File No: NA/827

June 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT- AMENDED

Phenol, 3-amino-2-chloro-6-methyl, hydrochloride

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Director
Chemicals Notification and Assessment

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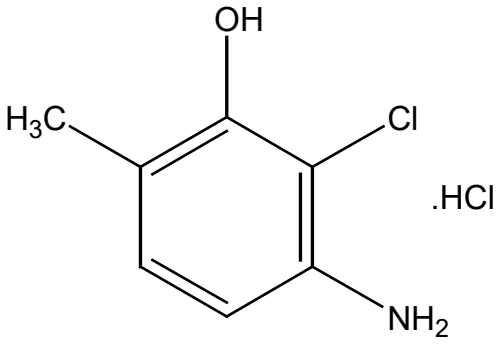
1. APPLICANT

Schwarzkopf Pty. Ltd. of 20 Rodborough Road, Frenchs Forest, NSW 2086 (ABN 21 000 076 782) and Cosmetic Products Pty. Ltd. of 1 Wella Way, Sommersby, NSW 2250 (ABN 19 000 128 101) have submitted a joint limited notification statement in support of their application for an assessment certificate for Phenol, 3-amino-2-chloro-6-methyl, hydrochloride. No application for information regarding the chemical to be exempt from publication was made by Schwarzkopf Pty. Ltd. or Cosmetic Products Pty Ltd.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	Phenol, 3-amino-2-chloro-6-methyl, hydrochloride
Chemical Abstracts Service (CAS) Registry No.:	80419-48-3
Other Names:	5-Amino-6-chloro-o-cresol, hydrochloride. 2-Chloro-6-methyl-3-aminophenol hydrochloride. 2-Hydroxy-3-methyl-6-amino-chlorobenzene hydrochloride
Marketing Name:	Napro Vital Colors 68 Cherry Fire
Molecular Formula:	$C_7 H_8 N Cl O . HCl$
Structural Formula:	



Molecular Weight:	194

Method of Detection and Determination:	The notified substance was identified using ultraviolet/visible (UV/Vis) and infra-red (IR) spectroscopy.
Spectral Data:	IR peaks are located at approximately 3,300, 2,700, 2,550, 1,500, 1,200 and 800cm^{-1}. UV/Vis maxima were located at approximately 281 and 204 nm.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	Beige crystals
Melting point	144-183°C
Specific Gravity:	1.0 (approx)
Vapour Pressure:	2.4kPa at 20°C
Water Solubility:	8.75g/L, calculated using ACD software. The water solubility calculation was performed on the uncharged base form of the chemical and the hydrochloride salt would be expected to have higher solubility.
Partition Co-efficient (n-octanol/water):	Log P_{ow} = 1.73, calculated using ACD software for the uncharged form of the chemical. The partition coefficient would be expected to be lower for the salt.
Hydrolysis as a Function of pH:	Not determined. The notified chemical contains no groups expected to undergo hydrolysis.
Adsorption/Desorption:	Log K_{oc} = 2.3, calculated using ACD software. The notified chemical is expected to be mobile in soils and sediments.
Dissociation Constant:	Not determined. Dissociation constant calculations were performed using ACD software for separate parts of the chemical structure. The phenolic hydroxyl group has a pKa of 8.0-10.0 and the aniline amino group has a pKa of approximately 4.6.
Particle Size:	< 10μm: 10% 10-100μm: 85% > 100μm: 5%
Flash Point:	Not flammable.
Flammability Limits:	Not determined. The notified chemical is combustible but not flammable.

Autoignition Temperature:	Not determined. The notified chemical is not expected to autoignite.
Explosive Properties:	Not explosive.
Reactivity/Stability:	Stable. The notified chemical will react with strong oxidising agents.

3.1 Comments on Physico-Chemical Properties

No test reports on determination of physico-chemical properties were provided. Instead, all data were estimated from Quantitative Structure Activity Relationships (QSARs) by the notifiers using a commercial ACD software package. For neutral species, QSAR estimates may be acceptable as physico-chemical parameters to within ± 1 order of magnitude, (depending on the true validity of the regression equations used), but for charged molecules QSAR estimates may be seriously in error (Kaiser et al., 1999). Consequently, the estimated data listed below should be treated with caution.

