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July 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

2,4-Diaminophenoxyethanol sulfate

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health and Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Sustainability, Environment, Water, Population and Communities.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Full Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Tigi Australia Pty Ltd (ABN 12 073 743 861)
Suite 1, Level 1, 7 Eden Park Drive
Macquarie Park NSW 2113

Combe Asia-Pacific Pty Ltd (ABN 69 122 678 684)
443-449 Toorak Road
Toorak VIC 3142

Unilever Australia Limited (ABN 66 004 050 828)
20 Cambridge Street
Epping NSW 2121

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: non-hazardous impurities, import volume,

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: melting point/boiling point, vapour pressure, density, hydrolysis as a function of pH, partition coefficient, adsorption/desorption, particle size, flammability, autoignition temperature.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
LVC/735, LVC/762

NOTIFICATION IN OTHER COUNTRIES
Europe

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
2,4-Diaminophenoxyethanol sulphate
Jarocol DPE (H2SO4)

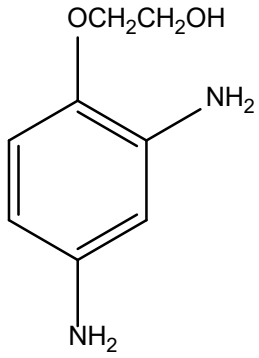
CAS NUMBER
70643-20-8

CHEMICAL NAME
Ethanol, 2-(2,4-diaminophenoxy)-, sulfate (1:1)

OTHER NAME(S)
2,4-Diaminophenoxyethanol sulphate (INCI)
Ethanol, 2-(2,4-diaminophenoxy)-, sulfate (1:1) (salt) (9CI name)
[4-(2-hydroxyethoxy)-1,3-phenylene]diammonium sulphate
1,3-Diamino-4-(2-hydroxyethoxy)benzene sulfate

MOLECULAR FORMULA
$C_8H_{12}N_2O_2.H_2SO_4$

STRUCTURAL FORMULA



Free base shown. Notified chemical is the sulfate salt.

MOLECULAR WEIGHT
266.27 Da

ANALYTICAL DATA
Reference IR and HPLC spectra were provided.

Identity of Analogue Chemical Used in Estimating the Physical, Chemical and Toxicological Properties of the Notified Chemical

The main analogue used in the assessment of the notified chemical is Ethanol, 2-(2,4-diaminophenoxy)-, dihydrochloride; CAS number: 66422-95-5 (INCI name: 2,4-diaminophenoxy ethanol HCl). This differs from the notified chemical only in the counter ion of the salt, with the free base of the analogue and the notified chemical being identical. The water solubility and partition coefficient of the notified chemical and the analogue chemical are within similar ranges and thus absorption of the two chemicals across biological membranes is not expected to be significantly different. It is reasonably considered that the analogue and the notified chemical will have comparable physical/chemical and toxicological properties.

3. COMPOSITION

DEGREE OF PURITY > 97%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS

Chemical Name	1,3-Benzenediamine, 4-methoxy-		
CAS No.	615-05-4	*Weight %*	Not detectable to ≤ 0.0015%
Hazard Properties	Carc.Cat.2;R45, Muta.Cat.3; R68 Xn; R22		
Chemical Name	1,3-Benzenediamine		
CAS No.	108-45-2	*Weight %*	Not detectable to ≤ 0.0014%
Hazard	Muta. Cat. 3; R68 T; R23/24/25 Xi; R36 R43		

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: White crystalline, odourless solid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	120°C (free base form of notified chemical)	Calculated (weighted value)
	84 °C (free base form of notified chemical)	CIR (2006)
	242.5°C (dihydrochloride form of notified chemical)	SCCS (2010)

	198 - 216ºC (dihydrochloride form of notified chemical)	CIR (2007)
Boiling Point	350ºC (free base form of notified chemical)	Calculated (Adapted Stein and Brown method)
Density	Not available	
Vapour Pressure	7.73 x 10^{-8} kPa at 25ºC	Calculated (Modified Grain method)
Water Solubility	50 – 100 g/L (pH 1.9)	SCCS (2010)
Hydrolysis as a Function of pH	Not determined	The notified chemical is not expected to hydrolyse under environmental conditions
Partition Coefficient (n-octanol/water)	log Pow = 0.612	SCCS (2010)
Adsorption/Desorption	log K_{oc} = -0.182	Calculated using KOCWIN (v2.00); US EPA (2009)
Dissociation Constant	Not determined	The notified chemical is a salt and is expected to be ionised at environmental pH (4-9)
Particle Size	Not determined	Not imported as raw material
Flash Point	> 110°C	Based on flash points of structurally related chemicals
Flammability	Not determined	Not expected to be highly flammable
Autoignition Temperature	> 475ºC	Based on the autoignition temperatures of structurally related chemicals
Explosive Properties	Not determined	Based on the structure, the notified chemical is not expected to be explosive.

DISCUSSION OF PROPERTIES

Reactivity

The notified chemical is stable under normal storage and handling conditions.

Dangerous Goods classification

Based on the submitted physical-chemical data in the above table the notified chemical is not classified according to the Australian Dangerous Goods Code (NTC, 2007). However the data above do not address all Dangerous Goods endpoints. Therefore consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the chemical.

5. INTRODUCTION AND USE INFORMATION

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

The notified chemical will be imported as a component of a number of formulated hair dye products at concentrations up to 4%.

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

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

PORT OF ENTRY

Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
Tigi Australia Pty Ltd
Unilever Australia Ltd
Combe Asia-Pacific Pty Ltd

TRANSPORTATION AND PACKAGING
Finished hair dye products containing the notified chemical will be imported in tubes or bottles (typically less than 100mL) in shippers containing several packs of the products. The shippers will be transported by road from the wharf to a warehouse and subsequently to distributors.

USE
The notified chemical will be used as a component of permanent (oxidative) hair dye formulations at concentrations up to 4%. Some of the products will be available to hair salons only, whilst others will be available to members of the public.

OPERATION DESCRIPTION
No manufacture or reformulation will occur in Australia.

