Australian Government
Department of Health
Therapeutic Goods Administration

Final decisions and reasons for decisions by delegates of the Secretary to the Department of Health

31 January 2017

(Chemicals not referred to the November 2016 ACCS/ACMS meeting)

Notice under subsection 42ZCZX of the Therapeutic Goods Regulations 1990 (the Regulations)

The delegate of the Secretary to the Department of Health hereby give notice of delegate's final decisions for amending the *Poisons Standard* (commonly referred to as the *Standard for the Uniform Scheduling of Medicines and Poisons* - SUSMP) under subsection 42ZCZX the Therapeutic Goods Regulations 1990 (the Regulations). This notice also provides the reasons for each decision and the date of effect (implementation date) of the decision.

The delegates' final decisions and reasons relate to scheduling proposals considered as delegate-only matters, i.e. not referred to an expert advisory committee.

Matters not referred to an advisory committee

A delegate may decide not to refer a scheduling proposal to an expert advisory committee for advice and instead may make a delegate-only decision. When deciding not to refer a matter to a committee, the delegate considers the scheduling guidelines as set out in the *Scheduling Policy Framework for Chemicals and Medicines* (SPF, 2015), available at SPF, February 2015.

Publishing of the amendments to the Poisons Standard

The amendments to the Schedules, Appendices or other parts of the *Poisons Standard* are published electronically on the Federal Register of Legislation (FRL) as amendments to the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) prior to the date of effect (implementation date) of the final decisions. Further information, including links to the *Poisons Standard* on the Federal Register of Legislation (FRL), is available at SUSMP.

Glossary

Abbreviation	Name
AAN	Australian Approved Name
AC	Active constituent
ACCC	Australian Competition and Consumer Commission
ACCM	Advisory Committee on Complementary Medicines (formerly Complementary Medicine Evaluation Committee [CMEC])
ACNM	Advisory Committee on Non-prescription Medicines (formerly Medicines Evaluation Committee [MEC])
ACPM	Advisory Committee on Prescription Medicines (formerly Australian Drug Evaluation Committee [ADEC])
ACSOM	Advisory Committee on the Safety of Medicines (formerly Adverse Drug Reactions Advisory Committee [ADRAC])
ADEC	Australian Drug Evaluation Committee (now Advisory Committee on Prescription Medicines [ACPM])
ADI	Acceptable daily intake
ADRAC	Adverse Drug Reactions Advisory Committee (now Advisory Committee on the Safety of Medicines [ACSOM])
AHMAC	Australian Health Ministers' Advisory Council
APVMA	Australian Pesticides and Veterinary Medicines Authority
AQIS	Australian Quarantine and Inspection Service (now Biosecurity)
ARfD	Acute reference dose
ASCC	Australian Safety and Compensation Council
ASMI	Australian Self-Medication Industry
ARTG	Australian Register of Therapeutic Goods
CAS	Chemical Abstract Service

Abbreviation	Name
CHC	Complementary Healthcare Council of Australia
CMEC	Complementary Medicine Evaluation Committee (now Advisory Committee on Complementary Medicines [ACCM])
CMI	Consumer Medicine Information
COAG	Councils of Australian Governments
CRC	Child-resistant closure
CTFAA	Cosmetic, Toiletry & Fragrance Association of Australia
CWP	Codeine Working Party
DAP	Drafting Advisory Panel
ECRP	Existing Chemicals Review Program
EPA	Environmental Protection Authority
ERMA	Environmental Risk Management Authority (New Zealand)
EU	European Union
FAISD	First Aid Instructions and Safety Directions
FDA	Food and Drug Administration (United States)
FOI	Freedom of Information Act 1982
FSANZ	Food Standards Australia New Zealand
GHS	Globally Harmonised System of Classification and Labelling of Chemicals
GIT	Gastro-intestinal tract
GP	General practitioner
HCN	Health Communication Network

Abbreviation	Name
IMAP	Inventory Multi-tiered Assessment Prioritisation
INN	International Non-proprietary Name
IUPAC	International Union of Pure and Applied Chemistry
ISO	International Standards Organization
LC_{50}	The concentration of a substance that produces death in 50 per cent of a population of experimental organisms. Usually expressed as mg per litre (mg/L) as a concentration in air.
LD_{50}	The concentration of a substance that produces death in 50 per cent of a population of experimental organisms. Usually expressed as milligrams per kilogram (mg/kg) of body weight.
LOAEL	Lowest observed adverse effect level
LOEL	Lowest observed effect level
MCC	Medicines Classification Committee (New Zealand)
MEC	Medicines Evaluation Committee (now Advisory Committee on Non-prescription Medicines [ACNM])
MOH	Ministry of Health (New Zealand)
NCCTG	National Coordinating Committee on Therapeutic Goods
NDPSC	National Drugs and Poisons Schedule Committee
NHMRC	National Health and Medical Research Council
NICNAS	National Industrial Chemicals Notification & Assessment Scheme
NOAEL	No observed adverse effect level
NOEL	No observable effect level
NOHSC	National Occupational Health & Safety Commission
OCM	Office of Complementary Medicines

Abbreviation	Name
OCS	Office of Chemical Safety (formerly Office of Chemical Safety and Environmental Health [OCSEH])
OCSEH	Office of Chemical Safety and Environmental Health (now Office of Chemical Safety [OCS])
ODA	Office of Devices Authorisation
OMA	Office of Medicines Authorisation (formerly Office of Prescription and Non-prescription Medicines)
OOS	Out of session
OTC	Over-the-counter
PACIA	Plastics and Chemicals Industries Association
PAR	Prescription animal remedy
PBAC	Pharmaceutical Benefits Advisory Committee
PEC	Priority existing chemical
PGA	Pharmaceutical Guild of Australia
PHARM	Pharmaceutical Health and Rational Use of Medicines
PI	Product Information
PIC	Poisons Information Centre
PSA	Pharmaceutical Society of Australia
QCPP	Quality Care Pharmacy Program
QUM	Quality Use of Medicines
RFI	Restricted flow insert
SCCNFP	Scientific Committee on Cosmetic and Non-Food Products
SCCP	Scientific Committee on Consumer Products

Abbreviation	Name
SPF	Scheduling Policy Framework
STANZHA	States and Territories and New Zealand Health Authorities
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
SVT	First aid for the solvent prevails
TCM	Traditional Chinese medicine
TGA	Therapeutic Goods Administration
TGC	Therapeutic Goods Committee
TGO	Therapeutic Goods Order
TTHWP	Trans-Tasman Harmonisation Working Party
TTMRA	Trans-Tasman Mutual Recognition Agreement
WHO	World Health Organization
WP	Working party
WS	Warning statement

Contents

Amendment to delegate-only final decisions not referred to an expert advisory committee

On 16 January 2017, the delegate made four delegate-only decisions. Following the release of the final decisions, feedback from industry indicated that some of the chemicals are used more broadly than initially considered. Hence, these four delegate-only decisions will undergo review to enable further consideration of their broader use pattern. It is anticipated that scheduling advice will be sought from the Advisory Committees on Medicines and Chemicals Scheduling (ACMS/ACCS).

