Australian Government
Department of Health
Therapeutic Goods Administration

Notice of interim decisions to amend (or not amend) the current Poisons Standard

TGA Health Safety Regulation

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1 Notice of interim decisions made under Regulation 42ZCZN of the *Therapeutic Goods Regulations 1990*

This web publication constitutes a notice for the purposes of regulation 42ZCZP of the *Therapeutic Goods Regulations 1990* (the **Regulations**). In accordance with regulation 42ZCZP, this notice sets out:

- the interim decisions made by a delegate of the Secretary under regulation 42ZCZN in relation to proposed amendments to the current Poisons Standard which were referred to an expert advisory committee under subdivision 3D.2 of the Regulations in March 2021;
- the proposed date of effect of the proposed amendments (in circumstances where the interim decision proposes an amendment to the current Poisons Standard).

In accordance with regulation 42ZCZP, interested persons (including the applicant requesting the amendment) are invited to make submissions to the Secretary in relation to these interim decisions on or before **17 August 2021**.

We have changed the way to make submissions.

Submissions should now be provided through our consultation hub. Submissions will be considered by the Delegate in making the final decision.

Please note that in accordance with subregulation 42ZCZQ(4) of the Regulations, the Secretary must publish all relevant submissions received, unless the Secretary considers the information to be confidential information.

2 Interim decisions on proposed amendments referred to the Advisory Committee on Medicines Scheduling (ACMS #33, March 2021)

2.1 Interim decision in relation to metoclopramide

Proposal

The applicant proposed an amendment to include metoclopramide in Appendix H of the Poisons Standard to allow direct-to-consumer advertising of pharmacist only medicines containing the substance.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision not to amend the current Poisons Standard in relation to metoclopramide.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to metoclopramide;
- The 31 public submissions, including five written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #33);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard; and
- Appendix 1 - Guidelines for advertisements for medicines containing Schedule 3 substances (tga.gov.au).

Summary of ACMS advice to the Delegate

The Committee advised that the current scheduling for metoclopramide remains appropriate.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Benefits:
  - Useful for vomiting, nausea and treatment of migraines due to anti-emetic properties.
- Risks:
  - Over 300 adverse reports where this medicine was the single suspected drug. Effects included drowsiness, confusion, diarrhoea, fatigue. Rarer side effects include extrapyramidal movement disorders and tardive dyskinesia, which may be irreversible. Associated neuroleptic malignant syndrome may be life-threatening.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Migraine – dosage controlled for short periods. Symptomatic relief of headache, nausea and vomiting associated with migraines.
- No information provided on extent of use, however migraines are experienced by over 3 million Australians.
- Short-term treatment (1-2 days).

c) the toxicity of a substance

- Tolerable in prescribed doses which must be clearly labelled.
- Reported side effects include drowsiness, disorientation, extrapyramidal reactions, seizures in infants, tardive dyskinesia and extrapyramidal disorders may be irreversible.
- Increase in gut motility causes interactions with many other drugs.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- Packaging of 10 dosage units (Schedule 3 preparations).
- Each tablet contains 5mg metoclopramide 500mg paracetamol.
- Dosage is 1-2 tablets initially, followed by one tablet every 4 hours to a maximum of 6 tablets in a 24-hour period.

e) the potential for abuse of a substance

- The potential for using this medicine beyond the Schedule 3 uses of the substance (for reasons other than migraine) is high, particularly if awareness is raised in the community of its availability at a pharmacy. There is a risk of misuse for its Schedule 3 indications for hangovers, especially in young people, who are at the highest risk of serious extrapyramidal adverse effects (half the cases reported to NSW PIC were patients under 20 years old)

f) any other matters that the Secretary considers necessary to protect public health

- nil.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision not to amend the scheduling of metoclopramide in the current Poisons Standard.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance.

I find that the evidence presented by the applicant is insufficient to overturn the 2018 decision not to include metoclopramide in Appendix H. The same arguments continue to apply regarding the sedating properties of metoclopramide, the potential for misuse and increased pressure on pharmacists to supply metoclopramide off-label.