The water solubility calculation was performed on the uncharged base form of the chemical and the hydrochloride salt would be expected to have significantly higher solubility.

The notifiers claim that the determination of hydrolysis is not applicable to the chemical on the grounds that the chemical does not have any hydrolysable groups. This is accepted.

Partition co-efficient was also calculated using the uncharged form of the chemical and it would be expected to be appreciably lower for the salt.

The calculated Log K_{oc} of the chemical, (estimated on the basis of an uncharged molecule), indicates that it would have some mobility in soils and sediment. In reality since the chemical would be charged and has a high water solubility, the mobility in soil is likely to be appreciable.

A dissociation constant calculation was performed on the separate parts of the structure of the chemical. The phenolic hydroxyl group has a pKa of 8.0-10.0 and the aniline amino group has a pKa of approximately 4.6.

4. PURITY OF THE CHEMICAL

Degree of Purity:	> 94 %
Hazardous Impurities:	None.
Non-hazardous Impurities (> 1% by weight):	

Name	CAS No.	Weight %
p-Amino-o-cresol	2835-96-3	2.0
5-Amino-4-chloro-2-methylphenol	110102-86-8	2.8
2, 4-dichloro-6-methyl-3-aminophenol hydrochloride	None assigned	0.8

Additives/Adjuvants: None.

5. USE, VOLUME AND FORMULATION

Phenol, 3-amino-2-chloro-6-methyl, hydrochloride will be used as an oxidation (semi-permanent) dye for hair dye formulations. Schwarzkopf Pty Ltd will import up to 250kg/year of the notified chemical for 5 years in ready-to-use hair dye creams for the domestic market. The products will be imported in 50 mL tubes in cardboard boxes and the notified chemical will be present at ≤ 0.3%.

Cosmetic Products Pty Ltd will import up to 200kg/year of the notified chemical for 5 years in powdered dye concentrates for the local formulation of cream and liquid hair dye products for professional salons and the domestic market. The dye concentrates will be imported in 5kg laminated, vacuum-sealed plastic bags in 100-120 kg sealed plastic drums. Depending on the dye colour, the notified chemical will be present in the dye concentrates at 0-20%, and up to 4% in the finished products.

6. OCCUPATIONAL EXPOSURE

Import, Transport and Storage

The notified chemical will be imported as a component of a hair dye cream in 50 mL plastic tubes. In this form, the notified chemical will be present at ≤ 0.3%. The chemical will also be imported as a powdered dye concentrate in laminated, vacuum-sealed aluminium-lined polyethylene bags in plastic drums. The preformed product will be transported by road from dockside to Schwarzkopf warehouses prior to distribution to retail outlets. The dye concentrate will be transported by road to a single Cosmetic Products warehouse for reformulation and the hair dye product will then be transported to hair salons or retail outlets. Dockside, warehouse and transport workers will only be exposed in the event of accidental puncture of the product containers.

Reformulation

Plant operators working up to 8 hours/day for 150 days/year will open pre-weighed bags containing powdered dye concentrate and pour the concentrate manually into a 100kg mixing vessel containing hot water. After closing the lid and mixing until dissolution, the solution is then pumped to a closed 250kg mixing vessel where other ingredients are added to produce a liquid or cream hair dye product. The product is then pumped to an automatic multi-head filling machine and then into 60g tubes or 60mL bottles.

Exposure to the notified chemical may occur by inhalation during the opening and pouring of bags of powdered concentrate. Contact may also occur via slops and spills to the skin and

eyes during connection of transfer lines between mixing vessels and also during equipment cleaning and maintenance. Inhalation exposure is controlled by general and local exhaust ventilation at mixing points and the use of negative pressure respirators by workers during the opening of concentrate bags. Dermal exposure of workers is controlled by impervious gloves, coveralls and safety glasses.

Quality control staff working up to 4 hours/day for 150 days/year will sample and test raw materials and final formulations. Inhalation and dermal exposure to the notified chemical is possible for these workers. Inhalation exposure will be controlled by the forced ventilation of test areas. Dermal exposure will be controlled by the use of gloves, laboratory coats and safety glasses.