Summary of amended delegate-only final decisions

Substance	Final Decision
m-Aminophenol	**Schedule 6 – Delete Entry** Implementation date: 1 February 2017
Resorcinol (1,3-benzenediol)	**Schedule 6 – Delete Entry** Implementation date: 1 February 2017
2-Chloro-6-(ethylamino)-4-nitrophenol	**Schedule 6 – Delete Entry** Implementation date: 1 February 2017
2,4-Diaminophenoxyethanol hydrochloride	**Schedule 6 – Amended Entry** 2,4-DIAMINO-PHENOXYETHANOL in hair dye preparations **except** in preparations containing 4 per cent or less of 2,4-diaminophenoxyethanol when the immediate container and primary pack are labelled with the following: KEEP OUT OF REACH OF CHILDREN WARNING – this product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dying eyelashes and eyebrow; to do so may be injurious to the eye. Written in letters not less than 1.5 mm in height. **Appendix E, Part 2 – Current Entry** 2,4-DIAMINO-PHENOXYETHANOL Standard statements: A [For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)], E1 (If in eyes wash out immediately with water.). **Appendix F, Part 3 – Amended Entry** 2,4-DIAMINO-PHENOXYETHANOL Warning statement: 21 (WARNING – This product contains

Substance	Final Decision
	ingredients which may cause skin irritation to certain individuals. A preliminary test according to accompanying directions should be made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye.). **Index – Current Entry** **2,4-DIAMINO-PHENOXYETHANOL** Schedule 6 Appendix E, Part 2 Appendix F, Part 3 Implementation date: 1 February 2017

1. *m*-Aminophenol

Scheduling proposal

The chemicals scheduling delegate initiated a scheduling proposal to delete the Schedule 6 entry for *m*-aminophenol.

Current scheduling status and relevant scheduling history

m-Aminophenol is currently in Schedule 6 of the Poisons Standard.

In August 2016, the chemicals scheduling delegate received an application to create a new Schedule 6 entry for *m*-aminophenol. The delegate made a delegate-only decision in January 2017 with a 1 February 2017 implementation date. Prior to this date, *m*-aminophenol was unscheduled and had not previously been considered for scheduling.

Australian regulatory information

New Zealand, ASEAN countries and the EU have restricted the use of *m*-aminophenol in cosmetics (see *International regulations* below); however, there are currently no restrictions in Australia on the use of the chemical in cosmetics or domestic products.

Considering the use of this chemical in permanent hair dyes in Australia and other potential domestic uses (based on overseas information), the main routes of public exposure are expected to be through the skin and inhalation from products applied as aerosols.

In the absence of regulatory controls, the characterised critical health effects (acute toxicity and skin sensitisation) have the potential to pose an unreasonable risk under the identified uses. The risk could be mitigated by implementing restrictions for the use of the chemical in hair dyes and other cosmetic products.

International regulations

Use of the chemical in cosmetics in the EU is subject to the restrictions described in EU Cosmetics Regulation 344/2013 (as an amendment to the listing under Annex III of Regulation 1223/2009). The use of the chemical in hair dyes is restricted to a maximum concentration of 1.2% applied to hair after mixing under oxidative conditions (1:1 ratio with hydrogen peroxide). If the chemical is present at lower concentrations, sensitisation labelling is required.

Use of the chemical in cosmetics and domestic products is also restricted in several other countries as follows:

- ASEAN Cosmetic Directive Annex III Part 1: List of substances which cosmetic products must not contain except subject to restrictions and conditions; and
- New Zealand Cosmetic Products Group Standard—Schedule 5, Table 1: Components cosmetic products must not contain except subject to restrictions and conditions.

Under the above regulations, the use of the chemical in hair dyes is restricted to a maximum concentration of 1.2% applied to hair after mixing under oxidative conditions.

Scheduling application

Delegate-initiated application.

The delegate's proposed amendments to the Poisons Standard are as follows:

Schedule 6 – Delete Entry

~~*m*-AMINOPHENOL **except** when in hair dye preparations containing 1.2 per cent or less of *m*-aminophenol when the immediate container and primary pack are labelled with the following statements:~~

> ~~KEEP OUT OF REACH OF CHILDREN, and~~
>
> ~~WARNING – This product contains ingredients which may cause skin sensitisation to certain individuals, and when used for eyelash or eyebrow tinting may cause injury to the eye. A preliminary test according to the accompanying directions should be made before use.~~
>
> ~~written in letters not less than 1.5 mm in height.~~

Appendix E, Part 2 – Delete Entry

~~*m*-AMINOPHENOL~~

~~Standard statements: A [For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)], E1 (if in eyes wash out immediately with water).~~

Appendix F, Part 3 – Delete Entry

~~*m*-AMINOPHENOL~~

~~Warning statements: 28 ((over) (repeated) exposure may cause sensitisation).~~

Index – Delete Entry

~~***m*-AMINOPHENOL~~

~~Schedule 6~~
~~Appendix E, Part 2~~
~~Appendix F, Part 3~~

The delegate's reasons for the proposal include:

- Information has been received from industry to indicate that the wording of the Schedule 6 entry may require further amendment to account for the use of *m*-aminophenol in other industry sectors.
- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).

Substance summary

The following toxicology information was extracted from the NICNAS IMAP Human Health Tier II assessment report for 3-aminophenol. Further information can also be found in the SCCP report for m-aminophenol.

