations/Bodyweights/Food and Water consumption

Transient increased salivation approximately 3 minutes after dosing was observed in the mid dose group from day 11 and in the high dose group from day 5 followed by more prolonged increased salivation up to one hour after dosing. The only other clinical signs were in the high dose group and were red/brown staining of the external body surface, fur wetting, noisy respiration and incidents of hunched posture, distended abdomen, pallor of the extremities, dehydration, tiptoe gait, fur loss, pilo-erection, diarrhoea and vocalisation as the study progressed. Laboured respiration and/or gasping and decreased respiratory rate were observed mainly in one male and one female.

Bodyweight gain was reduced in males of the high dose group throughout the study correlated with reduced food consumption by 20%, 13% and 9% in weeks 1, 2 and 3,

respectively, compared with controls.

Water consumption was elevated in males and females of the high dose group as measured from day 15 onwards.

Clinical chemistry/Haematology

Clinical chemistry

High dose animals exhibited elevated aspartate aminotransferase (ASAT) and alanine aminotransferase and mid dose males exhibited elevated ASAT. These changes were considered to be toxicologically significant but had no histopathological correlate.

High dose males exhibited a statistically significant increase in albumin/globulin ratio within the normal range and a reduction in alkaline phosphatase and chloride concentration in the absence of changes in other electrolytes. High dose females exhibited an elevated inorganic phosphorus concentration but no change in calcium concentrations. These changes were considered to be of no toxicological significance.

Haematology

Slight increases in erythrocyte count, haematocrit and platelet count were observed in males of the high dose group but these were not considered toxicologically relevant and the minimal increase in erythrocyte numbers was insufficient to suggest a polycythaemia. Other statistically significant changes were either sporadic or not dose-related.

Organ weights/Macroscopic findings

Organ weights

High dose animals exhibited increased absolute and relative (to bodyweight) adrenal weights which were considered to be toxicologically significant. High dose males exhibited a reduction in absolute liver weights but not relative liver weights. Therefore these changes were not considered to be toxicologically relevant. A reduction was observed in absolute brain weights and reduced (in males) brain and testes weights relative to body weight in high dose males considered to be related to reduced bodyweight gain. High dose animals exhibited reduced heart weight relative to bodyweight and mid and high dose males exhibited reduced absolute heart weight but these changes had no histopathological correlates. Elevated absolute and relative ovary weights were observed in high dose females and elevated absolute ovary weights in mid dose females. The intergroup differences were small and considered to be fortuitous.

Macroscopic findings

Two males and three females in the high dose group exhibited signs of gastric irritation, viz., pallor, thickening and/or ulceration of the non-glandular gastric epithelium and one male exhibited a fluid-filled gastrointestinal tract.

Histopathology

Treatment-related gastric changes were observed in high dose animals. Epithelial acanthosis, hyperkeratosis, subepithelial inflammatory cell infiltrates, ulceration and erosion were observed in the forestomach.

Reduced secretory contents observed in the seminal vesicles of three high dose males were probably the result of poor nutritional status.

All other changes were not toxicologically significant.

Comment

In high dose animals the increased salivation from day 5 onwards succeeded by red/brown fur staining, fur wetting and noisy respiration were characteristic of oral administration of an irritant substance. Increased water consumption, clinical signs and both the macroscopic and microscopic findings supported this view. Elevated adrenal weights, although treatment-related, had no histopathological correlates and the cause was not clearly established. Elevated ASAT and alanine aminotransferase in high dose animals also had no histopathological correlates and the precise aetiology could not be determined.

Mid dose animals exhibited transient increased salivation from day 11 and males exhibited increased ASAT. The effects were considered to be minimal.

Result

The NOEL was determined to be 15 mg/kg/day for 28 days. The effects at 150 mg/kg/day were considered not to be serious damage to the health of the animals and represents the NOAEL.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Corning Hazelton, 1996)

Strains:	TA 1535, TA 1537, TA 1538, TA 98, TA 100.
Metabolic activation:	S9 fraction from Aroclor 1254-induced Sprague-Dawley rat liver.
Concentration range:	1, 5, 10, 50, 100 and 500 microgram/plate (+S9); 0.5, 1, 5, 10, 50, 100 microgram/plate (-S9).
Test method:	OECD TG 471
Comment:	The background lawn was slightly and moderately reduced at 50 and 100 microgram/plate, respectively in the absence of S9 and severely reduced at 500 microgram/plate the presence of S9.
Result:	The notified chemical was non mutagenic under the conditions of the test.