End-use in hair salons
A typical operation description for the use of products available to hair salons will involve the following:
Prior to application to the hair of a customer, the oxidative colouring agent (containing the notified chemical at up to 4% and typically in a tube containing up to 65 mL) and the hydrogen peroxide developer will be mixed in a plastic bowl with an applicator brush at a ratio of 1:1, 1:1.5, or 1:2 (mL dye formulation + mL developer formulation), resulting in a final use concentration of up to 2%. The finished mixed product will be applied to the hair by brush. This will be left in contact with the hair for the required time (up to 50 minutes) followed by rinse off with water and shampoo. The application may be repeated at intervals of approximately 4-6 weeks.

End-use by consumers
There will be several types of hair dye products available for home use by members of the public.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

EXPOSURE DETAILS
Transport and Storage
Exposure is not expected during transport, storage, or distribution as long as the packaging remains intact.

Hair salons
Products containing the notified chemical are expected to be available to hair salons Australia-wide. The number of employees would range typically between two to ten per salon and these workers may use products containing the notified chemical for an average of 2 hours/day for 200 days/year.

Professional salon workers may be exposed to the notified chemical primarily by skin contact, with potential for eye contact from splattering during mixing, application or rinsing. Hairdressers may receive repeated or prolonged dermal contact to hair colour products containing the notified chemical. Good occupational hygiene practices would minimise exposure. These practices include use of personal protective equipment, consisting of impervious gloves and a plastic apron.

An Australian survey of 184 hairdressers and 193 trainee hairdressers found a high percentage (91.9% and 90.2% respectively) of respondents used gloves when in contact with hair dye products (Nixon et al, 2006). Gloves are most likely to be worn during the application stage of the dyeing process, while they are not usually worn when preparing the dye, shampooing/rinsing the hair or when cutting/drying the dyed hair (Lind et al, 2005 and Hueber-Becker et al, 2007). In a recent study using ^{14}C-PPD (*p*-phenylenediamine) the exposure during the various stages of the dyeing process was quantified. The mean daily exposure (6 dye processes) during the latter stages when gloves are usually not worn (i.e. shampooing/rinsing and cutting/drying) was found to be 0.064% of the daily used PPD (Hueber-Becker et al, 2007). Based on this value, as well as the same conservative estimate of the number of dye processes (i.e. 6 per day) and the amount of notified chemical

used per application (4% of 65 mL = 2.6 g) and the corresponding amount applied per day (2.6 g x 6 applications = 15.6 g/day), an estimate for hairdresser exposure to the notified chemical if gloves are not used during the shampooing/rinsing and cutting/drying stages is calculated as 10 mg/day (ie. 0.064% of 15.6g/day). In the Hueber-Becker study, 0.381% of the daily used PPD was collected off the gloves used during the application phase. Therefore, if gloves were not worn during the application stage (and using the same assumptions listed above) the hairdresser would be exposed to 59.4 mg/day of the notified chemical (ie. 0.381% of 15.6 g/day) during application. This would result in a total exposure of 69 mg of notified chemical per day (ie. 59.4 mg/day + 10 mg/day) as a worst case during application of the hair dye and the shampoo/rinsing and cutting/drying of hair when gloves are not worn at any time throughout the process. Inhalation exposure in the Hueber-Becker study could not be quantitated but was not considered to be significant.

While gloves are considered to be protective against exposure to the notified chemical, inappropriate glove use during the use of hair dye product, including use of the wrong type or re-using gloves, may lead to increased exposure to the notified chemical. In their occupational exposure study using the hand-rinse method in Sweden, Lind et al (2005) found that dermal exposure to a number of hair dye chemicals occurred even when gloves were worn. The majority of the hairdressers in the study used the gloves more than once, and the gloves were often turned inside-out after rinsing with water and re-used. Natural rubber latex gloves were often used for 2-3 months or until they were discarded as damaged or torn. This is consistent with findings from a survey of Australian hairdressers, where it was found that 70% of participants re-used disposable gloves (Nixon et al, 2006). In one salon hairdressers were given one pair of disposable gloves a week and the used gloves were washed in a washing machine and dried in a dryer before re-use, which is likely to seriously affect the barrier properties of the gloves. In addition, it was found to be common practice in a number of salons to wash the gloves while still on the hands, dry them and turn them inside out, then re-use the gloves with the outer contaminated surface being on the inside of the glove. In these situations the gloves are likely to be a source of contamination, rather than a protective measure.

The type of glove may also affect whether or not the gloves provide adequate protection. In the Australian survey 70% of participants used natural rubber latex (NRL) gloves (Nixon et al, 2006), and in the Swedish study the majority also used NRL gloves, with polyvinylchloride (PVC), polyethene (PE) and nitrile (NR) also being used (Lind et al, 2005). In permeability studies of hair dye chemicals through different types of gloves (NRL, PVC, NR, PE and neoprene (NP, not disposable)) it was found that all gloves gave protection for ≥ 30 min (Lind et al, 2007; and Lee and Lin, 2009). In terms of breakthrough time (elapsed time between application of chemical to the glove and its subsequent presence in the collection medium on the other side of the glove) the order was NP > NRL > NR > PVC > PE. Although suitable for the time periods expected during hair dyeing, most of the disposable gloves did show breakthrough of the chemicals and therefore are not suitable to be re-used. Due to the possible allergenicity of NRL the preferred disposable glove appears to be the nitrile (NR) glove (Lind et al, 2007; Nixon et al, 2006).

6.1.2. Public exposure

It is expected that during transport, formulation and storage, exposure of the general public to the notified chemical will be negligible.

Salon application

Some of the products are designed for the salon market and intended for one application per bottle. For such products, public exposure to hair colourant products containing the notified chemical is likely to be intermittent (based on use pattern) and widespread. In these products, the notified chemical (up to 4%) will be diluted 1:1 to 1:2 with developer, leading to maximal exposure concentrations of up to 2%. The hair dye will be used at a maximum of approximately once per month, at up to 2.6 g of the notified chemical (4 % in 65 mL liquid product) each application. It is estimated that consumers will be exposed to these hair dye products for up to one hour daily, 12 days per year primarily by dermal route (mainly on the scalp), with the possibility of accidental ocular and oral exposure.