I have considered arguments from the applicant and those written public submissions supportive of direct to consumer advertising, that metoclopramide does not possess inherent sedative properties. While not inherently sedating, metoclopramide's sedating effects are additive to those of alcohol, hypnotics, narcotics, tranquilisers and sedative medications. The TGA Guidelines for advertisements for medicines containing Schedule 3 substances[1] allows for the exclusion of a Schedule 3 substance from Appendix H where it is determined that the potential public health impact from direct to consumer advertising is adverse. I find that the sedating potential of metoclopramide requires increased patient education to ensure its continuing safe use and that there is potential for inappropriate use that may be exacerbated by advertising.

Metoclopramide is indicated for short-term use of 1 -2 days only and it has significant adverse effects when used in those under 18 years of age, with longer courses of treatment and at higher doses. Adverse effects associated with metoclopramide, while rare, may be irreversible. These include tardive dyskinesia (movement disorder with abnormal movement of face, mouth and tongue) and extrapyramidal movement disorders (abnormal involuntary movements such as writhing, dystonia, akinesia, tremors and rigidity). In the event of associated medicine-induced neuroleptic malignant syndrome, this adverse effect is potentially life-threatening. I have noted with concern that that the NSW Poisons Information Centre (PIC) received 84 calls regarding adverse reactions to therapeutic doses of metoclopramide from 2014 - 2020, with 66 requiring medical attention.

Taking into account the potential for serious adverse effects from use of metoclopramide, even at therapeutic doses, I find that direct consumer advertising of this substance is not in the interest of protecting public health.

I am not satisfied by claims that the proposed wording for an Appendix H entry, which specifies the indication for use, would adequately mitigate the pressure on pharmacists to supply metoclopramide off-label. Nor would it be sufficient to dissuade consumers from using the medication for reasons other than migraine.

Material to my decision has been consideration of whether direct to consumer advertising of metoclopramide would be in line with the quality use of the medicine. In forming my view that it would not, I have taken into account the submissions from the NSW PIC regarding adverse events from use of metoclopramide at therapeutic doses, particularly in children and adolescents under the age of 20 and the Australian Medical Association (AMA) regarding off-label use by patients and the risk of dystonic reactions (involuntary, slow, and sustained contractions of muscle groups in either sustained or intermittent patterns, which may result in twisting, repetitive movements, and abnormal posturing), particularly in patients aged 12- 17.

[1] https://www.tga.gov.au/sites/default/files/appendix-1-guidelines-for-advertising-medicines-containing-schedule-3-substances.pdf

I have considered the views expressed by the applicant that it would be advantageous for Australian consumers to be aware, through direct to consumer advertising, that metoclopramide can be used for the symptomatic relief of headache, nausea and vomiting associated with migraine. I am of the view however, that the potential diversion of metoclopramide for uses other than nausea and vomiting associated with migraine is high, particularly if awareness is raised in the community of its availability at pharmacy. As previously noted, even under existing scheduling arrangements, the AMA submission cited anecdotal reports of patients being supplied with metoclopramide for conditions other than migraine. Greater community awareness from direct to consumer advertising could result in increased pressure on pharmacists to supply metoclopramide off-label.

On balance, I find that the potential adverse impacts on public health outweigh the benefits of direct to consumer advertising for metoclopramide. The sedating properties of the substance can impact on its safe use and there is the potential for inappropriate use and diversion that may be exacerbated by advertising.

2.2 Interim decision in relation to chloramphenicol

Proposal

The applicant proposed an amendment to include chloramphenicol in Appendix H of the Poisons Standard to allow direct-to-consumer advertising of pharmacist only medicines containing the substance.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision not to amend the current Poisons Standard in relation to chloramphenicol.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to chloramphenicol;
- The 62 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #33);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard; and
- Appendix 1 - Guidelines for advertisements for medicines containing Schedule 3 substances (tga.gov.au)

Summary of ACMS advice to the Delegate

The Committee advised that the current scheduling for chloramphenicol remains appropriate.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included: (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters considered necessary to protect public health.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Benefits:
  - Chloramphenicol is the most common first-line antibiotic prescribed for bacterial conjunctivitis, otherwise known as 'red eye' or 'pink eye'.
- Risks:
  - Increased demand for inappropriate use of antibiotics. Most eye infections are not bacterial.
  - Antibiotic overuse.
  - Consumer self-diagnosis.
  - Inherent difficulties in differentiating viral and bacterial conjunctivitis without professional medical advice.

b) the purposes for which a substance is to be used and the extent of use of a substance