End-Use

The number of commercial salons across Australia likely to use the notified chemical is estimated in the 1,000s. 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 1 hour/day for 200 days/year. Prior to application to the hair, the hair colour product containing the notified chemical at up to 4% depending on colour is diluted with 50% developer and mixed in a plastic bowl with an applicator brush. The colour is applied by brush, left in contact with the hair for the required colour time (up to 30 minutes), and rinsed away with water.

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. Personal protective equipment to control exposure, where worn, would be cuff length disposable plastic or latex gloves and a plastic apron.

Retail Outlets

Retail hair colour products containing the notified chemical are packaged in 50 or 60 mL bottles and sold to the public through retail outlets. Retail workers should only be exposed to the chemical in the event of an accidental spill.

7. PUBLIC EXPOSURE

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

Public exposure to hair colourant products containing the notified chemical is likely to be intermittent (based on use pattern) and widespread (sold to the public and limited only by the commercial successes of the products). In the products from both companies, the notified chemical (≤ 0.3 % or 4%) will be diluted 1:1 with developer, leading to maximal exposure concentrations of ≤ 0.15 or 2%, respectively. Exposure will primarily occur via the dermal route, with the possibility of accidental ocular and oral exposure.

Calculations for a typical exposure from a hair colourant product were included in the submission. Using the highest concentration of notified chemical in a hair colourant product (4% in a volume of 50 mL = 2g), with a 1:1 dilution with developer provides a total application of 1g. Assuming a dermal absorption of 0.1 % (from a rat toxicokinetic study)

gives a dermal absorption per application of 1mg and a systemic exposure (assuming a body weight of 60 kg) of 0.015 mg/kg.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Reformulation Site (Cosmetic Products Pty Ltd):
Residue in the individual import bags is estimated to be 0.1% of the contents, which equates to a maximum of 200g/annum (based on the 200 kg/annum import volume for Cosmetic Products). The bags are not washed, a licensed waste disposal contractor disposes of the bags, with residue, and containers, presumably these will be taken to landfill.

One hundred and fifty batches of hair dye will be processed per year, ie. 3 per week. For each 100 kg batch there will be approximately 2 kg of product left in the process equipment, containing 0.08kg of the notified chemical. This will mean an annual release of 12 kg of the notified chemical from equipment cleaning. All equipment washwater is sent to the on-site treatment plant. The treatment plant consists of a 100,000 L averaging tank, a solids separator, a grease remover, automatic pH adjustment and a dissolved air flotation tank. The treated effluent, which is likely to contain the waste notified chemical, then enters the sewer.

All process areas are bunded so that any spill will be contained and disposed of by licensed waste contractors or sent to the on-site wastewater treatment plant. The notifiers have estimated that each is responsible for a 1% loss in spills equating to 4.5 kg/year of notified chemical.

User Sites:
Once the dye has been applied to hair and allowed to develop, the dye solution is rinsed from the hair and ultimately reaches the domestic sewer. Greater than 50% of the notified chemical is claimed to be adsorbed to hair. As a worst case scenario, it is assumed that 50% of the notified chemical (225 kg) will be released to the sewer with the rinse water.

The notifiers have estimated that 2% of the hair dye product will remain as residue in the bottles and tubes after use, ie. 9 kg/annum of the notified chemical. These containers will then be disposed of with domestic garbage and end up in a landfill.

A summary of estimated maximum annual amount of waste notified chemical generated is:

Source	Amount	Destination
Bag residue, 0.1%	0.2kg	Landfill
Equipment cleaning, 2%	12kg	Sewer
Spills, 1%	4.5kg	Sewer
Bottle residues, 2%	9kg	Landfill
Rinse water (users), 50%	225kg	Sewer
TOTAL	250.7kg	

8.2 Fate

Nearly all of the waste generated during the reformulation process and end use of the hair dye containing the notified chemical will be disposed of to the sewer. The chemical is expected to

remain dissolved in the water compartment due to its high water solubility and low P_{ow} and K_{oc} and will be rapidly diluted by the receiving waters (Lyman et al., 1982).

Residues remaining in the 'empty' import bags and bottles will be disposed of to landfill. Due to its high water solubility the chemical is likely to leach out of a landfill as the bags and bottles are destroyed but in very low concentrations and in a diffuse manner.

