File No: LTD/1055

16 April 2003

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

RO 1525

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 the Environment and Heritage.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at:

Library
National Occupational Health and Safety Commission
25 Constitution Avenue
CANBERRA ACT 2600
AUSTRALIA

To arrange an appointment contact the Librarian on TEL + 61 2 6279 1161 or + 61 2 6279 1163.

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

Director
Chemicals Notification and Assessment

TABLE OF CONTENTS

FULL PUBLIC REPORT

RO 1525

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT
Henkel Australia Pty Ltd., 135-141 Canterbury Road Kilsyth Vic 3137 (ABN: 82 001 302 996)

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Chemical Name CAS Number, Molecular formula, Structural Formula, Spectral data, Purity, Identity and weight of impurities and additives, import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT
The Applicant has not previously notified this chemical in Australia.

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Napro Live (Various shades of hair dye containing the notified chemical)

METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD: The notified chemical can be identified by IR and HPLC

3. COMPOSITION

DEGREE OF PURITY
High

HAZARDOUS IMPURITIES
1 % unknown impurities

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported as a component of a finished product.

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

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

Kilograms	<500	<500	<500	<500	<500

USE
The notified chemical will be used as a component of permanent hair dye at a concentration of <5%.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Sydney, NSW

IDENTITY OF MANUFACTURER/RECIPIENTS
Henkel Australia Pty Ltd Pty Ltd
20 Rodborough Rd, Frenchs Forest NSW 2086

TRANSPORTATION AND PACKAGING
The hair dye containing the notified chemical will be imported in 40 mL plastic bottles within a hair dye kit. The packaged goods will be transported by road from the wharf to the notifier's warehouse where it will be stored prior to distribution by road to retail and hair salon outlets.

5.2. Operation Description

End-use
Hair dye kits containing the notified chemical will be sold to both retail and salon markets. The hair dye in each kit is intended for single use.

5.3. Occupational Exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Transport and warehousing	10	1-2 hr	20 days/year
Retail workers	5000	0.5 hr	100 days/year
Salon workers	1000	0.5 hr	200 days/year

Exposure Details
Waterside, transport and warehouse workers will only handle the imported product packed in boxes. Supermarket workers will unpack the boxes and place the containers on supermarket shelves.

Salon workers will open the hair dye kit, remove and open the bottles of hair dye. They will pour a small amount of the dye (40 mL) into a small mixing vessel, mix with developer and apply it to the customer's hair by brush. Disposable gloves are supplied with each kit. The hair is then rinsed into the basin and dried with a towel.

EDUCATION & TRAINING
The MSDS will be made available to all workers. Salon workers are trained in the safe use of salon chemical products. No other specific training is proposed.

PREVALENCE OF WORK-RELATED INJURIES & DISEASES
No injuries or diseases related to exposure to the chemical are known. The chemical is not known to exacerbate any existing health conditions.

OTHER OCCUPATIONAL HAZARDS
No other occupational hazards are known.

OCCUPATIONAL HEALTH MONITORING (BIOLOGICAL MONITORING & ATMOSPHERIC MONITORING)
No biological or atmospheric monitoring is proposed.

5.4. Release

RELEASE OF CHEMICAL AT SITE
No manufacturing or reformulation will take place in Australia.

RELEASE OF CHEMICAL FROM USE
Average Release

It can be assumed that 90% of the notified chemical will be released to sewer and 10% will remain as residue in empty containers and will be disposed of to landfill via domestic garbage collection. Thus, <450 kg/year of the notified polymer will be released to sewer and <50 kg/year will end in landfill.

Assuming the average wastewater discharged to the sewer in Australia is approximately 200 L/person/day and that the population of Australia is approximately 19.5 million, the wastewater discharged to the sewer is approximately 3 900 ML/day. Therefore, the maximum PEC can be calculated as follows:

PEC = (450/365) / 3900 = 0.315 µg/L

Point Source Estimate

Based on a hair dye which contains <5% of the notified chemical and 40 g being used per application, the amount of notified chemical per application is <2000 mg.

The average water usage in a shower is assumed to be approximately 60 L (US EPA 1995). Therefore, <33 mg/L (ppm) notified chemical will be released to sewer for each use.

The PEC in metropolitan and rural areas is estimated to be <0.03 ppm (1:1000 dilution) and <0.8 ppm (1:40 dilution), respectively.

5.5. Disposal

Empty containers will be disposed to landfill via household garbage collection.