Home application

Some hair dye products containing the notified chemical (up to 4%) may also be used by members of the public in home settings. The application instructions of products designed for home application typically indicate that gloves must be worn when using the dye, though it is unknown whether the gloves provided are of the most suitable type to ensure minimal breakthrough of the notified chemical. In addition, the instructions indicate that an allergy patch test must be performed 48 hours before use.

The method of application used by consumers is likely to be similar to that used by salon workers (see above). As such, exposure is expected to be similar, though slightly higher, than experienced by consumers when the products are applied in salons, due to the greater potential for dermal (particularly to the hands) and accidental ocular exposure when application takes place by members of the public. If gloves are worn when using the dye this should act to reduce dermal exposure to the notified chemical.

There are a number of additional types of hair dye products for home use containing the notified chemical (up to 4%) with different use instructions to those used by hair salon workers. Examples of products may include shampoo-in haircolour and brush-in colour gels. The products are mainly recommended for grey hair and for use by men. Typically, for each product the colour base containing the notified chemical at up to 4% concentration will be diluted with developer (hydrogen peroxide solution) in a ratio of 1:1, so that the final maximum concentration of notified chemical applied will be 2%.

Shampoo-in products:
The mixture will be applied to the head and lathered evenly into the hair similarly to shampoo. The quantity used per application will be dependent upon the length of the hair and as such, the entire mixture may not be used. In this case, users are directed to discard any unused mixture. Up to 1.2 g of the notified chemical (4 % in 30 mL liquid product) will be used per application. The mixture will be kept in the hair for 5 minutes and then rinsed out, followed by shampooing of the hair. Typically reapplication will occur on a monthly basis. The method of reapplication (ie. application to grey roots) differs from the first time application described above. The mixture will be applied to the roots only and after 4 minutes it will be combed through the hair followed by rinsing. The mixture may also be used on grey sideburns or hair on the temple by applying for a few seconds and subsequently wiping away.

Brush-in colour gel:
Hair: The product containing the notified chemical (up to 4%) and the developer will be contained in separate resealable tubes. Up to 1.6 g of the notified chemical (4% in 40 g liquid product) will be used per application. It will be squeezed along one side of the applicator brush, with an approximately equal amount of developer on the separate and opposite side of the brush. Mixing with the developer does not occur prior to application to the hair. Rather, the brush will be run through the hair, resulting in some mixing on the hair (though it may not be complete or thorough). As such, the scalp may be exposed to concentrations of the notified chemical up to 4%. It will be kept on the hair for up to 10 minutes, followed by rinsing with warm water. Reapplication is expected to occur approximately once per month.

Facial hair: Up to 0.56 g of the notified chemical (4% in 14 g liquid product) will be used per application. The mixed product (containing the notified chemical at up to 2%) will be applied to facial hair using an applicator brush, left on the hair for up to 5 minutes, and then rinsed out, followed by shampooing. It is anticipated that reapplication would occur no more than once a week. It is also noted that the product instructions imply that the provided gloves should be reused during subsequent applications when the remaining contents of the tubes are used. This practice may lead to increased levels of exposure to the notified chemical due to the possible presence of residues on the gloves.

For each of the above types of products outlined above, exposure to the public will be primarily dermal through the scalp, beard area of face, and hands (if gloves are not used properly), but some accidental ocular or oral exposure is also possible. The public will be exposed to the notified chemical at a concentration of up to 4% from dermal contact with the hair dye during dilution and typically up to a concentration of 2% from contact of the hair dye with the scalp and face (beard area) during the dyeing process (note that there is some potential for the scalp to be exposed to concentrations of up to 4% of the notified chemical when using brush-in colour gel designed for the hair, due to possible incomplete mixing with the developer).

6.2. Human health effects assessment

No toxicity data are available on the notified chemical. The results from toxicological investigations conducted on the analogue chemical, 2,4-diaminophenoxy ethanol HCl, are summarised in the table below. These results are summarised in a report by the Scientific Community on Consumer Safety (SCCS, 2010) and/or the Cosmetic Ingredient Review Expert Panel (CIR, 2007). The studies included in the SCCS report tend to be more recent than those from the CIR report and were conducted in accordance with OECD Test Guidelines. As such, results from studies reported by the SCCS are generally considered more reliable for the purposes of the hazard and risk assessment of the notified chemical.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity (1)	LD50 ~1000 mg/kg bw; harmful toxicity
Rat, acute oral toxicity (2)	LD50 = 1113 mg/kg bw; harmful toxicity
Mice, acute oral toxicity (1)	LD50 = 1745 mg/kg bw; harmful toxicity
Mice, acute oral toxicity (2)	LD50 = 1160 mg/kg bw; harmful toxicity
Rabbit, skin irritation (4% solution) (1)	slightly irritating
Rabbit, skin irritation (2)	slightly irritating
Rabbit, eye irritation (4% solution) (1)	slightly irritating
Rabbit, eye irritation (4% solution) (2)	slightly irritating
Rabbit, eye irritation (3)	irritating, irreversible effects
Guinea pig, skin sensitisation – adjuvant test	evidence of sensitisation
Guinea pig, skin sensitisation – non-adjuvant test.	no evidence of sensitisation
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Rat and mice, repeat dose oral toxicity – 12 weeks	NOAEL/LOAEL not reported
Rat, repeat dose oral toxicity – 90 days (1)	NOAEL/LOAEL not reported
Rat, repeat dose oral toxicity – 90 days (2)	NOAEL = 20 mg/kg bw/day
Genotoxicity – bacterial reverse mutation	mutagenic
Genotoxicity – in vitro mammalian cell gene mutation test	non mutagenic
Genotoxicity – in vitro chromosome aberration test in human lymphocytes	genotoxic
Genotoxicity – in vitro micronucleus test in human lymphocytes	genotoxic
Genotoxicity – in vivo rat bone marrow micronucleus test	non genotoxic
Genotoxicity – in vivo rat liver unscheduled DNA synthesis assay	non genotoxic
Dermal percutaneous absorption: in vitro human dermatomed skin (2% mixture)	1.74 μg/cm^2 (range 0.38-4.33 μg/cm^2) oxidative 6.55 μg/cm^2 (range 1.56-16.61 μg/cm^2) non-oxidative
Developmental and reproductive effects	NOAEL = 20 mg/kg bw/day
Carcinogenicity	non-carcinogenic in mice no conclusion in rat study

Toxicokinetics, metabolism and distribution.