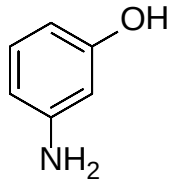

Figure 1: Chemical structure of *m*-aminophenol

Table 1A: Chemical properties and identifiers of *m*-aminophenol

Property/identifier	*m*-Aminophenol
Molecular formula	C_6H_4
Molecular weight	109.13 g/mol
CAS name	Phenol, 3-amino-
CAS number	591-27-5
IUPAC and/or common and/or other names	3-hydroxyaniline (IUPAC); m-aminophenol (INCI)
SUSMP name	Not listed in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). Based on previously considered isomers, *p*-aminophenol (March 2016 ACCS meeting cycle) and o-aminophenol (July 2014 ACCS meeting cycle), the recommended SUSMP name is *m*-aminophenol.

Table 1B: Acute toxicity end-points for *m*-aminophenol

Toxicity	Species	*m*-Aminophenol	SPF (2015) Classification
Acute oral toxicity LD_{50} (mg/kg bodyweight (bw))	Rat	812-1000	Schedule 6
Acute dermal toxicity LD_{50} (mg/kg bw)	N/A	No data	N/A
Acute inhalational toxicity LC_{50} (mg/m^3/4h)	Rat	1162	Schedule 6
Skin irritation	Rabbit	No irritation (2% *m*-aminophenol in a suspension of 0.5% methylcellulose in purified water)	N/A

Toxicity	Species	*m*-Aminophenol	SPF (2015) Classification
Eye irritation	Rabbit	Mild irritation (2% *m*-aminophenol in a suspension of 0.5% methylcellulose in purified water)	N/A
Skin sensitisation (LLNA)	Mouse	Moderate to strong skin sensitiser (EC3 0.24-3.2%)	Schedule 6
Skin sensitisation (Guinea pig maximisation test (GPMT))	Guinea pig	Sensitiser. Positive reactions in 100% of animals tested at 5%, following 1% intradermal induction and 1% topical induction.	

Acute toxicity

m-Aminophenol has moderate acute oral and inhalation toxicity, warranting hazard classification. No data were available for acute dermal toxicity.

Irritation

The available data from animal and human studies indicate that the chemical is not irritating to the skin or eyes.

Sensitisation

Based on the available animal and human data, the chemical is considered to be a moderate to strong skin sensitiser and is recommended for classification.

- In an in vivo mouse LLNA conducted in accordance with OECD Test Guideline (TG) 429, 28 female CBA/J mice (four animals/group) were administered the chemical at concentrations of 0 , 1 , 2.5 , 5 , 10 or 25% (w/v) in dimethylformamide. Stimulation indices (SI) of 0, 7.6, 12.6, 10.4, 7.2 and 6.0 were reported, respectively. In a second experiment, concentrations of 0, 0.05, 0.1, 0.5, 1.0 and 2.5% of the chemical in the same vehicle were administered to the animals. SIs of 1.0, 1.4, 5.9, 9.0 and 11.0 were reported, respectively. The calculated EC3 value (0.24%) indicated strong sensitisation potential for the chemical.
- In another mouse LLNA study, CBA/Ca mice were administered the chemical at concentrations of 0, 2.5, 5 or 10% (w/v) in acetone/olive oil (ratio of 4:1). SIs of 0, 2.8, 3.5 and 5.7 were reported, respectively. The EC3 value was reported to be 3.2%.
- In a non-guideline GPMT, guinea pigs were administered the chemical at a concentration of 1.0% (v/v) in acetone/olive oil (ratio of 4:1) by intradermal injection, followed by topical induction with a 10% solution of the chemical one week later. After two weeks, a topical challenge dose of 5% resulted in positive reactions observed in all animals tested.

Repeat-dose toxicity

Based on the available information, *m*-aminophenol is not considered to cause serious damage to health through repeated oral exposure at low doses. Systemic toxicity has not been demonstrated via the dermal route. No information was available for repeated dose toxicity by inhalation.

Genotoxicity

Based on the weight of evidence from the available *in vitro* and *in vivo* genotoxicity studies, m-aminophenol is not considered to be genotoxic.

Carcinogenicity

Based on the available data and the lack of genotoxicity, m-aminophenol is not expected to be carcinogenic.

Reproduction and developmental toxicity

Based on the available information, *m*-aminophenol is not expected to be a reproductive or developmental toxin.

Observation in humans

Sensitisation:

Sensitisation in humans exposed to the chemical has been observed both in repeat insult patch tests and during diagnostic patch testing.

In two semi-occlusive repeat insult patch tests, 0.1 mL doses of *m*-aminophenol (3% solution in Schultz vehicle II or similar) were applied to the backs of 98 and 99 test subjects over a six week period. There were 10 consecutive induction patch applications at 48–72 hours, followed by one day of no application. Challenge patch applications on previously unexposed skin on backs of humans were conducted 48 hours following the rest period. In both studies, irritant effects (erythema) were observed in several subjects during the induction phase. In the first study (98 subjects), no reactions to the challenge patches were observed. In the second study (99 subjects), two subjects showed reactions following application of the challenge patches, as well as following application of additional rechallenge patches on different parts of the body.

In an Australian case study, 164 hairdressers and hairdressing apprentices who presented with allergic contact dermatitis at a dermatology clinic were patch-tested against 36 chemicals used in hair salons. Four subjects, previously exposed to *m*-aminophenol in the workplace, had positive reactions when patch tested with the chemical.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- NICNAS IMAP Tier II Report;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling Policy Framework (SPF 2015) criteria; and
- Other relevant information

Delegate's final decision

The delegate's final decision is to delete the Schedule 6 entry for *m*-aminophenol.

The implementation date is **1 February 2017**.

The delegate considered the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989*: (a) the risks and benefits of the use of the substance; (b) the purposes for which the substance is to be used and (c) the toxicity of the substance.

The reasons for the decision comprise the following:

- Information has been received from industry to indicate that the wording of the previous Schedule 6 entry may require further amendment to account for the use of *m*-aminophenol in other industry sectors.
- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).

2. Resorcinol

Scheduling proposal

The chemicals scheduling delegate initiated a scheduling proposal to delete the Schedule 6 entry for resorcinol.

Current scheduling status and relevant scheduling history

Resorcinol is currently in Schedule 6 of the Poisons Standard.

In August 2016, the chemicals scheduling delegate received an application to create a new Schedule 6 entry for resorcinol (1,3-benzenediol). The delegate made a delegate-only decision in January 2017 with a 1 February 2017 implementation date. Prior to this date, resorcinol was unscheduled and had not previously been considered for scheduling.

Australian regulatory information

Resorcinol was reported to be used in permanent hair dye preparations in Australia (NICNAS, 2007) and in overseas hair lotions and shampoos.