5.6. Public Exposure

The notified chemical will be used as a component of permanent hair dye at a maximum concentration of <5%. The hair dyes will be sold into the consumer market. The directions for use and warnings are clearly stated on the label. With each application 40 mL of the dye (2000 mg of the notified chemical) is mixed with developer in a 1:1 ratio and is then applied to the hair. Thus, the concentration of the notified chemical applied to the hair is less than 2.5%. The dye remains in contact with the hair for 15 minutes and is then rinsed off with water and the hair is shampooed and conditioned. The application is repeated once every 2 months.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Light grey powder

Melting Point/Freezing Point >300ºC

METHOD EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
TEST FACILITY Henkel (2001a)

Boiling Point >300ºC at 101.3 kPa

METHOD EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks No melting was observed up to the thermal decomposition temperature of 346ºC.
TEST FACILITY Henkel (2001b)

Density Not determined

METHOD OECD TG 109 Density of Liquids and Solids.
EC Directive 92/69/EEC A.3 Relative Density.
Remarks The density of the notified chemical has not been measured. However, it will be imported into Australia in a liquid hair dye with a density of approximately 1.0 g/mL.

Vapour Pressure 2.3×10^{-9} kPa at 20ºC.

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Vapour pressure was determined using differential scanning calorimetry (DSC). Additional thermogravimetric analysis was performed to assist in the interpretation of DSC results. A vapour pressure was also estimated based on Lyman *et al*. (1982). The results indicate the notified chemical is only very slightly volatile according to Mensink *et al*. 1995.
TEST FACILITY Henkel KGaA (2001c)

Water Solubility 183 g/L at 30ºC

METHOD EC Directive 92/69/EEC A.6 Water Solubility (Flask method).
Remarks A GLP study was performed where excess test substance was dissolved in water and stirred at 30ºC for 24 h then allowed to stand until equilibrium was reached. The concentration of test material was determined by Liquid chromatography. The notified chemical is readily soluble in water (Mensink *et al*. 1995).
TEST FACILITY Henkel KGaA (2001d)

Hydrolysis as a Function of pH Not determined
Remarks The notified chemical does not contain any groups that can undergo hydrolysis.

Partition Coefficient (n-octanol/water) log Pow = -4.0265 at 22.3 ºC

METHOD EC Directive 92/69/EEC A.8 Partition Coefficient (Shake Flask method).
Remarks A GLP study was performed using three ratios of n-octanol/water (1:1, 1:2, 2:1) and concentrations of 0.01 mol/L test substance. Test concentrations in each phase were determined by liquid chromatography. The notified chemical is not lipophilic.
TEST FACILITY Henkel KGaA (2001e)

Adsorption/Desorption Not determined

Remarks Based on the extremely low water/octanol partition coefficient and high water solubility, the notified chemical is unlikely to bind to organic matter in soils, but being a salt it may have an affinity toward silicates.

Dissociation Constant Not determined

Remarks The notified chemical contains phenol groups, which are expected to have pKa values of 8-10 and aryl amino groups, which will have pKa values of 1-5. However, since the notified chemical is in a salt form, it is expected to be fully dissociated in water, except at very low pH.

Particle Size Not determined

Remarks The notified chemical is imported in a liquid product.

Flash Point Could not be determined.

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks No flash point was determined as the notified chemical is a solid with a melting point >300ºC.
TEST FACILITY Henkel (2001f)

Flammability Limits Not flammable

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
EC Directive 92/69/EEC A.12 Flammability (Contact with Water).
TEST FACILITY Henkel (2001g)

Autoignition Temperature 216ºC

METHOD 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
TEST FACILITY Henkel (2001h)

Explosive Properties Not explosive.

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks The notified chemical is not sensitive to heat, impact or friction.
TEST FACILITY Henkel (2001i)

Reactivity

Remarks The notified chemical is stable under normal conditions of use. The chemical is hydrolytically, and thermally stable. However, the chemical will undergo oxidation.

Oxidizing Properties Not an oxidising substance.