- TGA-approved ARTG specific indication is 'For the treatment of bacterial conjunctivitis and other superficial ocular infections caused by chloramphenicol sensitive organisms'.
- Chloramphenicol is a Schedule 3 medicine for ophthalmic use only. Pharmacists can supply chloramphenicol as a Schedule 3 medicine only for the treatment of bacterial conjunctivitis for patients aged 2 years and older.

c) the toxicity of a substance

- In rare cases, chloramphenicol can have fatal side effects, including bone marrow hypoplasia with aplastic anaemia. The mechanism of these adverse events is unknown.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- Not applicable.

e) the potential for abuse of a substance

- Nil.

f) any other matters that the Secretary considers necessary to protect public health

- Broader policy on antimicrobial resistance.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision not to amend the current Poisons Standard in relation to chloramphenicol. My view is that the current scheduling of chloramphenicol is appropriate. The detailed reasons for my decision follow.

I have taken into account the purposes for which chloramphenicol is to be used and the extent of its use. Chloramphenicol is the most common first-line antibiotic prescribed for bacterial conjunctivitis, otherwise known as 'red eye'. Pharmacists can supply chloramphenicol as a Schedule 3 medicine only for the treatment of bacterial conjunctivitis for patients aged 2 years and older. Most eye infections are not bacteria and there are inherent difficulties in

differentiating viral, bacterial and allergic conjunctivitis. It follows that pharmacist advice is necessary before chloramphenicol can be safety supplied to consumers.

Having considered Appendix 1 - Guidelines for advertisements for medicines containing Schedule 3 substances, it is my view that chloramphenicol is unsuitable for direct advertising to the public, as greater consumer awareness is likely to increase the demand for inappropriate use of antibiotics and exacerbate consumer self-diagnosis.

I have not identified, and the applicant has not provided, sufficient evidence to suggest that the benefits of greater consumer awareness through advertising outweigh the delegate's concerns, raised in 2018, on the potential for promoting antibiotic resistance and the inherent difficulties in differentiating viral and bacterial conjunctivitis without professional medical advice.

The argument made by the applicant that advertising can facilitate early antibiotic treatment for bacterial conjunctivitis by informing consumers they can consult a pharmacist for early treatment and avoid potential for spreading the disease is noted with concern. The literature indicates two-thirds of bacterial conjunctivitis cases self-resolve, and do not require treatment. I consider that advertising could promote inappropriate self-diagnosis by consumers, and result in selection bias from consumers attending community pharmacies and compromise the process of professional clinical consultation by community pharmacists. On balance, I have not identified sufficient grounds to persuade me to accept the notion that advertising is in the interest of promoting public health. My view is that advertising chloramphenicol to consumers may promote unnecessary and improper overuse of antibiotics.

Antimicrobial resistance is one of the biggest threats to human today.[2] The applicant's claim that increased consumer and medical practitioner general awareness around antibiotic resistance is a mitigating factor against improper use, is inconsistent with a number of public health initiatives currently in place, which I find relevant to my interim decision. I understand that advertising would be inconsistent with the objectives of the National Antimicrobial Resistance Strategy, and Australia's commitment as part of the National Medicines Policy. Advertising will increase the difficulty to implement the Quality Use of Medicines (QUM) principle of using medicines safely and effectively. This National Strategy aims to recognise that there may be better ways than medicine to manage many disorders and many factors should be considered in choosing suitable medicines if a medicine is considered necessary. Advertising would be inconsistent with the objectives of the National Antimicrobial Resistance Strategy, and Australia's commitment as part of the National Medicines Policy. Finally, advertising will undermine the fundamental role of health professionals in antimicrobial stewardship.

I have had particular regard for the public submissions from a number of peak organisations, including the Pharmaceutical Society of Australia, the Pharmacy Guild, the Australian Medical Association and the Queensland Nurses and Midwives' Union, all of whom were opposed to the proposal to advertise chloramphenicol.

I find that advertising chloramphenicol direct to the public can be misleading to consumers and may suggest chloramphenicol is safe and inherently of low-risk, which will increase inappropriate demand from consumers, and exacerbate antibiotic resistance.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters considered necessary to protect public health.

[2] https://www.amr.gov.au/about-amr

2.3 Interim decision in relation to prochlorperazine

Proposal

The applicant proposed an amendment to include prochlorperazine in Appendix H of the Poisons Standard to allow direct-to-consumer advertising of pharmacist only medicines containing the substance.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision not to amend the current Poisons Standard in relation to prochlorperazine.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to prochlorperazine;
- The 60 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #33);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (e) the potential for abuse of a substance;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard; and
- Appendix 1 - Guidelines for advertisements for medicines containing Schedule 3 substances (tga.gov.au).