Currently, there are no restrictions in Australia on using this chemical in hair dyes, hair lotions and shampoos. In the absence of any regulatory controls, the characterised critical health effects (skin and eye irritation, and skin sensitisation) have the potential to pose an unreasonable risk under the identified uses. The risk could be mitigated by implementing concentration limits and labelling requirements for use in hair dyes, hair lotions and shampoos.

International regulations

The EU has restricted the use of this chemical in oxidative hair colouring products at a maximum concentration of 2.5%. It is mixed with hydrogen peroxide in a 1:1 ratio just prior to use, which corresponds to a concentration of 1.25% when applied to hair (SCCS, 2010). Restricted use in hair lotions and shampoos was also reported to be the maximum authorised concentration in the finished cosmetic product of 0.5%.

Resorcinol is listed on the EU Cosmetic Directive 76/768/EEC Annex III Part 1: List of substances which cosmetic products must not contain except subject to the restrictions and conditions laid down below (Galleria Chemica): (a) Hair dye substance in oxidative hair dye products for general and professional use—after mixing under oxidative conditions the maximum concentration applied to hair must not exceed 1.25% (w/w); and (b) Hair lotions and shampoos— maximum authorised concentration in the finished cosmetic product of 0.5% (w/w).

Resorcinol is also listed on the following:

- The Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex III—Part 1 List of substances which cosmetic products must not contain except subject to restrictions and conditions laid down;
- New Zealand Cosmetic Products Group Standard—Schedule 5—Table 1: Components cosmetic products must not contain except subject to the restrictions and conditions laid down;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient 'Hotlist'); and

- Chile list of Cosmetic Ingredients with limited use or concentration.

Scheduling application

Delegate-initiated application.

The delegate's proposed amendments to the Poisons Standard are as follows:

Schedule 6 – Delete Entry

~~RESORCINOL **except**:~~

~~a) in hair dye preparations containing 1.25 per cent or less of resorcinol when the immediate container and primary pack are labelled with the following statements:~~

~~KEEP OUT OF REACH OF CHILDREN, and~~

~~WARNING – This product contains ingredients which may cause skin sensitisation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye.~~

~~written in letters not less than 1.5 mm in height; or~~

~~b) in hair lotions/shampoo products containing 0.5 per cent or less of resorcinol when the immediate container and primary pack are labelled with the following statement:~~

~~WARNING – This product contains ingredients which may cause skin sensitisation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used on the eyelashes or eyebrows; to do so may be injurious to the eye.~~

~~written in letters not less than 1.5 mm in height.~~

Appendix E, Part 2 – Delete Entry

~~RESORCINOL~~

~~Standard statements: A [For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)], E1 (if in eyes wash out immediately with water).~~

Appendix F, Part 3 – Delete Entry

~~RESORCINOL~~

~~Warning statements: 28 ((over) (repeated) exposure may cause sensitisation).~~

Index – Delete Entry

~~RESORCINOL~~
~~cross reference: 1,3-benzenediol~~

~~Schedule 6~~
~~Appendix E, Part 2~~
~~Appendix F, Part 3~~

The delegate's reasons for the proposal include:

- Information has been received from industry to indicate that the wording of the Schedule 6 entry may require further amendment to account for the use of resorcinol in other industry sectors.

- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).

Substance summary

The following toxicology information was extracted from the NICNAS IMAP Human Health Tier II assessment. Further information can also be found in the European Commission Scientific Committee on Consumer Safety (SCCS) report.

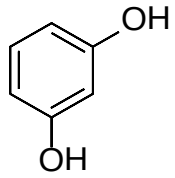

Figure 2: Chemical structure of resorcinol

Table 2A: Chemical properties and identifiers of resorcinol

Property/identifier	Resorcinol
Molecular formula	$C_6H_6O_2$
Molecular weight	110.1 g/mol
CAS name	1,3-Benzenediol
CAS number	108-46-3
IUPAC and/or common and/or other names	Resorcinol (INCI name); benzene-1,3-diol (IUPAC); 1,3-dihydroxybenzene; and 3-hydroxyphenol.

Table 2B: Acute toxicity end-points for resorcinol

Toxicity	Species	Resorcinol	SPF (2015) Classification
Acute oral toxicity LD_{50} (mg/kg bw)	Rats (Sprague Dawley)	200-980 mg/kg bw/day.	N/A
Acute dermal toxicity LD_{50} (mg/kg bw)	Rabbits	> 2000 mg/kg bw/day.	N/A
Acute inhalational toxicity LC_{50} (mg/m^3/4h)	Rats (Harlan Wistar)	> 7800 mg/m 3/1–hour (equivalent to 7.8 mg/L or 1732 ppm); and > 2800 mg/m 3/8–hours (equivalent to 2.8 mg/L or 622 ppm)	N/A

Toxicity	Species	Resorcinol	SPF (2015) Classification
Skin irritation	Rabbit (albino)	Slight to severe skin irritant in diluted and semi-solid state, respectively (flaked and industrial grade).	Schedule 6
	Rabbit (New Zealand White)	Not irritating to skin (2.5% solution in water; 98.8% purity)	
Eye irritation	Rabbit (albino)	Severe eye irritant (see below)	Schedule 6
Skin sensitisation (Guinea Pig Maximisation Test: GPMT)	Guinea pigs (Pirbright white)	Sensitiser (relative incidence of the positive reactions in animals was > 30%) (99.9% purity)	Schedule 6
Skin sensitisation (mouse local lymph node assay: LLNA)	Mice (CBA/Ca)	Moderate sensitiser with EC = 1.4 and 6.3% (unspecified purity)	

Acute toxicity

The acute toxicity end-points of resorcinol are summarised in Table 2B.