In an *in vitro* percutaneous absorption study using human dermatomed skin (conducted in accordance with OECD draft guideline 428, SCCS 2010) the absorption of a formulation containing the radiolabelled analogue chemical at 4% was investigated under oxidative (1:1 mix with developer and 1.8% p-phenylenediamine) and non-oxidative (1:1 mix with water) conditions. 20 mg/cm^2 of each mixture (oxidative and non-oxidative) containing 2% analogue chemical (therefore 0.4 mg/cm^2 of analogue chemical) was applied to the surface of the separate skin samples and left for 30 minutes before being washed off. After 24 hours the concentration of analogue chemical was measured in the following compartments: skin washes, stratum corneum (isolated by tape strippings), living epidermis/dermis, unexposed skin and receptor fluid. Most of the analogue chemical applied to the skin was removed with the skin wash (90% and 94% in oxidative and non-oxidative conditions, respectively). The amount of analogue chemical considered as absorbed from a typical hair colouring mixture containing 2% analogue chemical was estimated as set out in the following table:

	Oxidative conditions	*Non-oxidative conditions*
Mean absorption	1.74 μg/cm^2 (0.4 % of applied dose)	6.55 μg/cm^2 (1.6 % of applied dose)
Range of absorption	0.38-4.33 μg/cm^2 (0.095-1.1 % of applied dose)	1.56-16.61 μg/cm^2 (0.39-4.2 % of applied dose)

In a dermal absorption study in rats (test guideline not noted) using both the pure compound and formulation containing 0.4% analogue chemical, following mixing with hydrogen peroxide, 20 mg/cm^2 of the mixture was applied to 25 cm^2 for a period of 40 minutes. Excess test substance was then removed from the skin and faeces and urine collected for 4 days prior to the animal being killed and necropsied. The quantity of chemical that penetrated was 0.84 μg/cm^2 (pure chemical application) and 0.47 μg/cm^2 (chemical in formulation). Penetration of the analogue chemical in the commercial formulation was 40% of the penetration of the pure compound (CIR

2007).

In another dermal absorption study in rats (test guideline not noted), radiolabelled analogue chemical at 0.4%, 0.8% and 1.2% in a commercial vehicle was mixed with equal quantities of hydrogen peroxide before use. 20 mg/cm^2 was applied to 25 cm^2 for a period of 40 minutes. The animals were subsequently killed and necropsied and the amount of test substance absorbed was determined. The penetration per cm^2 was 0.84 µg/cm^2 for the lowest concentration and 1.58 µg/cm^2 for the highest concentration (CIR 2007).

Results from the *in vitro* percutaneous absorption study using human dermatomed skin described above are considered most appropriate for use in the hazard and risk assessment of the notified chemical given that the study was conducted according to an OECD Test Guideline and is more recent than the studies described in the CIR report.

Acute toxicity.
The acute oral toxicity of the analogue chemical was tested in a number of studies. A study in rats (according to OECD TG 401) using a single dose of 1000 mg/kg bw resulted in the death of 1/5 males and 3/5 females. As such, the LD50 was estimated to be approximately 1000 mg/kg bw (SCCS 2010), suggestive of harmful acute toxicity via the oral route. This was supported by another study in rats (LD50 = 1113 mg/kg bw) and two studies in mice (LD50s = 1745 mg/kg bw and 1160 mg/kg bw) (CIR 2007).

There was no information available on the acute dermal or inhalation toxicity of the notified chemical or known analogues.

Irritation
The skin irritation potential of the analogue chemical was examined in two separate studies. One study (according to OECD TG 404) showed the analogue chemical to be slightly irritating, with the only skin reaction (slight erythema) being observed in one animal at the 48 hour observation (SCCS 2010). When tested in rabbits (test guideline not noted) as a 4% solution (pH 8.5), it was also found to be slightly irritating (CIR 2007).

The eye irritation potential of the analogue chemical was examined in three separate studies. When tested in rabbit eyes as a 4% solution, it was found to be slightly irritating (CIR 2007 and SCCS 2010), with signs of irritation clearing by day 7 and day 2, respectively in each study. When tested neat in a separate study (according to OECD TG 405), marked ocular reactions, including moderate to marked chemosis, slight to moderate redness of conjunctivae, slight to moderate corneal opacification and slight iridial lesions were observed. Ocular reactions were still present at the end of the study (day 15), but were less marked (SCCS 2010). Based on the presence of reactions at the end of the study period the tested chemical should be classified as R41 Risk of serious damage to eyes.

Skin Sensitisation.
The skin sensitisation potential of the analogue chemical was examined in a number of studies, as summarised below. Overall, these tests confirm that the analogue chemical should be classified as a skin sensitiser.

Local Lymph Node Assay - LLNA (mouse) (according to OECD TG 429): Five treated groups received analogue chemical at concentrations of 0.5, 1, 2.5, 5 and 10% in DMSO. A dose-related increase in stimulation index was observed, and the threshold positive value of 3 was exceeded at concentrations of 5 and 10% (SCCS 2010). The EC3 value was calculated to be 3.2%, and the analogue chemical was considered to be a skin sensitiser.

Buehler Test (guinea pig) (according to OECD TG 406): Following challenge with 500 mg neat analogue chemical cutaneous reactions included purple colouration and very slight erythema in 2/20 animals, with the slight erythema observed at the 48-hour reading only (SCCS 2010). It was concluded that neat analogue chemical did not produce sensitisation reactions under the conditions of the test.

Modified Magnusson and Kligman (adjuvant) sensitisation study (guinea pig): Following challenge with 25% of the analogue chemical, erythema was observed in 3 of the 10 animals, all of which recovered in 5 days. No details of reactions in the control animals were provided (CIR 2007). Based on these reported test results the analogue chemical should be considered to be a dermal sensitiser.

Repeated Dose Toxicity
The oral repeated dose toxicity of the analogue chemical was examined in a number of studies.