Summary of ACMS advice to the Delegate

The Committee advised that the current scheduling for prochlorperazine remains appropriate.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included: (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (e) the potential for abuse of a substance.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Benefits:
  - Treatment of nausea associated with migraine.
- Risks:
  - Prochlorperazine acts across multiple systems in the body: CNS depression, extrapyramidal, QT prolongation and anticholinergic effects are frequent with prochlorperazine. Prochlorperazine was shown to inhibit histaminergic, cholinergic

and alpha-1 adrenergic receptors. The blockade of alpha-1 adrenergic receptors may result in sedation, muscle relaxation, and hypotension.

- Known drug-drug interactions: Additive effects are likely when combined with commonly used agents including anti-psychotics, sedatives and some antidepressants. Prochlorperazine can interact with other depressant medicines and substances and enhance CNS depressant.
- Prochlorperazine carries a significant fall risk.
- Mask other conditions: Antiemetic effect of prochlorperazine, for which patients access this substance as a Schedule 3 medicine, may mask signs of overdose of toxic drugs or obscure the diagnosis of other conditions (e.g. intestinal obstruction and brain tumour).

b) the purposes for which a substance is to be used and the extent of use of a substance

- When supplied as a Schedule 3 medicine, the TGA-approved ARTG specific indication for prochlorperazine is 'for the treatment of nausea associated with migraine'.
- As a Schedule 3 medicine, prochlorperazine is indicated only for the treatment of nausea associated with migraine, in limited pack sizes.
- Consumers are aware that treatments for migraine are available without prescription, especially now that triptans are in Appendix H. Advertising prochlorperazine may increase pressure on pharmacists to supply it, rather than the pharmacist recommending the best medicine for each patient.

c) the toxicity of a substance

- As described above:
  - CNS depression
  - extrapyramidal
  - QT prolongation
  - anticholinergic effects
  - interactions with other (some common) medicines
  - may mask signs of overdose with other toxic substances

d) the dosage, formulation, labelling, packaging and presentation of a substance

- Not applicable.

e) the potential for abuse of a substance

- Potential for abuse or misuse based on evidence that prochlorperazine can alter mood and perception. Consumers may purchase prochlorperazine for indications other than 'for the treatment of nausea associated with migraine' with the knowledge that the active ingredient is the same as what is found in Schedule 4 products.

f) any other matters that the Secretary considers necessary to protect public health

- Nil.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision not to amend the current Poisons Standard in relation to prochlorperazine. My view is that the current scheduling of prochlorperazine is appropriate. The detailed reasons for my decision follow.

I have not identified, and the applicant has not provided, sufficient evidence to adequately mitigate the delegate's concerns, raised in 2018, on the potential negative impact on public health related to possible misuse, abuse or diversion.

Having considered Appendix 1 - Guidelines for advertisements for medicines containing Schedule 3 substances, I find that the potential for abuse may be exacerbated by advertising, and that the significant known drug-drug interactions and sedating potential require increased patient education to ensure the continuing safe use of prochlorperazine.

There are a number of safety considerations I find relevant to my deliberations on the appropriateness of direct advertising of prochlorperazine to the public, these include:

- prochlorperazine acts across multiple systems in the body: CNS depression, extrapyramidal, QT prolongation and anticholinergic effects are frequent. Prochlorperazine was shown to inhibit histaminergic, cholinergic and alpha-1 adrenergic receptors. The blockade of alpha-1 adrenergic receptors may result in sedation, muscle relaxation, and hypotension.
- Drug-Drug interactions: Additive effects are likely when prochlorperazine is combined with commonly used agents including anti-psychotics, sedatives and some antidepressants. Prochlorperazine can interact with other depressant medicines and substances and enhance CNS depressant.
- Prochlorperazine is required to have a sedation warning on the label as it is listed in Appendix K of the Poisons Standard.
- Potential for abuse or misuse: based on evidence that prochlorperazine can alter mood and perception. Consumers may purchase prochlorperazine for indications other than 'for the treatment of nausea associated with migraine' with the knowledge that the active ingredient is the same as what is found in more restricted Schedule 4 products.
- Mask other conditions: Antiemetic effect of prochlorperazine, for which patients access this substance as a Schedule 3 medicine, may mask signs of overdose of toxic drugs or obscure the diagnosis of other conditions (e.g. intestinal obstruction and brain tumour).
- Significant increased fall risk.