METHOD EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks No spreading of the flame was observed with any of the various mixtures of the notified chemical with cellulose. No flame or glow persisted when the Bunsen burner was removed.
TEST FACILITY Henkel (2001j)

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral	toxic (LD50 25 < LD50 < 200 mg/kg bw)
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	irritating
Guinea pig, skin sensitisation -non-adjuvant test.	no evidence of sensitisation.
Rat, oral repeat dose toxicity - 28 days.	LOAEL = 60 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	non mutagenic
Skin absorption study	Low skin absorption

7.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/Him:OFA, SPF
Vehicle	Deionised water
Remarks – Method	No deviations from test protocol

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 male	25	0/3
2	3 females	25	0/3
3	3 males	200	3/3
4	3 males	2000	3/3

LD50	25 < LD50 <200 mg/kg bw
Signs of Toxicity	Body weight gain was normal in surviving animals. Death was observed in the high dose group within one hour of dosing, while animals in the mid dose group survived for 2 to 4 days. Clinical observations in surviving animals (25 mg/kg) were piloerection, chromodacryorrhoea (coloured overabundant tears), discoloured urine and hunched posture lasting from 1 day (females) to 4 days (males). In the 200 mg/kg the additional symptoms pale skin, retention of faeces, tremor, sedation, dyspnoea were observed on the first day of administration and lasting until the death of the animal. In the high dose group, piloerection, hunched posture and sedation in one rat and unconsciousness in 2/3 rats was observed immediately after administration.
Effects in Organs	At necropsy, exsiccosis (drying), ulcers of the glandular stomachs mucosa with haemorrhages, a pale mucosa in the intestine and haemorrhages in the lung, a small spleen and clear exudate in the lung were observed in the males of the 200 mg/kg group. No findings were noted in animals in the 25 mg/kg group.
Remarks – Results	The test substance caused gastric ulceration and pulmonary haemorrhages with secondary circulatory problems and signs of general malaise at doses of 200 mg/kg b.w. and above, leading to 100% mortality. All signs noted in life and at necropsy may be directly or indirectly related to this main effect.
CONCLUSION	The notified chemical is toxic via the oral route.
TEST FACILITY	Seiberdorf (1998)

7.4. Irritation – skin

TEST SUBSTANCE Notified chemical

METHOD OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 females
Vehicle Deionised water
Observation Period 72 hours
Type of Dressing Semi-occlusive.
Remarks – Method No deviations from test protocol

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0	0	0	1	1 hr	0
Oedema	0	0	0	0	0	0

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

Remarks – Results The application site was stained grey in all animals from 1h to 24 h after patch removal.

CONCLUSION The notified chemical is non-irritating to skin.

TEST FACILITY Seiberdorf (1998b)

7.5. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 females
Observation Period 26 days
Remarks – Method No deviation from test protocol.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	2	3	2.67	3	17 days	0
Conjunctiva: chemosis	2.33	4	2.67	4	13 days	0
Corneal opacity	0	1	0	2	21 days	0
Iridial inflammation	0	0.33	0	1	17 days	0

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

Remarks – Results Discharge of the conjunctiva was not scored. All effects were reversible.

CONCLUSION The notified chemical is severely irritating to the eye.

TEST FACILITY Seiberdorf (1998c)

7.6. Skin sensitisation

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 406 Skin Sensitisation – Buehler method.
Species/Strain	Guinea pig/ Dunkin Hartley HsdPoc:DH
PRELIMINARY STUDY	Maximum Non-irritating Concentration: topical: 50% in white petrolatum (maximum concentration feasible)
MAIN STUDY	
Number of Animals	Test Group: 20 females Control Group: 10 females
induction phase	Induction Concentration: topical application 50%
Signs of Irritation	3/20 animals showed irritation with a score of 1 or 2 after the second or third induction.
CHALLENGE PHASE	
1st challenge	topical application: 50%
Remarks – Method	The test substance did not stain the skin of the guinea pigs and scoring was not impeded by skin dyeing.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	50%	1	1		
Control Group	50%	0	0		

Remarks – Results	The number of animals in the test group showing a positive reaction (Score of 2) after the challenge was 1/20 (5%).
CONCLUSION	The notified chemical is not a skin sensitiser under the conditions of the test.
TEST FACILITY	Seiberdorf (1998d)

7.7. Repeat dose toxicity (oral)

TEST SUBSTANCE

METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rats/Hsd:Sprague Dawley SD
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days; Dose regimen: 7/7 days per week; Post-exposure observation period: None
Vehicle	Distilled water
Remarks – Method	Distilled water was used as the vehicle in this study in place of 0.5% carboxymethylcellulose indicated by the protocol, due to the low solubility of the test item in the latter vehicle.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	5 m + 5 f	0	0
II (low dose)	5 m + 5 f	60	0

III (mid dose)	5 m + 5 f	80	0
IV (high dose)	5 m + 5 f	100	0

Mortality and Time to Death
None

Clinical Observations
Discolouration of urine was observed in all treated groups. Food consumption and body weight gain were not significantly affected.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
There were no remarkable changes in haematology. Urinalysis was not conducted. Statistically significant changes in clinical chemistry parameters (increased total cholesterol in high-dose males, decrease in alkaline phosphatase and alanine aminotransferase in high dose females, increase in glucose concentration in high dose animals) were within the range of historical control data.