9.3.2 Chromosomal Aberration Assay in Human Lymphocytes (CHE, 1997b)

Cells: human lymphocytes from males used in experiment 1 and from females in experiment 2.

Metabolic activation system: S9 fraction from Aroclor 1254-induced rat liver.

Dosing schedule:

Metabolic Activation	***Experiment Number***	*Test concentration (μg/mL)*	*Controls*
-S9	1	treatment time = 20 hours = harvest time; doses*: 0, 49.41, 70.59 and 100.8 microgram/mL	Positive: NQO (2.5 microgram/ mL)
	2	treatment time = 20 hours = harvest time; doses*: 0, 52.43, 65.54 and 81.92 microgram/mL	Negative: solvent control (DMSO)
		treatment time = 44 hours = harvest time; doses*: 0 and 65.54 microgram/mL	
+S9	1	treatment time = 3 hours, harvest time = 20 hours; doses*: 0, 159.4, 177.1 and 196.8 microgram/mL	Positive: cyclophosphamide (25 microgram/ mL)
	2	treatment time = 3 hours, harvest time = 20 hours; doses*: 0, 170, 180 and 190 microgram/mL	Negative: solvent control (DMSO)
		treatment time = 3 hours, harvest time = 44 hours; doses*: 0 and 190 microgram/mL	

NQO – 4-nitroquinoline-1-oxide
CP - cyclophosphamide
DMSO – dimethylsulphoxide
* doses selected for metaphase analysis

Test method: OECD TG 473

Comment: A single statistically significant increase above control values was observed in experiment 1 (-S9) at 70.59 microgram/mL for chromosomal aberrations excluding gaps. However, the lack of a dose response suggests this to be a fortuitous result.

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

9.4 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity in rats (LD50 > 5000 mg/kg) and low dermal toxicity (LD50 > 2000 mg/kg) in rabbits. The notified chemical was a slight skin irritant in rabbits and, at the least, a severe eye irritant in rabbits. The notified chemical was negative in a human repeat insult patch test, human photoallergy and human phototoxicity tests and was neither mutagenic in bacteria nor clastogenic in human lymphocytes.

The notified chemical did not exhibit appreciable organ toxicity in a 28-day repeated dose toxicity study in rats. The NOEL was 15 mg/kg/day and the NOAEL, 150 mg/kg/day.

The notified chemical is determined to be a hazardous substance in accordance with NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999) and is assigned the risk phrase R41: risk of serious damage to eyes.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Full test reports on the ecotoxicity studies for notified substance were provided by the notifier. The authors of the studies indicate that the ecotoxicity tests were conducted on a 80.5% w/w preparation of the notified chemical in propylene glycol, however, the notifier indicates that the percentage of the notified chemical was 85%.

Test	***Species***	***Results***
96 h Acute Toxicity OECD TG 203	Rainbow Trout *Oncorhynchus mykiss*	LC_{50} = 10.7 mg/L
48 h Acute Toxicity OECD TG 202	*Daphnia magna*	EC_{50} = 0.57 mg/L
72 h Growth Inhibition OECD TG 201	Algae *Selenastrum capricornutum*	E_bC_{50} = 0.064 mg/L E_rC_{50} = 0.234 mg/L NOEC = 0.016 mg/L
Inhibitory Effect OECD TG 209	Activated Sewerage Sludge	EC_{50} (3 h) = 109 mg/L

* NOEC - no observable effect concentration

The tests on fish (CHE, 1997c) were performed using a static methodology. Observations were performed at 1, 24, 48, 72 and 96 hours. The test was performed using seven specimen fish per loading rate at a temperature of 14ºC. The tests were conducted using Escalol HP-610 made up at nominal concentrations of 6.25, 12.5, 25, 50 and 100 mg/L prepared from the serial dilution of a stock solution. Analysis of the test solutions at 0, 24 and 96 h found measured concentrations of Escalalol HP-610 ranged from 5.517 – 72.498 mg/L. The results of the definitive study showed that sub-lethal effects such as swimming abnormally and lying on the bottom of the test vessel were experienced at nominal concentrations of 6.25 and 12.5 mg/L. After 96 h, 43% mortality was observed at a test substance concentration of 12.5 mg/L and 100% mortality was observed at nominal concentrations above 25 mg/L. The 96-hour

LC_{50} for the notified chemical to *Oncorhynchus mykiss* is 10.7 mg/L and were based on mean measured concentrations in the test media.