Skin irritation

Based on the weight of evidence, the chemical is considered to be slightly to severely irritating to skin when administered diluted in an aqueous solution or in semi-solid state (flaked or industrial grade):

- In a non-guideline (Federal Hazardous Substance Labelling Act (FHSLA)) skin irritation study, 0.5 g of the chemical (flaked grade) in saline was applied to the clipped belly skin (abraded and intact) of albino rabbits (six males) for 24 hours under occlusive patches. Observations were made at 24 and 72 hours post-treatment, and animals were kept under observation for a maximum of two weeks. Treatment-related effects were moderate irritation on intact skin and necrosis on abraded skin. Effects were more pronounced at 72 hours post-treatment. In the two week recovery period, necrotic areas were still encrusted or scarred. The primary dermal irritation index (PDII) was reported to be 4.4;

- In similar non-guideline (FHSLA) studies, a 24-hour occluded application of the chemical (flaked and industrial grade) at 0.5 g to the bellies of male albino rabbits produced moderate irritation on intact skin and necrosis on abraded sites. The chemical (industrial grade) was reported to cause slight to severe irritation of the intact areas, and from severe irritation to necrosis of the abraded areas, 24 hours after exposure. In the 2-week post-recovery period, necrotic areas were still encrusted or scarred. The primary dermal irritation index (PDII) for the chemical was reported to be 4.4 (flaked grade) and 5.4 (industrial grade); and

- In a study conducted according to the OECD Test Guideline 404 (acute dermal irritation/corrosion), 0.5 mL of the chemical (2.5% aqueous solution) (98.8% purity) was applied to the clipped back skin of New Zealand White rabbits (three males/group) for four hours under

semi-occlusive patches. Observations were made at one, 24, 48 and 72 hours post-treatment. No adverse cutaneous reactions were reported at this low concentration.

Eye irritation

Data from one study using the chemical (flaked and industrial grade diluted in an aqueous solution and semi-solid state, respectively) indicated that the chemical should be considered a severe eye irritant:

- In a non-guideline (FHSLA) study, 0.1 g of the chemical (flaked and industrial grade) was instilled into the eyes of albino rabbits (6 males). Treatment-related effects upon administration included inflamed conjunctivae, opaque corneas and visible discomfort in animals. At 24 hours post-exposure, observations included severe conjunctivitis, iritis, corneal opacity occluding most of the iris and corneal ulcerations. Irreversible effects on the eyes were reported and by day 14, all treated eyes had kerataconus (thinning of and irregularly shaped cornea) and pannus (abnormal layer of fibrovascular tissue or granulation tissue over the cornea) formation. Total mean eye irritation Draize scores were reported to be 105/110 at 24, 48 and 72 hours and the chemical was considered to be a severe eye irritant;

- The chemical was mildly irritating in six albino rats administered 0.1 g of the chemical (dry powder). Reported mean irritation scores were 56.3, 45.0 and 39.9 out of 110 over the observation period at 24, 48 and 72 hours, respectively. No further study details were available; and

- In a study conducted according to OECD TG 405 (acute eye irritation/corrosion), 0.1 mL of the chemical (2.5% solution in water (98.8% purity)) was instilled into the eyes (conjunctival sacs) of New Zealand White rabbits (three males) and left for 72 hours. Mean scores of zero were reported for chemosis, iris lesions and corneal opacity over 24, 48 and 72 hours. For redness of the conjunctivae, a mean score of 0.1 was reported.

Skin sensitisation

Based on the available animal and human data, the chemical is considered to be a moderate to strong contact skin sensitiser and is recommended for classification:

- In a GPMT conducted in accordance with OECD TG 406, Pirbright white guinea pigs (treatment group 10 animals, control group 5 animals and accompanying group 20 animals used for range finding) were administered 2% (w/v) solution of the chemical (99.9% purity as white flakes in sodium chloride) by intradermal injection followed by occlusive, epicutaneous application of 25% the chemical. At the challenge exposure using 25% of the chemical (occlusive epicutaneous application), very slight to distinct erythema was observed on the skin of 2-3 animals at 24 and 48 hours observation periods. At the second challenge and compared to the control group, very slight to distinct erythema was reported in 7/10 guinea pigs at 24 hours and on 5/10 guinea pigs at 48 hours and minor swelling was also observed in one animal at 24 hours after patch removal. The relative incidence of the positive reactions in animals was over the threshold value of 30% and the chemical was considered to be a skin sensitiser;

- In a study conducted in accordance with OECD TG 429, positive skin sensitisation was reported in LLNA studies in two independent experiments. A positive control of a-hexylcinnamaldehyde (HCA), a moderate sensitiser, at the concentration of 25% (v/v) in DMF was used. In the first experiment (range finding), female CBA/J mice (four animals/dose including negative and positive controls) were administered 25 µL of the chemical (in vehicle dimethylformamide at 2.5, 5, 10, 25 or 50%) applied to the dorsal surface of each ear, once daily for three consecutive days. Stimulation indices (SI) of 3.83, 4.14, 3.97, 3.51 and 3.30 were reported, respectively. Positive lymphoproliferative responses (SI > 3) were reported at all concentrations, but no clear dose-response relationship was observed. In the second experiment, mice (four/dose) were administered daily applications of 0.1, 0.5, 1, 5 or 25% chemical (w/v). Treatment resulted in stimulation indices of 1.58, 2.87, 1.97, 3.51 and 5.74, respectively. A dose-related increase in SI was seen and the threshold positive value of three was exceeded. The effective concentration at which

a three-fold increase in SI was achieved (EC3) was reported to be 1.4% and the chemical was considered to be a moderate skin sensitiser; and

- The chemical (purity unspecified) was not reported to be sensitising according to two non-guideline skin sensitisation (LLNA) studies in mice (concentrations of up to 2.5% and 25% w/v were tested, respectively). No further study details were available and the reliability of both studies was questioned due to outdated study methods (OECD, 2008). However, the chemical was reported to be a sensitiser in mice in a LLNA study (OECD TG 429). A group of CBA/Ca female mice (four/dose) were treated at daily concentrations of 0, 1, 5, 10, 25 and 50% (w/v) of the chemical (purity unspecified) in acetone/olive oil (ratio of 4:1). SIs of 1.0, 0.7, 2.2, 5.2, 8.4 or 10.4 were measured respectively, and an EC value of 6.3% was determined (REACH; OECD, 2008).

Observation in humans

Human patch-testing using the chemical elicited allergic skin reactions in 0.7–0.8% of 1694 dermatitis patients. In further case histories of 34 dermatitis patients, the chemical was reported to cause reactions after epicutaneous testing.

No dermatitis of the hands was reported for 42 workers from a tyre factory after an epicutaneous test with the chemical.

In human patch tests with the chemical (2% in petrolatum), four out of 302 hairdressers suffering from contact dermatitis reported a positive reaction. No further details were available. In another case, one patient who developed contact dermatitis after application of paint to the skin was patch tested with the chemical (5% in petrolatum) and showed a positive result after 48 hours. In a third case, three female patients suffering from acne and contact dermatitis gave a positive patch test for the chemical (2% in petrolatum) after 48 and 72 hours.