Effects in Organs
Terminal body weights and organ weights:
At necropsy, organ weights were comparable in all groups.

Pathology – Macroscopic
Macroscopic findings were not remarkable.

Pathology – Microscopic
Histopathology of the control and high dose group showed changes in the kidney. These kidney changes were subsequently observed in the other treatment groups as well. Brown pigmentation was observed in the cytoplasm of the proximal renal tubules. Mild chronic interstitial inflammation, mostly in the cortical area, as well as basophillia and tubular dilation were observed.

CONCLUSION
The Lowest Observed (Adverse) Effect Level (LO(A)EL) was established as 60 mg/kg bw/day in this study, based on histological changes in the kidney. The NO(A)EL was not established.

TEST FACILITY Research Toxicology Centre (2000)

7.8. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102.
Metabolic Activation System	Rat liver S mix.
Concentration Range in Main Test	a) With metabolic activation: 33 to 5000 µg/plate. b) Without metabolic activation: 33 to 5000 µg/plate.
Vehicle	Deionised water or DMSO
Remarks – Method	Both plate incorporation procedure (test 1) and Pre incubation procedure (test 2) were used in the study.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	None*	1000#, 5000**	-	-

Test 2	1000#, 2500*	-	-
Absent			
Test 1	1000#, 2500*	-	-
Test 2	-	-	-

* TA 98, **TA 100, # TA 1537

Remarks – Results	No substantial increase in revertant colony numbers of any of the five tester strains was observed following treatment at any dose level, with or without metabolic activation.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	RCC-CCR (1998)

7.18T. Skin Absorption Studies

TEST SUBSTANCE	Notified Chemical
METHOD	Test guidelines for *In Vitro* Assessment of Dermal Absorption and Percutaneous Penetration of Cosmetic Ingredients (Diembeck *et al*, 1999)

STUDY DESIGN AND OBJECTIVE

The study investigated the dermal absorption and percutaneous penetration of the test substance in pig skin *in vitro.* The test substance was studied as an ingredient (at 3-6%) in two formulations representative of direct hair dyes (A) and oxidation hair dyes in combination with a developer mix (B). Two independent experiments were performed with each formulation using six integrity checked dermatomed skin preparations in each experiment. The experiments were performed in flow-through penetration cells with an application area of 0.5 cm^2. The ^{14}C-labelled test substances were applied topically to the horny layer of the skin in quantities of 22.9 mg (A) and 22.2 mg (B) respectively, which corresponded to 469 µg (A) and 453 µg (B) of the test chemical. The non-occlusive exposure under room temperature controlled conditions lasted 30 minutes before rinsing.

After 48 hours, the *stratum corneum* was removed by repeated stripping with adhesive tape to obtain the adsorbed test substance. The remaining skin was taken to determine the absorbed test substance. The penetration was calculated from the ^{14}C-amount in the fractionated receptor fluid consisting of phosphate buffered saline plus 3% bovine serum albumin. The overall amount of bioavailable test substance is defined as the sum of absorbed and penetrated quantities.

RESULTS

Adsorption: Most of the radioactivity was detected in the first tape, then a gradual decrease with the number of tapes was noted.
Absorption: Low amounts of radioactivity were detected in the dermis and the residual epidermis, including the remaining hair stubs and hair shafts.
Percutaneous penetration: The penetration with formulation B was just below the detection limit of ca. 0.01% of dose.
Penetration rate: The penetration rate gained its maximum at ca. 1.5 h after the start of exposure and then decreased, with both formulations.
Mass balance: The total recovery of test substance equivalents is within the limits of 100 ± 15% as set in the recovery plan.