The immobilisation tests with daphnia (CHE, 1997d) were also performed under static conditions with observations performed at 24 and 48 hours. The test was performed in quadruplicate using 5 daphnids per flask at a temperature of 21ºC. The tests were conducted with Escalalol HP-610 made up at nominal concentrations of 0.63, 1.3, 2.5, 5.0 and 10 mg/L. Analysis of the test solutions at 0 and 48 h found measured concentrations of Escalalol HP-610 ranged from 0.338 – 8.827 mg/L. After 48 h, 100% immobilisation was observed at nominal test concentrations above 1.3 mg/L. The 48-hour EC_{50} for the notified chemical to *Daphnia magna* is 0.57 mg/L and were based on mean measured concentrations in the test media.

Algae were exposed to the test substance at nominal concentrations of 0.0078, 0.016, 0.031, 0.063 and 0.13 mg/L for 72 h at 24˚C under constant illumination and shaking (CHE, 1997e). Both biomass and growth rate of *Selenastrum capricornutum* was adversely affected by the test substance, giving a 96 h E_bC_{50} of 0.064 mg/L, E_rC_{50} of 0.234 mg/L and NOEC of 0.016 mg/L based on initial measured concentrations of which only the highest two could be determined. At 72 h all were below the level of quantification except at the highest exposure concentration. Analysis of the test solutions after 72 h in the absence of algae showed measured concentrations ranging from below the limits of quantification to 0.076 mg/L. The results from this study should therefore be treated with caution because the authors had difficulty in determining the concentrations of the test substance, as in most cases they were below the limit of quantification (0.0478 mg/L) and the 95% confidence limits lie outside the concentration range tested. The actual toxicity could be higher.

The activated sludge study was conducted using sludge obtained from Burley Mentson sewage treatment works in Yorkshire (CHE, 1996c). Based on the results of the range finding studies, the definitive study was conducted on nominal concentrations of 50, 100, 150, 200 and 250 mg/L. Synthetic sewerage and activated sludge were added to the aqueous solutions of the test substance to give the required concentrations. The reference material used in the study was 3,5-dichlorophenol. Activated sludge at the nominal concentrations of 50, 100, 150, 200 and 250 mg/L after 3 h experienced 13, 46, 69, 79 and 87% inhibition, respectively. The 3-hour EC_{50} for the notified substance to activated sludge is 109 mg/L.

The ecotoxicity data indicates the notified substance is practically non-toxic to activated sludge, moderately toxic to fish, highly toxic to daphnia and very highly toxic to algae based on measured concentrations.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The intended use pattern of the notified chemical is expected to result in the majority of the chemical being eventually released to the environment. However, this will be in dilute manner as the notified chemical contained within the hair care products will be released from domestic use at low concentrations. The ecotoxicity data indicates the notified substance is practically non-toxic to activated sludge, moderately toxic to fish, highly toxic to daphnia and very highly toxic to algae based on measured concentrations.

In a worst case based on maximum annual imports of 1 tonne per annum, all of which is

released to sewer and assuming that none is removed during sewage treatment processes, assuming a national population of 19,000,000 and that each person contributes an average 150 L/day to overall sewage flows, the predicted concentration in sewage effluent on a nationwide basis is estimated as 0.96 microgram/L.

Amount of Escalol entering sewer annually	1000 kg
Population of Australia	19 million
Amount of water used per person per day	150 L
Number of days in a year	365
Estimated PEC	0.96 microgram/L (0.96 ppb)

When released to receiving waters the concentration is generally understood to be reduced by a further factor of at least 10, and so the Predicted Environmental Concentration (PEC) is approximately 0.1 microgram/L.