The biodegradation and bioaccumulation potentials were not determined but it would not be expected to present a significant bioaccumulation hazard to aquatic organisms due to its water solubility and low partition co-efficient (Lyman et al., 1982).

9. EVALUATION OF TOXICOLOGICAL DATA

Summaries of results from toxicological studies for the notified chemical were provided in a COLIPA (European Cosmetic, Toiletry and Perfumery Association) document No: A 094 (Sterzel and Steiling, 1996). Individual animal results were not reported.

9.1 Acute Toxicity

Summary of the acute toxicity of phenol, 3-amino-2-chloro-6-methyl, hydrochloride.

Test	*Species*	*Outcome*	*Reference*
Acute oral toxicity	rat	LD_{50} = 1360 mg/kg	Potokar (1992a) in Sterzel and Steiling (1996)
Acute oral toxicity	mice	LD_{50} = 1260 mg/kg	Potokar (1992b) in Sterzel and Steiling (1996)
Skin irritation (10% aqueous solution)	rabbit	Non-irritating	Potokar (1992c) in Sterzel and Steiling (1996)
Eye irritation (5% aqueous solution)	rabbit	Slight irritant	Potokar (1992f) in Sterzel and Steiling (1996)
Repeated application skin irritation (10%)	mice	Non-irritating	Potokar (1992e) in Sterzel and Steiling (1996)
Repeated application skin irritation (10%)	rabbit	Non-irritating	Potokar (1992d) in Sterzel and Steiling (1996)
Skin sensitisation	guinea pig	Slightly sensitising	Potokar (1992g) in Sterzel and Steiling (1996)

9.1.1 Oral Toxicity

9.1.1.1 Oral Toxicity – Rats (Potokar, 1992a in Sterzel and Steiling, 1996)

Species/strain:	TNO-Wistar rats
Number/sex of animals:	10 or 20 per group, males
Observation period:	14 days
Method of administration:	Gavage
Test method:	Not provided
Clinical observations:	Apathy, staggering, enhanced and later stage hindered breathing, abnormal abdominal position, yellow-orange discolouration of the urine.
LD_{50}*:*	1360 mg/kg
Result:	The notified chemical was of moderate acute oral toxicity in rats.

9.1.1.2 Oral Toxicity – Mice (Potokar, 1992b in Sterzel and Steiling, 1996)

Species/strain:	CF1 mice
Number/sex of animals:	10 per group, males
Observation period:	14 days
Method of administration:	Gavage
Test method:	Not provided
Clinical observations:	Apathy, enhanced breathing, abnormal abdominal position, cramps, abnormal utterances
LD_{50}*:*	1200 mg/kg
Result:	The notified chemical was of moderate acute oral toxicity in mice.

9.1.2 Skin Irritation of a 10% Aqueous Formulation (Potokar, 1992c in Sterzel and Steiling, 1996)

Species/strain:	Rabbits, New Zealand White

Number/sex of animals:	6 males
Observation period:	48 hours
Method of administration:	Notified chemical (3g) dissolved in 10mL distilled water, 5 mL ammonium (conc) and 30mL ethanol (96%) and 0.5mL applied to shaved, intact skin by dermal patch for 2 hours.
Test method:	Not provided.
Comment:	No signs of irritation or corrosivity were observed. Individual Draize scores were not provided.
Result:	A 10% aqueous formulation of the notified chemical was not irritating to the skin of rabbits.

9.1.3 Eye Irritation of a 5% Aqueous Formulation (Potokar, 1992f in Sterzel and Steiling, 1996)

Species/strain:	Rabbits, New Zealand White
Number/sex of animals:	6 males
Observation period:	48 hours
Method of administration:	0.1mL of 5% notified chemical in water instilled into conjunctival sacs of right eyes.
Test method:	Not provided.
Comment:	No effects on the cornea or iris were observed. Slight conjunctival oedema and erythema were observed for up to 24 hours after instillation. Individual Draize scores were not provided.
Result:	A 5% aqueous formulation of the notified chemical was slightly irritating to the eyes of rabbits.

9.1.4 Skin Sensitisation (Potokar, 1992g in Sterzel and Steiling, 1996)

Species/strain:	Guinea pigs, Pirbright White
Number of animals:	20 per group
Induction procedure:	Intradermal injections using 5% notified chemical in water followed one week later by topical application using 5% cream of notified chemical in Vaseline under occlusive dressing for 48 hours.