Mean of test results

Parameter	Formulation A [%]	Formulation B [%]	Formulation A [µg/cm^2]	Formulation B [µg/cm^2]
Skin rinsings	89.5	85.2	-	-
Adsorption	3.3	2.6	31	24
Absorption	0.91	0.39	8.2	3.5
Penetration	0.11	0.009	1.0	0.085
Bioavailability	1.02	0.40	9.2	3.6
Mass balance	94.7	89.1	-	-

CONCLUSION
The bioavailability of formulation A is 1.02% of the dose (9.2 µg/cm^2) and of formulation B 0.4% of the dose (3.6 µg/cm^2). The results showed that a low proportion of the notified chemical was absorbed by the skin and penetrated the skin.

TEST FACILITY Austrian Research Centres (2000)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE RO 1525

METHOD OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.

Inoculum	Municipal sewage sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Oxygen consumption and dissolved organic carbon.
Remarks - Method	The Theoretical Oxygen Demand of the reference and test substance was calculated from the empirical formula. The ThOD was 470 mg O_2/g for sodium acetate trihydrate, and $ThOD_{(NO3)}$ was 1869 mg O_2/g for the test substance.

RESULTS

Test substance		*Sodium acetate*	
Day	*% degradation*	*Day*	*% degradation*
4	0	4	73
14	3	14	89
28	5	28	91

Remarks - Results There was no significant degradation of the test substance during the 28-day test period. In comparison, the reference substance attained 91% degradation by the end of the test, indicating the test was valid.

CONCLUSION The notified chemical is poorly biodegradable.

TEST FACILITY Henkel KGaA Ecology, Dusseldorf, Germany (2001p)

8.1.2. Bioaccumulation

No bioaccumulation data were provided. On the basis of the low partition coefficient and high water solubility, the notified chemical is not expected to bioaccumulate.

8.2. Ecotoxicological investigations

The notifier provided one test report for *Daphnia*.

8.2.2. Acute/chronic toxicity to aquatic invertebrates

TEST SUBSTANCE RO 1525

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test - static conditions.

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	Not measured
Analytical Monitoring	Test concentrations by HPLC
Remarks - Method	Two replicates of 10 Daphnia each were exposed to test concentrations for 48 hours. The concentrations in solution were determined at 0, 24 and 48 hours. The test media was clear or light reddish (high concentrations) at the start of the test, while a precipitate was formed in concentrations above 3 mg/L after about 24 hours. The EC_{50} was calculated by

interpolation between two values according to the probit method.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	-	2 X 10	0	0
0.1	-	2 X 10	0	0
0.3	-	2 X 10	1	2
1	<0.1	2 X 10	9	13
3	<0.1	2 X 10	18	20
10	<0.1	2 X 10	12	16
30	6.3	2 X 10	11	15
100	34.7	2 X 10	18	18

EC50	0.76 mg/L at 48 hours (nominal)
NOEC (or LOEC)	0.10 mg/L at 48 hours
Remarks - Results	The effects concentrations are reported as nominal concentrations because the analytical recovery of the test substance was below the detection limit. It was hypothesised that the poor recovery of test material was due to the formation of a precipitate (after 24 h in test concentrations >3 mg/L) through hydrolysis-oxidation between the test substance and salts in the test medium. However, since no test substance could be determined at the lower concentrations it may have been due to the enrichment method used, which involved drying the substance in a rotary evaporator at 70ºC.
CONCLUSION	The test substance is highly toxic to Daphnia (Mensink *et al*. 1995).
TEST FACILITY	Henkel KGaA Ecology, Dusseldorf, Germany (2001q)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

No manufacturing or reformulation of the notified chemical will take place. The notified chemical is a component in a finished hair dye product and as such almost all of the chemical could be released into sewer during end use when the dye is washed off hair. The product will be sold nationwide and hence release is expected to occur in a diffuse manner. The notifier estimates an average of 90% of the notified chemical will be released to sewer and 10% will remain as residue in empty containers. This equates to <450 kg/year of the chemical released to sewer and <50 kg/year released to landfill.

As with most permanent hair colouring products, the product containing the notified chemical consists of two components, the colour gel and a developer. These components are mixed together just prior to application, and are then immediately applied to the hair, where they penetrate the hair cuticles and continue to react to form the hair dye. Consequently, once the notified chemical is developed on the hair (usually after about 30 minutes), it will have reacted with other chemicals to form a dye, which becomes fixed to the hair, and from where it will be released very gradually. Some of the fixed dye may also photo-chemically degrade over time on the hair. Nevertheless, the worst-case predicted environmental concentration (PEC) for the notified chemical is calculated assuming the chemical is released gradually by repeated washing in its original form rather than in the form of a reacted and insoluble dye.