90 day oral repeat dose study (rat) (according to OECD TG 408) (SCCS 2010): NOAEL = 20 mg/kg bw/day
Dose: 0, 4, 20 and 100 mg/kg bw/day
Reported effects: No effects were observed at 4 and 20 mg/kg bw/day. At 100 mg/kg bw/day ptyalism (excessive salivation) was observed in both males and females and lower body weight gains were noted for males. The presence of urinary bilirubin, nitrites and glucose in the coloured urine (marked coloration from yellow to yellow-brown in both males and females) was detected at the end of the treatment period. The presence of these chemicals in the urine may have been due to an analytical interference, as there were no changes observed in the plasma levels of these chemicals. An increase in relative kidney weights was observed in males and females dosed with 100 mg/kg bw/day. Relative thyroid weights were observed to increase in females dosed with 20 mg/kg bw/day and for males and females dosed at 100 mg/kg bw/day. The increased thyroid weights in females at 20 mg/kg bw/day were not considered toxicologically significant since microscopic examination revealed no effects on the thyroid at this dose level. All these effects had reversed after a 4-week recovery period.

Deposition of brownish pigment in the thyroid (mainly in follicular epithelial cells) as well as brownish colouration of the thyroid was observed in all animals given 100 mg/kg bw/day. An augmented degree of spleen hemosiderosis (deposition of hemosiderin, a protein that stores iron) was also observed for most animals given 100 mg/kg bw/day. The microscopic changes to the thyroid and spleen were still observed at the end of the recovery period.

Plasma levels of the test substance were determined from samples taken on day 1 and week 13 of the study. Systemic exposure was found to increase proportionally with the dose level.

Similar types of effects were observed in two separate studies reported in the CIR 2007 (test guidelines not noted), as outlined below:

12 week oral repeat dose study (rat/mice): No NOAEL/LOAEL reported.
Doses: 0, 0.01, 0.03, 0.05, 0.1 and 0.2% in tap water, ad libitum
Reported effects: 1/10 male mice died in each of the 0.1% and 0.2% groups, with their deaths attributed to malnutrition (inability to drink water). Reduced body weight gains/feed consumption was observed in the top two dose levels. Water intake reduced in all treatment groups. Histopathologic observations (in 0.2% dose groups): kidney abnormalities (2/20 mice), lesions of pneumonia (7/20 mice) and pigment deposits in the epithelial cells of the thyroid follicles (1/20 mice, 20/20 rats) (CIR 2007).

90 day oral repeat dose study (rat): No NOAEL/LOAEL reported.
Dose: 56 mg/kg bw/day in a 5% Tween suspension, by gavage daily
Reported effects: dull coat, brown discolouration of urine, thyroid and trachea, reduced (not significant) bodyweight gain, no significant histological/clinical observations (CIR 2007).

Mutagenicity.
The mutagenicity of the analogue chemical was examined in a range of different studies that are outlined below. Based on these studies the analogue chemical is considered to be an *in vitro* mutagen/genotoxin. However, the results obtained from tests conducted *in vivo*, which explored the endpoints found to be positive *in vitro*, indicate that the test substance cannot be classified as an *in vivo* mutagen or genotoxin.

The SCCS report (2010) outlines the results for several studies on the genotoxicity of the analogue chemical, as follows:

- Bacterial gene mutation assay (according to OECD TG 471): Positive in one strain (*Salmonella typhimurium* TA98) in the presence of S9 metabolic activation.

In vitro:

- Mammalian chromosome aberration test (according to OECD TG 473): Positive result. Induced chromosome aberrations in cultured human peripheral blood lymphocytes with or without metabolic activation.
- Micronucleus test (according to OECD TG 487): Positive result. Induced micronuclei in cultured human peripheral blood lymphocytes with or without metabolic activation.
- Mammalian cell gene mutation test (according to OECD TG 476): In mouse lymphoma L5178Y cells statistically significant increases in gene mutations at the HPRT locus were observed in the absence of metabolic activation, but not in the presence of metabolic activation. The increase was small and dose-response was not obvious. Therefore this result was considered to be equivocal.

In vivo:

- Rat bone marrow erythrocyte micronucleus test (according to OECD TG 474): Negative result. Two isolated increases in micronucleus responses were observed, however these were considered to be of no biological relevance as the overall micronucleus responses were not statistically significant compared to the vehicle. There was no indication of bone marrow toxicity, however, the oral bioavailability of the test substance was indicated by the clinical signs observed at the two highest doses used and one death observed at the highest dose. Also, systemic exposure following oral dosing was shown in the 90 day oral repeat dose study where plasma samples were analysed.
- Rat *in vivo*/*in vitro* UDS (unscheduled DNA synthesis) assay (according to OECD TG 494): Negative result. Increased UDS response was observed in the lowest dose group (2/3 animals) but one of these animals had a response in only one out of the three slides examined. The UDS response in the medium and high dose groups were similar to the responses in the vehicle control animals, and so the changes at the lowest dose were considered to be unrelated to treatment.

The CIR report (2007) summarises the results of several genotoxicity studies (test guidelines not noted) on the analogue chemical. These include a number of bacterial cell assays, with some positive results in certain strains and/or conditions/concentrations, as well as negative results. There are also *in vitro* assays with some positive and some negative results, and *in vivo* assays, with negative results.

Carcinogenicity.
Studies on the carcinogenicity of the analogue chemical are reported in the CIR (2007) and SCCS (2010) reports. The studies were conducted in 1983 and there was no indication of GLP compliance.

2 year study (rats): no sufficient evidence of carcinogenicity (CIR 2007); no conclusion can be drawn from this study (SCCS 2010)
Dose: 0, 0.05 and 0.1% (Corresponding intake levels: 0, 20.9 and 35.5 mg/kg bw/day for male rats and 0, 27.8 and 60.9 mg/kg bw/day for female rats)
Results: Body weight gain was decreased for males and females in both treatment groups. Tumour incidences in control and treated groups were generally the same. Pigment deposition in the epithelial cells of thyroid follicles of both males and females was observed in the highest dose groups, though their distribution did not correlate with the occurrence of tumours. An increase in the C-cell adenoma was observed in the thyroid gland of male rats. The study authors indicated that this increase was not toxicologically significant as C-cell adenomas are common in old F344 rats. However, historical control values were not provided. The SCCS considered that no conclusion regarding the carcinogenicity of the analogue chemical could be made on the basis of this study.