Challenge procedure:	Fourteen days later, topical application of 25% cream of test substance in Vaseline under occlusive dressing for 24 hours.
Test method:	Magnusson and Kligman maximisation test; similar to OECD TG 406
Challenge outcome:	Twenty-five percent of test animals showed slight erythema 24 hours after challenge. No dermal effects were observed at 48 hours.
Comment:	Irritation was observed after topical application.
Result:	The notified chemical was slightly sensitising to the skin of guinea pigs.

9.2 Repeated Dose Skin Irritation

9.2.1 Repeated Dose Skin Irritation of 10% Aqueous Formulation – Mice (Potokar, 1992e in Sterzel and Steiling, 1996)

Species/strain:	Mice, hairless, hr/hr
Number/sex of animals:	5 males
Method of administration:	One drop of 10% aqueous formulation (3g notified chemical, 10mL distilled water, 5mL ammonium (conc.) in 30mL ethanol (96%)) applied to back, twice per day.
Dose/Study duration:	5 days
Test method:	Not provided.

Clinical observations:
No primary skin irritation could be observed during or after the application period. Individual Draize scores were not provided.

Result:
A 10% aqueous formulation of the notified chemical was not irritating to the skin of mice following repeated dermal application.

9.2.2 Repeated Dose Skin Irritation of a 10% Aqueous Formulation – Rabbits (Potokar, 1992d in Sterzel and Steiling, 1996)

Species/strain:	Rabbits, New Zealand White
Number/sex of animals:	6 males

Method of administration:	One drop of 10% aqueous formulation (3g notified chemical, 10mL distilled water, 5ml ammonium (conc.) in 30mL ethanol (96%)) applied to back every 30 seconds for 30 minutes.
Dose/Study duration:	30 minutes
Test method:	Burckhardt (1970)

Clinical observations:
No primary skin irritation could be observed during or after the application period. Individual Draize scores were not provided.

Result:
A 10% aqueous formulation of the notified chemical was not irritating to the skin of rabbits following repeated dermal application.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Banduhn, 1993 in Sterzel and Steiling, 1996)

Strains:	TA 98, 100, 1535, 1537, 1538
Metabolic activation:	Rat liver S9 mix – Aroclor 1254 and Phenobarbital induced enzymes
Concentration range:	4 – 2500 μg/plate (5 doses)
Test method:	Similar to OECD TG 471
Comment:	The notified chemical induced reverse mutations in strains TA 98, 100 and 1538 in the presence of Aroclor induced S9 rat liver enzymes. No reversions were reported in the absence of S9 mix or in the presence of Phenobarbital induced enzymes.
Result:	The notified chemical was mutagenic under the conditions of the test.

9.3.2 Chromosomal Aberration Assay in Chinese Hamster Lung Cells (Heidemann, 1989 in Sterzel and Steiling, 1996)

Cells:	Chinese hamster lung V79
Metabolic activation system:	Aroclor 1254 stimulated rat liver microsomes (S9 mix)

Dosing schedule:	Test concentrations 10 – 800 μg/mL at 18 hours and 1100 μg/mL at 7 and 28 hours.
Comment:	In pre-experiments, treatment with 1000 and 3000μg/mL were found to be toxic. Increases in numbers of cells with structural aberrations after treatment were observed at each fixation interval, except 7 hours (with S9 mix), both with and without metabolic activation.
Test method:	OECD TG 473
Result:	The notified chemical was clastogenic under the conditions of the test.

9.3.3 *In Vitro* Gene Mutation Assay at the HGPRT-Locus (Heidemann, 1988 in Sterzel and Steiling, 1996)

Cells:	Chinese hamster lung V79
Metabolic activation system:	Aroclor 1254 stimulated rat liver microsomes (S9 mix)
Dosing schedule:	Test concentrations 0, 35, 100, 200 and 350 μg/ml in absence of S9 mix and 0, 25, 100, 200 and 300 μg/ml in presence of S9 mix with a treatment period of 4 hours. Cultures were incubated for 6 days and then plated for 6-thioguanine resistance.
Test method:	OECD TG 476
Comment:	No relevant increases in mutant colony numbers were obtained in 2 independent experiments. The notified chemical did not induce gene mutations at the HGPRT locus.
Result:	The notified chemical was not mutagenic under the conditions of the test.