According to the Appendix 1 - Guidelines for advertisements for medicines containing Schedule 3 substances, when deciding if there is a reason for not permitting a substance to be advertised, the delegate will consider the potential impact on public health. The wide range of potential drug-drug interactions and its sedating potential, both of which warrant individual consultation with a pharmacist to ensure patient safety are noted with concern. Of particular relevance to Appendix 1 - Guidelines for advertisements for medicines containing Schedule 3 substances, is the sedation potential of prochlorperazine, which was a key consideration in my deliberations on the reasons not to advertise. On the balance of evidence, I find that the need for pharmacist oversight to manage the known safety risks outweigh the benefits of greater consumer awareness through advertising. It is my view that advertising may result in selection bias from consumers attending community pharmacies and this may undermine the process of professional clinical consultation insofar as the appropriate management of nausea associated with migraines.

In making my interim decision, I have had particular regard for the submissions from a number of peak organisations, including: the Pharmaceutical Society of Australia, the Pharmacy Guild,

the Australian Medical Association and the Queensland Nurses and Midwives' Union. These organisation were opposed to the proposal to advertise prochlorperazine.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of the substance; (b) the purposes for which a substance is to be used and the extent of use of the substance; (c) the toxicity of the substance; and (e) the potential for abuse of the substance.

2.4 Interim decision in relation to processed *Aconitum carmichaelii*

Proposal

The applicant proposed an amendment to the scheduling of processed *Aconitum carmichaelii* (*A. carmichaelii)* with the intent that it is down-scheduled to general sales level in certain preparations used in Traditional Chinese Medicine (TCM). *A. carmichaelii* is currently listed in Schedule 2 and Schedule 4 of the Poisons Standard, with exceptions at low levels of alkaloids.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision not to amend the current Poisons Standard in relation to processed *A. carmichaelii*.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to processed *A. carmichaelii*;
- The 331 public submissions, including 52 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #33);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACMS advice to the Delegate

The Committee advised that the current scheduling for processed *A. carmichaelii* remains appropriate.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Benefits:
  - The substance has established uses in Traditional Chinese Medicine, however it is difficult to assess benefits as traditional use is outside Western medicine paradigms.
- Risks:
  - Significant risk, with deaths reported even when used in countries where traditional use is well established and well documented and where pharmacopoeial standards apply.
  - The substance is a complex mix of alkaloids, for which toxicological data is incomplete.
  - Issues of potential bacterial and/or fungal contamination for the ingredient need to be addressed.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Traditional Chinese Medicine uses of *Aconitum* species include treatment of mental fatigue, loose stools, abdominal pain, faint pulse and oedema.

c) the toxicity of a substance

- Significant toxicity potential including cardiovascular, neurological and gastrointestinal systems related to the action on voltage-dependent Na+ channels. There is a lack of clarity regarding safe levels of many of the constituent alkaloids, and there are no specific antidotes for aconitum poisoning.
- The symptoms associated with *Aconitum* toxicity include numbness of the face, body and extremities, muscle weakness, involuntary salivation, nausea, vomiting, abdominal pain, diarrhea, hypotension, palpitations, sinus tachycardia, ventricular ectopic and ventricular arrhythmias. Deaths due to cardiac arrest and respiratory failure have been attributed to *Aconitum* species.
- Preparations of *Aconitum* spp. have a narrow therapeutic range. There is evidence that around 20 per cent of *Aconitum carmichaelii* lateral root preparations in China exceed the maximum levels of the main toxic alkaloids allowed by the national pharmacopoeia.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- The proposed guidelines for the packaging and labelling include a requirement that Traditional Chinese Medicine practitioners use a product processed/manufactured by a GMP licensed manufacturer, and each batch must have a certificate of analysis demonstrating evidence of compliance with quality standards. It is unclear how these guidelines would be enforced in an unscheduled product that was not included on the ARTG.
- Concerns with regards to preparation and uniformity of the ingredients, increasing the risk of contamination, particularly when prepared traditionally.
- Use of *A. carmichaelii* lateral root preparations requires the patient to further decoct the dried root to reduce toxicity, prior to ingestion.