The calculated diffuse daily PEC in the sewer is <0.315 µg/L, assuming water use of 3900 ML/day (200L per person for a population of 19.5 million), no partitioning from the sewer to the atmosphere or sediment, and no degradation. PEC values of <0.03 mg/L (1:1000 dilution) and <0.8 mg/L (1:40 dilution) were also calculated for metropolitan and rural areas, respectively.

The PEC would be further reduced by dilution in receiving waters. Assuming a conservative dilution ratio of 10:1 for oceans, and no dilution for a river, the PEC is 0.0315 µg/L for release into oceans, but no change to the PEC in rivers.

No PEC is calculated for soil. Less than 50 kg per year of the notified chemical is expected to be sent to landfill in used containers via domestic garbage. Release will also occur in a diffuse manner, resulting in very low concentrations in the soil should the containers rupture and the contents spill. The notified chemical contained in the hair dye is water-soluble and could potentially leach into soil and groundwater.

The notified chemical is poorly biodegradable according to the Manometric test for ultimate biodegradability, and may persist in the environment. However, its high water solubility and low P_{OW} should preclude it from bioaccumulating.

The notified chemical has an expected pKa of 8-10 for the phenol groups and 1-5 for the aryl amino groups suggesting it is unlikely to become neutral under environmental conditions of pH 4-9, except in extreme pH ranges. However, the notified chemical is a salt, and is expected to fully dissociate in water. Consequently, there may be some adsorption to ions in water, soil and sediment, evidenced by it forming a precipitate in the test media during the Daphnia test.

9.1.2. Environment – effects assessment

Only one ecotoxicity test was provided. The results indicate the test substance is highly toxic to *Daphnia magna*, with an LC50 of 0.76 mg/L and an NOEC of 0.1 mg/L. The PNEC is 0.76 µg/L, assuming a safety factor of 1000 (used when only one acute toxicity endpoint is available).

9.1.3. Environment – risk characterisation

Up to 90% of the imported volume, equating to less than 450 kg per year, of notified chemical could be released in a diffuse manner via sewage treatment facilities. A worst-case daily nationwide PEC in the sewer is 0.315 µg/L, assuming all of the dye is released gradually during hair washing. The PEC would be further reduced by dilution in receiving waters to 0.0315 µg/L

in oceans, but we assume no dilution in rivers.

The notified chemical is highly toxic to Daphnia, and it can be assumed that it will also be toxic to other aquatic organisms. The calculated PNEC is 0.76 µg/L, using a safety factor of 1000. The resulting risk quotient (PEC/PNEC) is <0.4 indicating a low risk, where RQ >1 indicates a potential risk.

No PEC has been calculated for soil. Despite the possible persistence of the notified chemical in the environment, the risk to the environment is expected to be low because the relatively small import volume and diffuse manner of release will result in very low concentrations in both the aquatic and soil environments.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

During transport, storage and retail handling the hair dyes will be in a packaged form and exposure is only likely to occur when packages are damaged and leaking.

In salons, dermal exposure to unprotected parts of the hands, and possibly the wrist and forearm may occur. EASE modelling predicts exposure could be 0.1 to 1.0 mg/cm^2/day (dye) (EASE, 1997), equivalent to 50 µg/cm^2/day notified chemical.

Using the maximum exposure predicted by EASE, the dose can be calculated as follows:

Exposure	0.05 mg/cm^2/day
Area of skin exposed (hands)	840 cm^2
Bodyweight	60 kg
Dermal absorption	1% (Henkel, 2000)
Estimated dose	0.007 mg/kg/day

Exposure duration is likely to be lower for salon workers than for users, as the dye would be washed off immediately after application, however, exposure could occur more frequently. Incidental exposure to the eye may occur from splashes.

9.2.2. Public health – exposure assessment

As gloves are provided with the dye kit, exposure is only likely to occur from skin contact on the scalp. Based on the amount of notified chemical in the dye kit, the potential dose can be calculated:

Amount of dye per application	40 g
Concentration of chemical	5%
Amount of chemical	2000 mg
Dermal absorption	1 % (Henkel, 2000)
Exposure frequency	6 days/year
Body weight	60 kg
Estimated dose	0.0055 mg/kg/day

9.2.3. Human health - effects assessment

Toxicological studies of the notified chemical submitted were acute oral toxicity, skin irritation, eye irritation, skin sensitisation, 28-day repeat dose (oral), genotoxicity (Bacterial Reverse Mutation Test), and skin absorption studies.