9.3.4 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Weill, 1989 in Sterzel and Steiling, 1996)

Species/strain:	Mice, OF1
Number and sex of animals:	5 males and 5 females per dose
Doses:	1200 mg/kg
Method of administration:	Gavage

Test method:	OECD TG 474
Comment:	Polychromatophile erythrocytes were examined at 24, 48 and 72 hours after administration of test substance.
Result:	The notified chemical was non clastogenic under the conditions of the test.

9.3.5 *In Vitro* Induction of Unscheduled DNA Synthesis – UDS Test (Timm, 1988 in Sterzel and Steiling, 1996)

Cells:	Wistar rat (CF HB strain) primary hepatocytes
Dosing schedule:	In separate experiments, test concentrations 0, 6.7, 66.7, 100, 333.3 and 666.7µg/mL and 600, 1000, 1300, 1600 and 2000 µg/mL for a treatment period of 3 hours.
Test method:	OECD TG 482
Comment:	No dose-related increases in incorporation of [^{3}H]-thymidine were observed.
Result:	The notified chemical was not mutagenic under the conditions of the test.

9.3.6 Embryotoxicity Including Teratogenicity in Rats (Becker, Frei, Mladenovic and Terrier, 1988 in Sterzel and Steiling, 1996)

Species/strain:	Rats, Wistar/HAN
Number and sex of animals:	125 females/dose
Doses:	0, 30, 90 and 270 mg/kg/day on days 6-15 of pregnancy
Method of administration:	Gavage
Comment:	Maternal responses: No specific findings except for slight reductions in food consumption and body weight gain in the highest dose group (270 mg/kg/day). Foetuses: No specific findings
Test method:	OECD TG 414
Result:	The reported No Observed Adverse Effect Level (NOAEL) for maternal toxicity was 90 mg/kg body weight/day. The NOAEL for embryotoxicity was 270mg/kg/day.

9.4 Subchronic Toxicity

9.4.1 Subchronic Oral Toxicity in Rats: 90 Day Study (Potokar, Pittermann and Bartnik 1986 in Sterzel and Steiling, 1996)

Species/strain:	Wistar rats MuRA Han 67 strain
Number/sex of animals:	10 per sex
Observation period:	13 weeks
Dose:	50mg/kg body weight of 1% suspension with traganth daily for 5 consecutive days over 13 weeks.
Method of administration:	Gavage
Test method:	OECD TG 408
Clinical observations:	No treatment-related pathology, biochemistry or clinical signs were observed.
Result:	The reported No Observed Effect Level for the notified chemical was ≥ 50mg/kg body weight/day.

9.5 Toxicokinetics

Approximately 81% of a basic (pH 9.5) cream containing 1.14 % of radioactive notified chemical without developer was absorbed percutaneously by Wistar rats over 48 hours (Bartnik and Zimmermann, 1988b). Absorbed radioactivity was excreted mainly in urine (83%) within 24 hours.

The same basic cream mixed with developer (H_2O_2) applied to rat skin for 30 minutes had a percutaneous absorption of 0.1% at 48 hours. Absorbed radioactivity was excreted equally in the urine and faeces with 80% excreted in the first 24 hours (Bartnik and Zimmermann, 1988a).

Excretion in the rat following single subcutaneous application of 1g of a 0.25% aqueous solution of radioactive notified chemical without developer was 89% over 24 hours and 96% over 96 hours, mostly in urine (Bartnik and Zimmermann, 1987a). Excretion of radioactivity following a single oral application of 49mg/kg body weight of a 1.7% aqueous solution of notified chemical without developer was 90% over 24 hours and 91% over 96 hours, mostly in urine (Bartnik and Zimmermann, 1987b).

Whole body autoradiography following a single oral administration of 50mg/kg body weight of a 1.7% aqueous solution of radioactive notified chemical showed labelling in skin, kidneys, liver, intestinal contents and especially the stomach at 1 hour. At 6 hours, labelling was observed in the stomach, intestine, colon, caecum and to a minor extent in the kidneys.