e) the potential for abuse of a substance

- Not applicable.

f) any other matters that the Secretary considers necessary to protect public health

- Possible scope for future discussion with the Chinese Medicine Board of Australia regarding the scheduling framework for TCM herbal medicines.
- The current entry in the Poisons Standard for Aconitum covers all species, whereas the application only refers to *A. carmichaelii*.
- ISO standards are currently in development but only for this particular product and does not cover any other aconitum species.
- Hong Kong and China reports of toxicity despite widespread use of Traditional Chinese Medicine practitioners.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision not to amend the scheduling of processed *A. carmichaelii* in the current Poisons Standard.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

A. carmichaelii is covered by the Schedule 2 and Schedule 4 entries for *Aconitum spp.* in the current Poisons Standard. In Australia, unless they are also registered medical practitioners, Traditional Chinese Medicine (TCM) practitioners are restricted to use of medicines that are exempt from scheduling. The current application seeks to amend the scheduling of *Aconitum spp*. to allow TCM practitioners to prescribe and supply processed *A. carmichaelii*, a common ingredient in TCM.

Having considered the matters set out in the application and the Scheduling Policy Framework's (SPF 2018), Scheduling Factors for inclusion of medicines in Schedule 2 and Schedule 4, I find there is insufficient evidence to support the down-scheduling of processed preparations of *Aconitum carmichaelii* used in TCM.

In accordance with the cascading principle for the scheduling of substances, exemption of a particular medicinal preparation to allow supply from general sales outlets (such as supermarkets) means that it does not meet the factors for Schedules 2, 3, 4 or 8. Medicinal preparations exempted from scheduling must also able to be supplied, with 'reasonable safety', as detailed in the Scheduling Handbook.

'Reasonable safety' indicates that:

- the consumer is able to identify and self-manage the condition for which the medicine is intended without health professional input
- the risk of the consumer confusing their condition with more serious diseases or conditions is very small
- the risks to health from the medicine are small and can be managed with packaging and labelling
- the risk of inappropriate use or misuse of the medicine is negligible.

On the basis of evidence provided with the application, I am not satisfied that processed *A. carmichaelii* for use in TCM, meets the standard for 'reasonable safety' and my reasons for this are detailed below.

Aconitum spp. exhibit neurological and cardiac toxicity due to the presence of various alkaloids including the highly toxic diester diterpenoid alkaloids (DDAs). As severe poisoning may occur after improper ingestion of DDA-containing medicines, *Aconitum* herbs are traditionally boiled or steamed prior to dispensing. This processing aims to covert the DDAs to monoester diterpenoid alkaloids (MDAs), which are less toxic but retain pharmacological activity. To ensure safety, once dispensed *Aconitum* herbs need to be further treated by the patient, by prolonged decoction immediately before consumption.

It is my understanding that adequate preparation and processing can reduce the content of the toxic DDAs to minimal or even undetectable levels. However, changes in decoction time can lead to clinically significant changes in the toxicity of the preparation. This means that the toxicity of *A. carmichaelii* is dependent on both the initial processing undertaken prior to dispensing and the way in which the patient uses the processed product. While it may be possible to be confident of the quality and DDA content of *A. carmichaelii* commercially manufactured under GMP conditions and with quality assessed by the TGA prior to use, I am not satisfied that the quality and the DDA content can be assured in products individually compounded as part of TCM practice. As improperly prepared *A. carmichaelii* can result in the ingestion of toxic levels DDAs, I am of the view that use of the medicine, and its availability at general sales level, present an unacceptable risk to public health.

I am also concerned that *A. carmichaelii* can be used in combination with other TCM herbal ingredients, potentially increasing health risks from use of the medicine. While the risk profile of properly prepared and decocted *A. carmichaelii* is well-defined, interactions are not well characterised. Interactions between *A. carmichaelii* and other products used in TCM, are reported to either decrease or increase the toxicity of *A. carmichaelii*[3],[4].