2 year study (mice): no evidence of carcinogenicity
Dose: 0, 0.04 and 0.07% in water, ad libitum (Corresponding intake levels: 0, 35.8 and 62.8 mg/kg bw/day for male mice and 0, 44.6 and 81.4 mg/kg bw/day for female mice)
Results: Tumour incidences in control and treated groups were the same. Pigment deposition in the epithelial cells of thyroid follicles of both males and females was observed in the highest dose groups. The distribution of the deposits did not correlate with the tumour occurrence.

Toxicity for reproduction.
The developmental toxicity of the analogue chemical was examined in a number of studies, as outlined below.

Prenatal developmental toxicity (rat) (according to OECD TG 414): NOAEL for maternal toxicity and embryo-foetal development = 20 mg/kg/day
Dose: 0, 4, 20, 125 mg/kg bw/day
Clinical signs of maternal toxicity: salivation, reduced body weight gain and food consumption, in the dam were noted in the 125 mg/kg bw/day dose group.
Effects on foetuses: At 125 mg/kg/bw there was a statistically significant reduction in the mean foetal weight. This corresponded with a statistically significant increased incidence of foetuses showing incomplete ossification of thoracic vertebra centrum or supernumerary short 14th rib.

Developmental toxicity (rat): No NOAEL/LOAEL reported.
Dose: 0, 50, 100, 200 mg/kg bw/day
Effects: In the 200 mg/kg bw/day dose groups, there was a significant dose related increase in the incidence of skeletal anomalies and skeletal variants. Lower litter weights and foetal mean weight were also observed at this dose. Clinical signs of toxicity (salivation, fur loss, reduced body weight gain) in the dam was noted in the 200

mg/kg bw/day dose group (CIR 2007).

Developmental toxicity (mice):
Dose: 15, 150, 1500 mg/kg bw (dermal application)
No teratogenic effects, no significant difference in skeletal development compared to negative controls (CIR 2007).

Health hazard classification
Based on the available toxicity data on the analogue chemical (2,4-diaminophenoxy ethanol HCl) the notified chemical should be classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrase:

R22 Harmful if swallowed
R43 May cause skin sensitisation by skin contact
R41 Risk of serious damage to eyes

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
The greatest potential for worker exposure to the notified chemical will be during the hair dyeing process in professional hairdressing salons.

The notified chemical was considered to be harmful if swallowed. However, the notified chemical will be present at relatively low concentrations (up to 4%) in hair dye products and good occupational hygiene practices are expected to be in place to avoid oral exposure. Therefore, the risk of acute oral toxicity during use of the hair dye product is considered minimal.

The notified chemical was considered to be a severe eye irritant. However, at the concentrations used in the imported hair dye products (up to 4%), the risk of these effects will be reduced, though the possibility of some eye irritation cannot be completely ruled out.

The notified chemical was considered to have the potential to cause skin sensitisation. The notified chemical will be present in the hair dye products (up to 4%) at concentrations above the cut-off for sensitisation classification (1%). Gloves are expected to be worn during the application of the hair dye, but are less likely to be worn when mixing the products, when shampooing/rinsing the dyed hair, or when cutting/drying dyed hair. In addition, inappropriate glove use, particularly the re-use of disposable gloves, may be common. Hairdressers are likely to have compromised skin barrier function due to frequent hand immersion in cleaning agents that tend to defat the skin. For some individuals, this is likely to induce increased susceptibility to sensitising agents. Therefore the risk of sensitisation exists. In order to reduce the risk of long-term adverse skin effects good occupational hygiene practices are required. These should include the wearing of appropriate gloves (such as neoprene, or nitrile/natural rubber latex for disposable gloves), and not re-using disposable gloves. The product labels and associated product leaflets provided by the notifier contain appropriate safety instructions regarding the potential for the product to cause skin sensitisation and the required safety measures to be taken (use of gloves, avoiding contact with skin and eyes). The inclusion of directions to not re-use disposable gloves would further reduce the risk of exposure.

Based on the weight of evidence the notified chemical is considered unlikely to be a genotoxin in vivo, and the analogue chemical was shown to cause reproductive/developmental effects only at doses causing maternal toxicity. Following repeated oral dosing (90 day study), microscopic changes were observed on the thyroid and spleen in the high dose animals that persisted after the completion of the recovery period. The NOAEL determined in the SCCS report on the analogue chemical was 20 mg/kg bw/day. In the absence of data on the repeated dose dermal toxicity of the notified chemical, oral toxicity data will be used for the risk assessment of the notified chemical, together with information on the dermal absorption of the analogue chemical (and thus the notified chemical).

Hairdressers may be exposed to the notified chemical on a daily basis. Based on studies conducted on PPD under similar use conditions, the worst case dermal exposure to the notified chemical was estimated to be 59.4 mg/day when gloves are not used during the application stage. Using the maximum dermal absorption value determined in the in vitro percutaneous absorption study under oxidative conditions (1.1% of applied dose) and a bodyweight of 60 kg this equates to a systemic exposure dosage (SED) of 10.9 μg/kg bw/day in the

absence of gloves. The calculation of the Margin of Exposure (MOE) is presented below:

NOAEL = 20 mg/kg bw/day
SED without gloves = 10.9 μg/kg bw/day
MOE without gloves (NOAEL/SED) = 1837

A MOE of greater than 100 is considered to be acceptable to account for intra- and inter-species differences, and therefore the risk of adverse effects after repeated exposure while hair dyeing is not considered unreasonable. The MOE would be further reduced if gloves were used, as is expected to be the case due to the sensitisation risk.

Overall, while the risk of sensitisation exists, the risk to hairdressers exposed to the notified chemical is not considered unreasonable if the appropriate good occupational hygiene practices are in place, including the use of impermeable gloves (such as neoprene), or the single use of disposable, impermeable gloves (nitrile or NRL preferred).

No toxicity information was available on the reaction products formed from the notified chemical under the oxidative conditions. Based on the estimates for exposure to the notified chemical the exposure of hairdressers to these intermediates is expected to be very low. However, the risk from exposure to these reaction products cannot be determined.