Repeat-dose toxicity

Based on the weight-of-evidence, the chemical is not considered to cause serious damage to health from repeated oral exposure.

No information was available for repeated dose toxicity by the dermal route.

There is insufficient evidence to evaluate repeated dose inhalation toxicity.

Genotoxicity

Based on the weight-of-evidence from the available *in vitro* and *in vivo* genotoxicity studies, the chemical is not considered to be genotoxic.

Carcinogenicity

Based on the available data, the chemical is not considered to be carcinogenic.

Reproduction and developmental toxicity

Based on the available data, the chemical is not considered to be a reproductive or developmental toxin.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- NICNAS IMAP Tier II Report;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling Policy Framework (SPF 2015) criteria; and

- Other relevant information.

Delegate's final decision

The delegate's final decision is to delete the Schedule 6 entry for resorcinol.

The implementation date is **1 February 2017**.

The delegate considered the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989*: (a) the risks and benefits of the use of the substance; (b) the purposes for which the substance is to be used and (c) the toxicity of the substance.

The reasons for the decision comprise the following:

- Information has been received from industry to indicate that the wording of the previous Schedule 6 entry may require further amendment to account for the use of resorcinol in other industry sectors.
- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).

3. 2-Chloro-6-(ethylamino)-4-nitrophenol

Scheduling proposal

The chemicals scheduling delegate initiated a scheduling proposal to delete the Schedule 6 entry for 2-chloro-6-(ethylamino)-4-nitrophenol.

Current scheduling status and relevant scheduling history

2-Chloro-6-(ethylamino)-4-nitrophenol is currently in Schedule 6 of the Poisons Standard.

In August 2016, the chemicals scheduling delegate received an application to create a new Schedule 6 entry for 2-chloro-6-(ethylamino)-4-nitrophenol. The delegate made a delegate-only decision in January 2017 with a 1 February 2017 implementation date. Prior to this date, 2-chloro-6-(ethylamino)-4-nitrophenol was unscheduled and had not previously been considered for scheduling.

International regulations

Use of the chemical in cosmetics in the European Union (EU) is subject to the restrictions described in EU Cosmetics Regulation 344/2013 (as an amendment to the listing under Annex III of Regulation 1223/2009). This chemical may be used at maximum concentrations of 3.0% in ready-for-use preparations of oxidising (permanent) and non-oxidising (semi-permanent) colouring agents for hair dyeing. Additionally, after mixing under oxidative conditions (i.e. with hydrogen peroxide) the maximum concentration applied to hair must not exceed 1.5% for both permanent and semi-permanent application types. The Cosmetics Regulation also mandates label warning statements relating to the sensitisation potential of the chemical.

Use of the chemical in hair dyes is also restricted in several other countries as according to inclusion in the following listings:

- the Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex III—Part 1, with the same use restrictions as described above for the EU; and
- the New Zealand Cosmetic Products Group Standard—Schedule 5—Table 1: Components cosmetic products must not contain except subject to restrictions and conditions laid down. While a maximum concentration (of 3.0%) only appears to apply to ready for use preparations of non-oxidising (semi-permanent) colouring agents for hair dyeing, the maximum concentration applied to hair must not exceed 1.5% for both permanent and semi-permanent application types.

Scheduling application

Delegate-initiated application.

The delegate's proposed amendments to the Poisons Standard are as follows:

Schedule 6 – Delete Entry

~~2-CHLORO-6-(ETHYLAMINO)-4-NITROPHENOL **except** when in hair dye preparations containing 1.5 per cent or less of 2-chloro-6-(ethylamino)-4-nitrophenol when the immediate container and primary pack are labelled with the following statements:~~

~~KEEP OUT OF REACH OF CHILDREN, and~~

~~WARNING – This product contains ingredients which may cause skin sensitisation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye, and~~

~~written in letters not less than 1.5 mm in height.~~

Appendix E, Part 2 – Delete Entry

~~2-CHLORO-6-(ETHYLAMINO)-4-NITROPHENOL~~

~~Standard statements: A [For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)], E1 (if in eyes wash out immediately with water).~~

Appendix F, Part 3 – Delete Entry

~~2-CHLORO-6-(ETHYLAMINO)-4-NITROPHENOL~~

~~Warning statements: 28 ((over) (repeated) exposure may cause sensitisation).~~

Index – Delete Entry

~~2-CHLORO-6-(ETHYLAMINO)-4-NITROPHENOL~~

~~Schedule 6~~
~~Appendix E, Part 2~~
~~Appendix F, Part 3~~

The delegate's reasons for the proposal include:

- Information has been received from industry to indicate that the wording of the Schedule 6 entry may require further amendment to account for the use of 2-chloro-6-(ethylamino)-4-nitrophenol in other industry sectors.
- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).

Substance summary

The following toxicology information was extracted from the NICNAS IMAP Human Health Tier II assessment report for phenol, 2-chloro-6-(ethylamino)-4-nitro-.

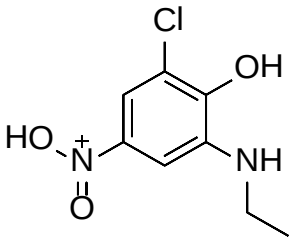

Figure 3: Chemical structure of 2-chloro-6-(ethylamino)-4-nitrophenol

Table 3A: Chemical properties and identifiers of 2-chloro-6-(ethylamino)-4-nitrophenol

Property/identifier	2-Chloro-6-(ethylamino)-4-nitrophenol
Molecular formula	$C_8H_9ClN_2O_3$
Molecular weight	216.62 g/mol
CAS name	Phenol, 2-chloro-6-(ethylamino)-4-nitro-
CAS number	131657-78-8
IUPAC and/or common and/or other names	2-Chloro-6-(ethylamino)-4-nitrophenol (INCI name)

Table 3B: Acute toxicity end-points for 2-chloro-6-(ethylamino)-4-nitrophenol

Toxicity	Species	2-Chloro-6-(ethylamino)-4-nitrophenol	SPF (2015) Classification
Acute oral toxicity LD_{50} (mg/kg bw)	Rat	1728	Schedule 6
Acute dermal toxicity LD_{50} (mg/kg bw)	Rat	>2000	Schedule 5
Acute inhalational toxicity LC_{50} ($mg/m^3/4h$)	-	No data	N/A
Skin irritation	Rabbit	Not irritating to the skin	N/A
Eye irritation	Rabbit	Insufficient data.	N/A
Skin sensitisation (Local lymph node assay, LLNA)	Mouse	Skin sensitiser	Schedule 6

Acute Toxicity

2-Chloro-6-(ethylamino)-4-nitrophenol has moderate acute oral toxicity, but low acute dermal toxicity based on results from animal tests. Additionally, the chemical is classified as hazardous with the risk phrase 'Harmful if swallowed' (Xn; R22) in the HSIS. The available data support this classification.