At 24 and 48 hours, radioactivity was detected in the colon, caecum and kidneys with a very small amount detected in bone at 96 hours. Approximately 91% of the notified chemical was eliminated in urine within 24 hours (Bartnik, Pittermann and Zimmermann (1987).

9.6 Overall Assessment of Toxicological Data

On the basis of summaries of toxicological studies, the notified chemical is likely to be of moderate acute oral toxicity, an eye irritant and a slight skin sensitiser. An eye irritation study using a 5% aqueous formulation of notified chemical revealed slight irritation. The level of eye irritation with neat chemical remains undetermined. Likewise, although acute and repeated dose skin irritation studies using a 10% aqueous formulation in two animal species showed no signs of irritation or corrosivity suggesting the notified chemical is not a skin irritant, the skin irritation properties of neat notified chemical remain undetermined.

The notified chemical was positive in two in vitro genotoxicity assays (reverse mutation assay and chromosomal aberration assay) but negative in two other in vitro assays (HGPRT-locus mutation assay and unscheduled DNA synthesis test) and one in vivo assay (bone marrow micronucleus assay). These results indicate the potential for the notified chemical to possess limited mutagenic properties.

Embryotoxicity studies revealed neither specific maternal or foetal responses to oral administration of notified chemical.

A subchronic oral toxicity study reported a No Observed Effect Level of ≥50mg/kg/day.

Absorption studies indicated that prolonged dermal contact with the notified chemical produces significant dermal absorption with excretion predominantly via the urine. Absorption is decreased when the developer solution is added before testing. Whole body autoradiography following oral administration showed significant rapid distribution of notified chemical to major organs within 1 hour.

According to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 1999), the notified chemical should be classified Hazardous (Xn) with the risk phrase R22 – Harmful if Swallowed.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No ecotoxicological data were provided.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified chemical is expected pose a low environmental hazard if used as specified.

The annual amount of waste notified chemical produced during the reformulation is 28.7 kg/annum. The majority (28.5 kg) of this waste will enter the sewer. The remainder will likely be disposed of to landfill (ie. in bags/containers) where it is likely to leach. The end-user containers will go to landfill, equating to about 9 kg of notified chemical waste annually.

All these inputs into the environment are likely to be at very low concentrations and in a very diffuse manner.

According to the submission, approximately 50% of the notified chemical will adsorb to hair meaning that the other 50% will be washed from the hair in the rinse water and will end up in the sewer. The use of the hair dye would be dispersed over Australia, so a Predicted Environmental Concentration (PEC) for the notified chemical could be calculated as follows:

Amount of notified chemical entering sewer	241.5 kg
Population of Australia	18 million
Amount of water used per person per day	150 L
Number of days in a year	365
Estimated PEC	0.24 ppb

While no aquatic toxicity data are available this PEC is likely to be well below toxic levels and a low hazard may be expected from the proposed use pattern.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment

Only limited toxicological data in the form of summaries were provided. These suggest that the notified chemical is likely to be of moderate acute oral toxicity, irritating to eyes and a slight skin sensitiser. Summaries of both acute and repeated dose skin irritation studies with 10% notified chemical revealed no irritation. However, eye irritation induced with 5% notified chemical suggests that application of neat notified chemical may induce skin irritation.

Although positive results were obtained in two *in vitro* mutagenicity assays, the balance of genotoxicity data indicate that the notified chemical would be at most weakly mutagenic or clastogenic.

Absorption studies indicate that prolonged dermal contact with the notified chemical produces significant dermal absorption with excretion predominantly via the urine. Absorption is decreased in the presence of a H_2O_2 developer solution.

These summarised toxicity data support the classification of the notified chemical as a hazardous substance with the risk phrase R22 - Harmful if Swallowed.

Occupational Health and Safety

The notified chemical will be imported as an ingredient of a hair colour product at 0.3% and in a dye concentrate at up to 20%. Because of the low dermal toxicity profile of the notified chemical and low risk of exposure except in the event of a spill, the risk of adverse health effects to dockside, transport or warehouse workers is expected to be negligible.