6.3.2. Public health

The public will be exposed to the notified chemical in hair dye products, at concentrations up to 4%, on an intermittent basis. The products containing the notified chemical are for salon use or home use. As such, the public is expected to be exposed primarily through the dermal route via the skin of the scalp, beard of the face, and also the hands (if gloves are not used correctly).

Although the notified chemical was shown to be severely irritating to eyes, the risk of severe irritancy effects will be reduced due to the relatively low concentration in use, and the safety warnings on the label to not use it for dyeing eyelashes or eyebrows.

The notified chemical was found to have the potential to cause skin sensitisation. As significant dermal exposure to the scalp is expected during hair dye application, the risk of members of the public developing an allergy to the notified chemical exists. Representative product labels and accompanying information leaflets have been provided by the notifier. These contain warnings and precautions regarding the possibility of allergic reaction, the need for a skin sensitivity test, other possible complications that may arise, and the advice to discontinue use if any such issues occur.

While the skin sensitivity test may detect some clients who have already developed an allergy to the notified chemical (or other sensitising hair dye components in the product), it is likely to also produce false negatives and will not prevent the induction of sensitisation in previously unexposed clients. This type of test is recommended for many hair dye products, but the proportion of compliance with these recommendations is unknown and may be affected by the practicalities of attending the salon 48 hours before every use of the hair dye product. In many instances the test may be performed before the first use of hair dye (before sensitisation could have occurred) but not before subsequent colourings when allergy may have been acquired. This is recognised in the company's safety information that indicates that the test should be conducted before each and every use of the product.

Concerns regarding the use of these types of 'self-tests' have been raised by the EU Scientific Committee on Consumer Products (SCCP, 2007), including: the risk of misleading and false negative results; the potential risk that these tests result in induction of sensitisation to hair dye chemicals; and the fact that very little data exists on the proportion of hair dye allergic individuals who produce a positive reaction in these type of tests.

Therefore, while the skin sensitivity test will not prevent allergic reactions to the notified chemical, and there are concerns surrounding its use, it is still considered to be a useful measure in reducing the risk of serious allergic reactions. The safety information provided on the product label and information leaflet are considered to be important means of communicating the risk of allergic reaction to the client.

As discussed above, the NOAEL from the 90 day oral study was chosen for use in the risk assessment. The maximum dermal absorption value from the in vitro percutaneous absorption study (4.33 μg/cm^2 ie. 1.1% of

applied dose) under oxidative conditions was used. Assuming a body weight of 60 kg for females, and that gloves are not worn during application, the MOE for products used on the scalp was calculated as set out below:

Max absorption through human skin *in vitro*:	A	= 4.33 μg/cm^2
Skin area surface:	SAS	= 1010 cm^2 (ie. ½ area head + ½ area hands)
Dermal absorption per treatment:	SAS x A x 0.001	= 4.37 mg
Typical body weight of human (female):		= 60 kg
Systemic exposure dosage (SED):	SAS x A x 0.001/60	= 0.07 mg/kg bw
No Observed Adverse Effect Level (13 week, oral rat)	NOAEL	= 20 mg/kg bw
Margin of Exposure:	NOAEL/SED	= 286

Assuming a body weight of 70 kg for males, and that gloves are not worn during application, the MOE for products designed for use on facial hair such as beards was calculated as shown below:

Max absorption through human skin *in vitro*:	A	= 4.33 μg/cm^2
Skin area surface:	SAS	= 305 cm^2 (ie. ¼ area of head)
Dermal absorption per treatment:	SAS x A x 0.001	= 1.32 mg
Typical body weight of human (male):		= 70 kg
Systemic exposure dosage (SED):	SAS x A x 0.001/70	= 0.02 mg/kg bw
No Observed Adverse Effect Level (13 week, oral rat)	NOAEL	= 20 mg/kg bw
Margin of Exposure:	NOAEL/SED	= 1000

MOE of greater than 100 is considered to be acceptable to account for intra- and inter-species differences, and therefore the risk of adverse systemic effects after repeated exposure while hair dyeing is not considered unreasonable for both types of products in the absence of gloves. It is also noted that the MOE has been calculated assuming daily use, which would not occur with hair dye products.

As no toxicity information was available on the reaction products formed from the notified chemical under the oxidative conditions the risk from exposure to these reaction products cannot be determined, however the exposure to these products is expected to be less than that of the notified chemical.

In summary, the risk to the public of adverse systemic effects associated with use of hair dye products containing the notified chemical is not considered unreasonable. In addition, whilst the risk to the public of skin sensitisation exists from the use such products, it is not considered to be unreasonable assuming that gloves are used appropriately and skin sensitivity testing is performed in accordance with the product use instructions.

It is also noted that the SCCS opinion on the use of the notified chemical in oxidative hair dye formulations concluded that "at a maximum final concentration of 2% (after mixing with hydrogen peroxide) does not pose a risk to the health of the consumer, apart from its sensitising potential."

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia as a component of a finished product. Accidental spills and leaks during transport are unlikely as the products containing the notified chemical are containerised, or in

packaging designed to withstand impact. However, in the case of an accidental release the notified chemical is expected to be collected and disposed of according to State/Territory regulations.

RELEASE OF CHEMICAL FROM USE
In bathrooms and hair salons the product containing the notified chemical will be mixed with hydrogen peroxide developer before application to hair. After some contact time, the product containing the notified chemical will be rinsed off hair and the majority of the notified chemical is expected to reach the sewer.

RELEASE OF CHEMICAL FROM DISPOSAL
Residue of the notified chemical in the empty containers (3%) is likely either to share the fate of the container and be disposed of to landfill, or to be washed to sewer when containers are rinsed before recycling.

7.1.2 Environmental fate

No environmental fate data were submitted. As a result of its use pattern, the notified chemical is expected to be coupled with other components of the colouring agent to form reaction products. The reaction products will be washed to sewer along with unreacted notified chemical or trapped on hair clippings which will be disposed of to landfill. EPI Suite calculations performed on several likely reaction products predicted similar physico-chemical and ecotoxicological endpoints to those calculated for the notified chemical. Hence, the fate of the notified chemical is taken to be representative of the reaction products expected to form during use.