The nationwide PEC estimate indicates that after discharge to receiving waters the environmental concentration of the notified chemical will be 2 orders of magnitude less than the demonstrated toxicity to algae (EC_{50} = 0.064 mg/L). This is close to the 100-fold safety margin recommended by the OECD (OECD, 1992) but note the discussion regarding the reliability of the result. However, the risk to aquatic organisms will be further mitigated by the removal of the notified chemical through association with dissolved organic carbon from soils and sediment. This is expected to bind to the notified chemical, neutralising its positive charge and removing it from the aquatic compartment thus making it less bioavailable and less toxic to aquatic organisms (Nabholz, 1993). Therefore even though the notified chemical is soluble in water, its concentration in the aquatic compartment is expected to be significantly less than the calculated PEC because it will adsorbed to soil and sediment due to its cationic nature and be removed from the aquatic compartment. If a total of 50 or 90% of the notified chemical was adsorbed to soil and sediment the revised PECs would be 0.048 and 0.0096 microgram/L, the latter being 3 orders of magnitude less than the demonstrated toxicity to algae.

Wastes containing the notified chemical including residues from imported drums and from repackaging will also be disposed of in landfill where it is expected to adsorbed to soil and sediment due to its cationic nature.

Therefore, the environmental exposure and overall environmental hazard from the notified chemical is considered to be acceptable.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment

The notified chemical was of very low acute oral toxicity in rats (LD50 > 5000 mg/kg) and low dermal toxicity (LD50 > 2000 mg/kg) in rabbits. The notified chemical was a slight skin irritant in rabbits and, at the least, a severe eye irritant in rabbits. The notified chemical was negative in a human repeat insult patch test, human photoallergy and human phototoxicity tests and was neither mutagenic in bacteria nor clastogenic in human lymphocytes.

The notified chemical did not exhibit appreciable organ toxicity in a 28-day repeated dose toxicity study in rats. The NOEL was 15 mg/kg/day and the NOAEL, 150 mg/kg/day.

The notified chemical is determined to be a hazardous substance in accordance with NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999) and is assigned the risk phrase R41: risk of serious damage to eyes.

The notified chemical is to be imported at a concentration of 65% and formulated into products at a maximum concentration of 1%. The products would not be classified as eye irritants in accordance with NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

Occupational Health and Safety

The notified chemical as imported is a severe eye irritant. If the plastic containers in which the notified chemical is to be imported are ruptured accidentally, any spillage should be contained as the notified chemical is a waxy solid and eye contact can be avoided.

The containers of the notified chemical are heated prior to weighing out either into a plastic bucket for manual addition to a large mixing vessel or into a large plastic container of diluent prior to addition to a similar large mixing vessel via a stopcock. Inhalation exposure is unlikely due to the low vapour pressure of the notified chemical but dermal exposure is possible. Ocular exposure would most likely occur via secondary transfer from gloves or possibly from splashes. Workers are said to be wearing either full protective equipment or overalls, industrial safety shoes, facemask and gloves. Under these conditions the risk of serious eye damage is minimised. Mixing and dispensing the final products is automated and worker exposure should be minimal. Quality control sampling should also result in limited worker exposure as the maximum concentration is less than 1% and there is minimal risk of eye irritation. Equipment washing and maintenance procedures should also result in minimal exposure and little risk of eye irritation.

One of the products, a hair colourant, is for consumer use. If the other product, a hair conditioner, is used in salons, there should be little risk of eye irritation in hairdressers due to the low concentration of the notified chemical in the product.

Public Health

The use of the finished hair protection products is likely to be widespread among consumers. The nature and extent of the public exposure to the notified chemical is likely to vary with the frequency of application, the care taken with applications, the amount of hair care product applied on any occasion and with the frequency of hair washing. The product will be applied to the hair but dermal contact with the notified chemical is likely and ocular contact is possible. Nevertheless the low concentration of the notified chemical in the proposed consumer formulations and the toxicological profile of the notified chemical suggest that it will not pose a significant hazard to public health when used in the proposed manner and at the proposed concentrations in the finished products.

13. RECOMMENDATIONS

Regulatory controls

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:
  - R41: risk of serious damage to eyes

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - concentration cut-off: ≥ 10%, risk phrase: R41; 5% ≤ conc ≤ 10%, risk phrase: R36: irritating to eyes

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:
  - spillage should be avoided and should be cleaned up and placed in container for disposal

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - chemical goggles with side shields or full facemask, gloves and protective clothing

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

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

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

13.1 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 Section 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.

No additional secondary notification conditions are stipulated.

14. MATERIAL SAFETY DATA SHEET

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

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

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Attachment 1

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

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

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

CORNEA

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

CONJUNCTIVAE

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

IRIS

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

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