During reformulation and repackaging of the imported dye concentrate into tubes and bottles, there is potential for exposure to occur via the lungs, skin and eyes, especially during opening and manually pouring the powdered concentrate. At this point, depending on the dye shade,

the notified chemical may be present at up to 20%. Exposure may also occur via skin and eyes from spills of reformulated dye containing ≤ 4% notified chemical during connection of transfer lines and cleaning of equipment. The notifiers state that transfer points are fitted with local exhaust ventilation and that typically for these operations workers are required to wear impervious gloves, coveralls, respirator and eye protection.

The manual handling of powdered dye concentrate is likely to cause liberation of chemical dust which, given the considerable fraction in the inspirable particle size range, may be associated with significant irritation. The Material Safety Data Sheet (MSDS) for the dye concentrate containing the notified chemical carries a warning of the possibility of serious eye damage. Also, because skin irritation tests submitted for the notified chemical were conducted with highly diluted solution, there exists the possibility of serious skin irritation during manual handling of the dye concentrate.

The engineering controls described, namely local forced ventilation and personal protective equipment consisting impervious gloves, coveralls, respirator and eye protection are required in order to maintain low dermal and inhalation exposure and low risk of adverse health effects from repeated or prolonged exposure to the notified chemical. If adequate exposure protection measures are not used, allergic sensitisation may occur from repeated exposure to the notified chemical, particularly during decanting of the dye concentrate where the chemical may be in high concentration.

Hairdressers may receive repeated or prolonged dermal contact to hair colour products containing the notified chemical. Although dermal sensitisation data for the chemical is below that required for hazard classification, positive findings and the unpredictable nature of sensitisation means the risk of skin sensitisation must be regarded. Moreover, hairdressers particularly 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. 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 long-term adverse skin effects.

The risk of adverse health effects to retail outlet workers is expected to be negligible except in the event of a spill.

Public Health

Given the low concentration of notified chemical in the hair colourant products, the likelihood of a low level of dermal and therefore systemic absorption and its intermittent use, the potential genotoxic hazard is likely to be low.

Concerning the potential for the notified chemical to cause skin irritation/sensitisation, packaging for the Schwarzkopf product includes warnings about potential skin irritation, a self-administered preliminary skin test before use and the preclusion of use for dyeing eyelashes and eyebrows due to possibility of eye injury. Consequently, the low concentration of the notified chemical in the finished products, plus its use strictly in accordance with the product information should minimise the potential skin irritation/sensitisation hazard for the public.

Based on the above information, it is considered that the notified chemical is unlikely to pose a significant health risk to public health when used in the proposed manner.

13. RECOMMENDATIONS

To minimise occupational exposure to phenol, 3-amino-2-chloro-6-methyl, hydrochloride the following guidelines and precautions should be observed:

Formulation workers:

- Protective eyewear, dust tight chemical resistant industrial clothing and footwear and impermeable rubber or PVC gloves should be used during occupational use of the products containing the notified chemical. Where engineering controls and work practices do not reduce particulate exposure to safe levels, a P3 particle negative pressure respirator or supplied air respirator should also be used;

- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal;

Hairdressers:

- Hairdressers should wear plastic gloves when using products containing the notified chemical. Spillage to the skin or eyes should be removed promptly;

- Hairdressers are encouraged to consult guidance documents published by state occupational health and safety authorities (WorkCover Corporation, 1996; WorkCover NSW, 1997) for identifying and managing health risks in hairdressing;

- The notifiers should advise the hairdressing industry of the availability of these recommendations and state government publications relevant to hairdressing in addition to current industry codes;

All workers:

- Good personal hygiene should be practiced to minimise the potential for ingestion;

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

If products containing the notified chemical are hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999), workplace practices and control procedures consistent with State and Territory hazardous substances regulations must be in operation.

Guidance in selection of protective eyewear may be obtained from Australian Standard (AS) 1336 (Standards Australia, 1994) and Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); for industrial clothing, guidance may be found in AS 3765.2 (Standards Australia, 1990); for impermeable gloves or mittens, in AS 2161.2 (Standards Australia/ Standards New Zealand, 1998); for occupational footwear, in AS/NZS 2210 (Standards Australia/ Standards New Zealand, 1994a); for respirators, in AS/NZS 1715 (Standards Australia/ Standards New Zealand, 1994b) and AS/NZS 1716

(Standards Australia/ Standards New Zealand, 1994c) or other internationally acceptable standards.

14. MATERIAL SAFETY DATA SHEET

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

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

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical may be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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