The notified chemical is not expected to readily biodegrade based on EPI Suite calculations (BIOWIN v4.10; US EPA, 2009). Due to its cationic functionality, some notified chemical is expected to be removed from the water phase in sewage treatment plants (STPs) via sorption to sludge and sediment. However, due to its high water solubility a portion of notified chemical is expected to be present in the water phase, and may be released from STPs to receiving waters where it will disperse and eventually degrade. The notified chemical has low potential to bioaccumulate, based on its low octanol/water partition coefficient (log Pow = 0.612) and its low bioconcentration factor (log BCF = 0.50) predicted by a regression-based method (BCFBAF v3.00; US EPA, 2009). A small proportion of notified chemical may be applied to land when effluent is used for irrigation or sewage sludge is used for soil remediation. Notified chemical residues in landfill, soil and sludge are expected to degrade biotically or abiotically to form water and oxides of carbon and nitrogen.

7.1.3 Predicted Environmental Concentration (PEC)

Under a worst case scenario, it is assumed that all of the total import volume of notified chemical will be released to sewers with no removal of the notified chemical by sewerage treatment plants (STPs). It is assumed the release of the notified chemical will occur over 365 days per annum into the total Australian effluent volume.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	2.74	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	0%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.65	µg/L
PEC - Ocean:	0.06	µg/L

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 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.647 µg/L may potentially result in a soil concentration of approximately 4.316 µg/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 21.58 µg/kg and 43.16 µg/kg, respectively.

7.2. Environmental effects assessment

No measured ecotoxicity data were submitted. The acute toxicity for the notified chemical was estimated using the aniline (amino-meta) structure-activity relationship (SAR) from the ECOSAR suite of models (USA EPA, 2009), and the endpoints are tabulated below.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	LC50 (96 h) > 100 mg/L	Not harmful
Daphnia Toxicity	LC50 (48 h) = 21.5 mg/L	Harmful
Algal Toxicity	EC50 (96 h) = 6.4 mg/L	Toxic

Under the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS), the notified chemical is considered to be not harmful to fish, harmful to daphnia and toxic to algae. Based on its acute toxicity to aquatic biota, the notified chemical is formally classified under the GHS as 'Acute Category 2; Toxic to aquatic life'. Since the biodegradability of the notified chemical is unknown, and based on the acute toxicity endpoints, it is formally classified under the GHS as 'Chronic Category 2; Toxic to aquatic life with long lasting effects'.

7.2.1 Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has been calculated from the estimated algal toxicity of the notified chemical and assessment factor of 1000. A conservative assessment factor was used as the endpoints of the notified chemical are representative of those for the reaction products expected to form during use of the notified chemical.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Alga)	6.40	mg/L
Assessment Factor	1,000	
PNEC:	6.40	µg/L

7.3. Environmental risk assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.65	6.4	0.10
Q - Ocean	0.06	6.4	0.01

The Risk Quotients (Q = PEC/PNEC) for the worst case discharge scenario have been calculated to be < 1 for the river and ocean compartments. Therefore, the notified chemical is not expected to pose an unreasonable risk to the aquatic environment based on its reported use pattern at the proposed import quantity.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data on the analogue chemical the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)]. The classification and labelling details are:

R22 Harmful if swallowed
R43 May cause skin sensitisation by skin contact
R41 Risk of serious damage to eyes

and

The classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2009) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Acute toxicity	4	Harmful if swallowed (oral)
Skin sensitiser	1	May cause an allergic skin reaction
Serious eye damage/eye irritation	1	Causes serious eye damage
Aquatic Environment	Acute Category 2	Toxic to aquatic life
	Chronic Category 2	Toxic to aquatic life with long lasting effects

Human health risk assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk of adverse systemic effects. However the risk for skin sensitisation to hairdressers cannot be ruled out, and therefore appropriate work practices, such as the 'single' use of impermeable gloves (neoprene, nitrile or natural rubber latex preferred), are required.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk of adverse systemic effects to the public. However the risk for skin sensitisation to hair dye users cannot be ruled out. Therefore appropriate communication of this risk and the recommendation for skin sensitivity testing before every use is required.

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia, should consider the following risk phrases for health hazard classification and safety phrases for the notified chemical:
  - R22 Harmful if swallowed
  - R41 Risk of serious damage to eyes
  - R43 May cause sensitisation by skin contact
  - S25 Avoid contact with eyes
  - S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
  - S36 Wear suitable protective clothing

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc ≥ 25%: R22; R41; R43
  - 10% ≤ Conc < 25%: R41; R43
  - 5% ≤ Conc < 10%: R36; R43
  - 1% ≤ Conc < 5%: R43

- The notified chemical should be considered for listing on the SUSMP based on the skin sensitisation results. The Full Public Report will be provided to the Medicines and Poisoning Scheduling Secretariat.

Health Surveillance

- As the notified chemical is a sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation.

Material Safety Data Sheet

- An Australian MSDS should be made available for all imported hair dye products being used in hairdressing salons.

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical in the imported hair dye products:
  - Avoid contact with skin
  - Avoid contact with eyes
  - Avoid skin contact with contaminated gloves
  - Do not re-use disposable gloves worn during handling of the hair dye product

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical in the imported hair dye products:
  - Impermeable gloves (neoprene, nitrile or natural rubber latex may be suitable)

  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 *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Public Health

- The following measures should be taken to minimise the risk of serious allergic reactions to the notified chemical:
  - Product labels and associated information leaflets for consumer products should include warnings regarding the risk of allergic reaction;
  - Hairdressers should advise clients of the risk of allergic reaction and provide the product information leaflet for clients to read;
  - Skin sensitivity tests should be conducted prior to each and every use of the hair dye products containing the notified chemical.

- The notified chemical should not be used for dyeing eyelashes or eyebrows.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the notified chemical is imported in solid form;
- the notified chemical is imported for reformulation in Australia;
- the concentration in hair dye products has increased from 4%;
- the notified chemical has begun to be formulated into products in Australia;
- additional information becomes available to the person as to the adverse effects of the oxidative reaction products created during hair dye use.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of hair dye formulations, or is likely to change significantly;
- the amount of chemical being introduced has increased from 1 tonne per annum, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

Material Safety Data Sheet
The MSDS of the notified chemical (and products containing the notified chemical) provided by the notifier were reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

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