The notified chemical is toxic via the oral route. The LD_{50} is between 25 and 200 mg/kg bw. Reversible symptoms (piloerection, chromodacryorrhoea (coloured overabundant tears), discoloured urine and hunched posture) lasting 1 to 4 days were observed at 25 mg/kg bw. All animals in the 200 mg/kg bw group died.

In the 28-day repeat dose (oral) study in rats, a LO(A)EL of 60 mg/kg bw/day was established based on microscopic changes to the kidney.

The notified chemical is severely irritating to the eye. Reversible ocular lesions, lasting up to 17

days occurred in all animals.

The notified chemical was not a skin irritant or sensitiser, and was not genotoxic based on the results of the tests submitted.

9.2.4. Occupational health and safety – risk characterisation

The toxicological studies presented for the notified chemical are limited, and a NOAEL was not established in either the acute or repeat dose tests. The margin of exposure (LOAEL/systemic exposure dose) for the notified chemical is estimated to be 8600, indicating a low risk of kidney effects from repeated exposure. However, there is some uncertainty concerning this estimate, as it is based on the LOAEL rather than the NOAEL, the exposure has been estimated rather than measured and the percent dermal absorption is based on animal rather than human studies.

Although the dermal absorption studies indicate that systemic absorption via the dermal route is likely to be low, salon workers may have compromised skin barrier function due to frequent hand immersion in cleaning agents that tend to defat the skin. Good occupational hygiene practices, such as the wearing of plastic or cotton lined gloves and prompt removal of contaminants from the skin will be required to reduce risk of adverse effects. Further, the wearing of eye protection when using dyes containing the notified chemical is recommended.

9.2.5. Public health – risk characterisation

The margin of exposure (LOAEL/systemic exposure dose) for the notified chemical is estimated to be 11000, indicating a low risk of kidney effects from repeated exposure. However, this estimate is the subject of uncertainties as detailed in the above section.

Warnings on the label indicate that the product is harmful when swallowed and an eye irritant. The warnings preclude the use of the product for dyeing eyebrows or eyelashes due to the possibility of eye injury. Safety directions state that eyes should be protected when using. Consequently, the use of the hair dye strictly in accordance with the product instructions should minimise the potential risk to the public.

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

10.1. Hazard classification

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*. The classification details are:
T: R25 Toxic if swallowed
Xi: R36 Irritating to eyes

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio: the chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is low concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is low concern to public health associated with the use of this chemical if used in accordance with product instructions.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the product containing the chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994a). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for the products containing the chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994b). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS
Hazard Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:
  - T: Toxic. R25 Toxic if swallowed
  - Xi: Irritant. 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 products containing the notified chemical:
  - Equipment and work stations should be designed to minimise contact with the product containing the notified chemical.
  - If accidental contact occurs, the product containing the notified chemical should be removed from the skin or eye immediately

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to products containing the notified chemical:
  - Gloves, safety glasses

  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.

Public Health

- The following measures should be taken by the notifier to minimise public exposure to the notified chemical:
  - Label for the product containing the notified chemical should carry the Warning Statement 88, Appendix F of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP): "This product is not recommended for dyeing eyelashes or eyebrows. To do so may be injurious to the eye."
  - The concentration of the notified chemical in hair dye formulations should not exceed 5%.

Environment

Disposal

- The notified chemical should be disposed of through household garbage.

Emergency procedures

- Spills/release of the notified chemical is unlikely given the nature of the packaging. The small container size would limit any release to the environment.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under subsection 64(1) of the Act; if
- The concentration of the notified chemical in the product exceeds 5%.
- Other toxicological data becomes available, e.g. a 90-day repeat dose toxicity study.

or

(2) Under subsection 64(2) of the Act:
- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

13. BIBLIOGRAPHY

Austian Research Centres, Toxicology (2000). Dermal absorption/Percutaneous Penetration of RO 1525 in vitro (Study No. EH 64). Wiena, Austrai, ARC(Unpublished report submitted by Henkel Australia Pty Ltd).

Diembeck, W et al, (1999) "Test Guidelines for *In Vitro* Assessment of Dermal Absorption and Percutaneous Penetration of Cosmetic Ingredients"; *Food and Chemical Toxicology* 37:191-205.