Irritation

The available data from animal studies indicate that 2-chloro-6-(ethylamino)-4-nitrophenol is not irritating to the skin, but is a potential eye irritant. However, insufficient details on the eye irritation study are available, which do not allow for hazard classification.

Sensitisation

2-Chloro-6-(ethylamino)-4-nitrophenol is classified as hazardous with the risk phrase 'May cause sensitisation by skin contact' (R43) in the HSIS. The positive results, reported in a local lymph node assay (LLNA), support this classification.

In an LLNA conducted according to OECD TG 429, the skin sensitising potential of 2-chloro-6-(ethylamino)-4-nitrophenol was tested in mice (5 animals/dose group) at concentrations ranging from 0.5–10% using a DMSO vehicle, and at 0.5–2.5% using an acetone/water/olive oil vehicle (mix ratio of 2:2:1). The estimated concentration needed to produce a three-fold increase in lymphocyte proliferation (EC3) value of 2.79% was determined based on the concentrations used with the DMSO vehicle; a stimulation index greater than three was not observed at the lower concentrations used with the acetone/water/olive oil vehicle (up to 2.5%).

Repeat-dose toxicity

Based on the available information, 2-chloro-6-(ethylamino)-4-nitrophenol is not considered to cause serious damage to health through repeated oral exposure.

Mutagenicity/Genotoxicity

Based on the weight of evidence from the available, well-conducted, *in vitro* and *in vivo* genotoxicity studies, the chemical is not considered to be genotoxic.

Carcinogenicity

No animal toxicity data are available on the carcinogenicity of the chemical. Based on the available genotoxicity data and mechanistic information, the chemical is not considered to be carcinogenic.

Reproduction and developmental toxicity

Based on the available information, the chemical is not expected to be a developmental toxin. No reliable data examining the effect of the chemical on fertility are available.

Observation in humans

No information was available.

Public exposure

Considering that the chemical is reported to be used in hair dye products in Australia, the main route of public exposure is expected to be dermal.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- NICNAS IMAP Tier II Report;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling Policy Framework (SPF 2015) criteria; and
- Other relevant information.

Delegate's final decision

The delegate's final decision is to delete the Schedule 6 entry for 2-chloro-6-(ethylamino)-4-nitrophenol.

The implementation date is **1 February 2017**.

The delegate considered the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989*: (a) the risks and benefits of the use of the substance; (b) the purposes for which the substance is to be used and (c) the toxicity of the substance.

The reasons for the decision comprise the following:

- Information has been received from industry to indicate that the wording of the previous Schedule 6 entry may require further amendment to account for the use of 2-chloro-6-(ethylamino)-4-nitrophenol in other industry sectors.
- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).

4. 2,4-Diaminophenoxyethanol

Scheduling proposal

The chemicals scheduling delegate initiated a scheduling proposal to amend the Schedule 6 entry for 2,4-diaminophenoxyethanol.

Current scheduling status

2,4-Diaminophenoxyethanol is currently in Schedule 6 of the Poisons Standard.

Relevant scheduling history

In March 2014, the Advisory Committee on Chemicals Scheduling (ACCS) included 2,4-diaminophenoxyethanol in Schedule 6 and Appendices E and F of the Poisons Standard. Although the applicant's scheduling proposal specifically referenced the sulfate salt, it was noted at the meeting that the hydrochloride salt (2,4-diaminophenoxyethanol dihydrochloride) was used in the toxicity assessment and that the sulfate salt and free alcohol will likely have comparable physical/chemical and toxicological properties. The implementation date was 1 October 2014.

In August 2016, the chemicals scheduling delegate received an application to amend the Schedule 6 entry for 2,4-diaminophenoxyethanol. The delegate made a delegate-only decision in January 2017 with a 1 February 2017 implementation date.

Australian regulatory information

2,4-Diaminophenoxyethanol hydrochloride is listed on the Australian Inventory of Chemical Substances (AICS) and is reported to be used in permanent hair dye preparations in Australia (NICNAS, 2007).

International regulations

The Association of South East Asian Nations (ASEAN), Canada, New Zealand and the European Union (EU) have restricted the use of this chemical in cosmetics. Following a safety evaluation, the Scientific Committee on Consumer Products (SCCP) concluded that the use of the chemical 'as an oxidative hair dye at a maximum concentration of 2.0% in the finished cosmetic product (after mixing with hydrogen peroxide) does not pose a risk to the health of the consumer, apart from its sensitising potential' (SCCP, 2006).

The chemical is listed on the following:

- The ASEAN Cosmetic Directive Annex III—Part 1: List of substances which cosmetic products must not contain except subject to restrictions and conditions laid down: 'After mixing under oxidative conditions the maximum concentration applied to hair must not exceed 2.0% (as hydrochloride)';
- The EU Regulation (EC) No 1197/2013 of the European Parliament and of the Council of 1 July 2014 on cosmetic products Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down: 'After mixing under oxidative conditions the maximum concentration applied to hair or eyelashes must not exceed 2.0% (as hydrochloride) and for professional use only'. The Cosmetic Regulation also mandates label warning statements relating to the sensitisation potential of the chemical;
- New Zealand Cosmetic Products Group Standard—Schedule 5: Components cosmetic products must not contain except subject to the restrictions and conditions laid down: 'In combination with hydrogen peroxide the maximum use concentration upon application is 2.0% as hydrochloride'; and
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient 'Hotlist').

Scheduling application

Delegate-initiated application.

The delegate's proposed amendments to the Poisons Standard are as follows:

Schedule 6 – Amended Entry

2,4-DIAMINO-PHENOXYETHANOL in hair dye preparations **except** in preparations containing 4 per cent or less of 2,4-diaminophenoxyethanol when the immediate container and primary pack are labelled with the following:

KEEP OUT OF REACH OF CHILDREN

WARNING – this product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dying eyelashes and eyebrow; to do so may be injurious to the eye.

Written in letters not less than 1.5 mm in height.