EASE for Windows Version 2.0, August (1997). *A system for the Estimation and Assessment of Substance Exposure (EASE)*. The Health and Safety Executive, UK

Henkel KGaA (2001a) Determination of the Melting Point of RO 1525 in accordance with EEC-Guideline A.1 (Study No 00-9216-5). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001b) Determination of the Boiling Point of RO 1525 in accordance with EEC-Guideline A.2 (Study No 00-9216-6). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001c) Determination of the Vapour Pressure of RO 1525 in accordance with EEC-Guideline A.4 (Study No 00-9216-4. Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001d) Determination of the Water solubility of RO 1525 in accordance with EEC-Guideline A.6 (Study No 00-9216-2. Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001e) Determination of the Partition Coefficient of RO 1525 in accordance with EEC-Guideline A.8 (Study No 00-9216-3) Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001f) Determination of the flash point accordance with EEC-Guideline A.9 (Study No 00-9216-7) Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001g) Determination of the flammability of RO 1525 in accordance with EEC-Guideline A.12 (Study No 00-9216-8). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001h) Determination of the Auto-flammability of RO 1525 in accordance with EEC-Guideline A.16 (Study No 00-9216-9). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001i) Determination of the explosive properties of RO 1525 in accordance with EEC-Guideline A.14 (Study No 00-9216-11). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001j) Determination of the oxidising properties of RO 1525 in accordance with EEC-Guideline A.17 (Study No 00-9216-10). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (1998?) Acute Dermal Irritation/Corrosion Test of RO 1525 in Rabbits in accordance with OECD Test Guideline No. 404 (Study No. HE48). Henkel KGaA, Wiena, Austraia (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (1998?) Acute Eye Irritation/Corrosion Test of RO 1525 in Rabbits in accordance with OECD Test Guideline No. 405 (Study No. HE49). Henkel KGaA, Wiena, Austraia (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (1998?) Acute Oral Toxicity Test of RO 1525 in Rats in accordance with OECD Test Guideline No. 423 (Study No. HE50). Henkel KGaA, Wiena, Austraia (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (1998?) *Salmonella typhimurium* Reverse Mutation Assay with RO 1525 in accordance with OECD Test Guideline No. 471 (Project No 613001). Itingen, Switzerland, Henkel KGaA (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (1998?) Skin Sensitisation Test of RO 1525 in Guinea Pigs, Buehler Test in accordance with OECD Test Guideline No. 406 (Study No. HE47). Henkel KGaA, Wiena, Austraia (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001p) Ultimate Biodegradation in Manometric Respirometry Test of RO 1525 in accordance with OECD Test Guideline No. 301F (Report No. R0100227). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Henkel KGaA (2001q) Acute Toxicity of RO 1525 to Daphnia Magna in accordance with OECD Test Guideline No. 202/1 (Study No. 00038801). Henkel KGaA, Dusseldorf, Germany (Unpublished report submitted by Henkel Australia Pty Ltd).

Lyman WJ, Reehl W and Rosenblatt D (1982). Handbook of chemical property estimation methods, McGraw-Hill.

Mensink BJWG, Montforts M, Wijkhuizen-Maslankiewicz L, Tibosch H and Linders JBHJ (1995). Report no. 679101022: Manual for Summarising and Evaluating the Environmental Aspects of Pesticides. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

National Occupational Health and Safety Commission (1994a) National Code of Practice for the Preparation of Material Safety Data Sheets [NOHSC:2011(1994)]. Australian Government Publishing Service, Canberra.

National Occupational Health and Safety Commission (1994b) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. Australian Government Publishing Service, Canberra.

National Occupational Health and Safety Commission (1995) Adopted National Exposure Standards for Atmospheric Contaminants in the Occupational Environment, [NOHSC:1003(1995)]. In: Exposure Standards for Atmospheric Contaminants in the Occupational Environment: Guidance Note and National Exposure Standards. Australian Government Publishing Service, Canberra.

National Occupational Health and Safety Commission (1999) Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(1999)]. Australian Government Publishing Service, Canberra.

Reasearch Toxicology Centre (RTC) S.p.A. (2001) 28-Day Subacute Oral Toxicity Study in Rats (Gavage) with RO 1525 in accordance with OECD Test Guideline No. 407 (Study No. 7796). Rome, Italy, RTC (Unpublished report submitted by Henkel Australia Pty Ltd).

US EPA. Exposure Factors Handbook. EPA/600/P-95/002A. June 1995.