Appendix E, Part 2 – Current Entry

2,4-DIAMINO-PHENOXYETHANOL

Standard statements: A [For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)], E1 (If in eyes wash out immediately with water.).

Appendix F, Part 3 – Amended Entry

2,4-DIAMINO-PHENOXYETHANOL

Warning statement: 21 (WARNING – This product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to accompanying directions should be made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye.).

Index – Current Entry

2,4-DIAMINO-PHENOXYETHANOL

Schedule 6
Appendix E, Part 2
Appendix F, Part 3

The delegate's reasons for the proposal include:

- Information has been received from industry to indicate that the wording of the current Schedule 6 entry may require further amendment to account for the use of 2,4-diaminophenoxyethanol in other industry sectors.
- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).

Substance summary

The following information was extracted from the NICNAS IMAP Human Health Tier II group assessment report for Ethanol, 2-(2,4-diaminophenoxy)-, hydrochloride.

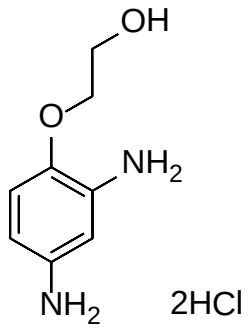

Figure 4: Structure of 2-(2,4-diaminophenoxy)ethanol

Table 4A: Chemical properties and identifiers of 2,4-diaminophenoxyethanol

Property/identifier	2,4-Diaminophenoxyethanol
Molecular formula	$C_8H_{12}N_2O_2.2HCl$
Molecular weight	241.119 g/mol
CAS name	ethanol, 2-(2,4-diaminophenoxy)-, hydrochloride (1:2)
CAS number	66422-95-5
IUPAC and/or common and/or other names	2,4-diaminophenoxyethanol HCL (INCI); 2,4-diaminophenoxyethanol hydrochloride.

Table 4B: Acute toxicity end-points for 2-(2,4-diaminophenoxy)ethanol hydrochloride

Toxicity	Species	2,4-diaminophenoxyethanol	SPF (2015) Classification
Acute oral toxicity LD_{50} (mg/kg bw)	Rat Mouse	1000 1160	Schedule 6
Acute dermal toxicity LD_{50} (mg/kg bw)	N/A	No data	N/A
Acute inhalational toxicity LC_{50} ($mg/m^3/4h$)	N/A	No data	N/A
Skin irritation	Rabbit	Non-irritant	N/A
Eye irritation	Rabbit	Irritant	Schedule 5/6
Skin sensitisation (local lymph node assay, LLNA)	Guinea pig Mouse	Moderate sensitiser	Schedule 6

Acute toxicity

The chemical is considered to have moderate acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) was approximately 1000 mg/kg bw in Sprague Dawley (SD) rats and 1160 mg/kg bw in Swiss albino mice. No data were available for acute dermal and inhalation toxicity.

Skin Irritation

Based on the limited available data, the chemical is not considered to be a skin irritant.

Eye Irritation

Based on the available data, the chemical is considered to be an eye irritant:

- In an eye irritation study conducted according to OECD TG 405 with three female New Zealand White rabbits, the undiluted 2,4-diaminophenoxyethanol hydrochloride was instilled into the conjunctival sac of the left eye of each animal. The eyes were not rinsed following instillation of the chemical. Moderate to marked chemosis, slight to moderate conjunctival redness, slight to moderate corneal opacification and slight iridial lesions were observed in the animals. These effects were not fully reversed at the end of the study (day 15). It was concluded that the undiluted chemical was irritating to rabbit eyes.
- In two other eye irritation studies carried out in three female New Zealand White rabbits and three albino Bouscat rabbits, a 4% solution of the chemical did not produce any irritation.

Sensitisation

Based on the available data, the chemical is considered to be a moderate skin sensitiser:

- One LLNA was conducted according to OECD TG 429 in female CBA/J mice (n=4/group). The chemical at 0.5, 1.0, 2.5, 5.0 or 10% dilutions produced a stimulation index (SI) of 0.92, 1.56, 1.17, 4.21 and 7.42, respectively. The estimated concentration needed to produce a three-fold increase in lymphocyte proliferation (EC3) was calculated to be 3.2%, indicating a moderate sensitising potential.

- In a Buehler test (OECD TG 406) conducted using ten Dunkin Hartley guinea pigs per sex, no sensitisation reaction was observed with topical induction and challenge applications of the undiluted chemical after 48 hours.

Repeat-dose toxicity

Based on the available data, 2,4-diaminophenoxyethanol hydrochloride is not expected to cause serious damage to health from repeated oral exposure. No information was available for repeated dose toxicity by dermal and inhalation routes.

Genotoxicity

Based on the negative results observed in several *in vitro* and *in vivo* genotoxicity studies, the chemicals are not expected to be genotoxic.

Carcinogenicity

Based on the available data, the chemical is not considered to be carcinogenic.

Reproduction and developmental toxicity

Based on the available data, the chemical is not expected to have reproductive and developmental toxicity.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- NICNAS IMAP Tier II Report;
- Section 52E of the *Therapeutic Goods Act 1989*; and
- Scheduling Policy Framework (SPF 2015) criteria.

Delegate's final decision

The delegate's final decision is to amend the Schedule 6 and Appendix F, Part 3 entries for 2,4-diaminophenoxyethanol as follows:

Schedule 6 – Amended Entry

2,4-DIAMINO-PHENOXYETHANOL in hair dye preparations **except** in preparations containing 4 per cent or less of 2,4-diaminophenoxyethanol when the immediate container and primary pack are labelled with the following:

KEEP OUT OF REACH OF CHILDREN

WARNING – this product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dying eyelashes and eyebrow; to do so may be injurious to the eye.

Written in letters not less than 1.5 mm in height.

Appendix F, Part 3 – Amended Entry

2,4-DIAMINO-PHENOXYETHANOL

Warning statement: 21 (WARNING – This product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to accompanying directions should be

made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye.).

The implementation date is **1 February 2017**.

The delegate considered the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989*: (a) the risks and benefits of the use of the substance; (b) the purposes for which the substance is to be used and (c) the toxicity of the substance.

The reasons for the decision comprise the following:

- Information has been received from industry to indicate that the wording of the previous Schedule 6 entry may require further amendment to account for the use of 2,4-diaminophenoxyethanol in other industry sectors.
- The delegate will review the previous January 2017 decision and seek advice from the scheduling committees (ACCS and ACMS).