In making my decision not to amend the current scheduling of *Aconitum spp*., I have taken into account the intended conditions for which processed *A. carmichaelii* will be used. TCM and 'Western' medicine use different diagnostic and therapeutic paradigms. As a result, the range of conditions that TCM is used for do not easily translate to common diagnoses in 'Western' medicine. Symptoms of conditions for which *A. carmichaelii*, might be indicated in TCM include: mental fatigue; extreme fatigue; low and faint voice; aversion to cold with cold limbs; loose stools or diarrhoea; oedema, especially pitting oedema of the lower limbs, faint or weak pulse; and ascites.[5]. These symptoms cover a range of 'Western' diagnoses that can be associated with a variety of conditions some of which are not minor aliments or suitable for self-diagnosis. Based on the available evidence, I am not satisfied that the use of *A. carmichaelii* at therapeutic doses would not potentially mask symptoms or delay diagnosis of serious conditions such as cardiovascular dysfunction or thyroid dysfunction.

I acknowledge arguments presented in the application and in public submissions supportive of the scheduling proposal that processed *A. carmichaelii* is an important herb in Chinese medicine, with a long history of use. However, in Australia, where TCM is not the predominant medical paradigm, there is greater likelihood of use outside the parameters of TCM and this has the potential to result in even greater risk of harm to consumers. I find the risk of harm is compounded by the lack of clinical evidence supporting the efficacy of *A. carmichaelii* or any other *Aconitum* species in any particular indication.

The limits of DDAs below which preparations would be exempted from scheduling, as proposed under the current application, are based on the maximum DDA limits and doses recommended in the Chinese Pharmacopoeia for *A. carmichaelii* (that is, maximum concentration of 0.02% DDAs in processed *A. carmichaelii* prior to decoction, equal to maximum 0.6 mg single dose and 3.0 mg total daily dose of DDAs). However, I am not certain that these levels are appropriate. No

[3] Singhuber J, Zhu M, Prinz S, Brigitte Kopp B. (2009) Aconitum in traditional Chinese medicine: a valuable drug or an unpredictable risk? J Ethnopharmacol, 126(1):18-30.
[4] Jing X. (2018) Monkshood Components and Adverse Reactions of Radix Aconiti. J Pract Trad Chinese Med. 12:73-75.
[5] Huang H (2020). On Fuzi. Prepared for Federation of Chinese Medicine & Acupuncture Societies of Australia Ltd.

toxicological basis for these levels has been proposed and the minimum toxic level of combined or individual DDAs in humans is not clear. Further, compounds found in *Aconitum spp*., especially DDAs, appear to have narrow therapeutic windows. Published scientific papers indicate that the minimum lethal dose of aconitine, one of the three major DDAs present in *A. carmichaelii,* for humans is estimated at 1-2 mg[6] and severe toxicity has been reported after ingestion of as little as 0.2 mg aconitine[7].

There are no specific antidotes for *Aconitum* poisoning, and symptoms occur within 2 hours of ingestion. The main acute and chronic toxicity effects of *Aconitum* preparations and purified alkaloids are observed in the cardiovascular, neurological and gastrointestinal systems. Symptoms often associated with *Aconitum* toxicity include numbness of the face, body and extremities, muscle weakness, involuntary salivation, nausea, vomiting, abdominal pain, diarrhoea, hypotension, palpitations, sinus tachycardia, ventricular ectopic, ventricular arrhythmias, and death due to cardiac arrest and respiratory failure[8],[9],[10],[11],[12]. I am concerned that access to *A. carmichaelii* at the general sales level may result in self-managed treatment of potentially serious and life-threatening conditions which require medical assessment, monitoring and treatment and for which, more appropriate medications are available. I find that the seriousness of potential adverse effects from the inappropriate use or misuse of *A. carmichaelii* preclude its exemption from Scheduling.

In relation to exempting *Aconitum species* for therapeutic use from scheduling, I have also considered the applicant's proposed guidelines for prescribing, packaging and labelling. These guidelines include requirements for TCM practitioners to use a product processed/manufactured by a GMP-licenced manufacturer and that each batch used must have a certificate of analysis demonstrating evidence of compliance with quality standards including DDA content. These guidelines have not been material to my decision as it is unclear how these guidelines would be enforced.

I am also concerned that if *A. carmichaelii* were to be exempt from scheduling, there would be no controls over who could supply it under state and territory medicines and poisons legislation. Although the registration requirements for Chinese medicine practitioners in Australia regulates the use of qualified practitioner titles and limits advertising of services, this registration would not directly determine who could supply and use *Aconitum spp.* preparations that meet the exemption criteria, making it available to the general public through general retail sales. This means that someone purporting to be providing natural or traditional types of medicine treatments could supply preparations containing *Aconitum spp.* that meet the exemption criteria, regardless of whether they have any training in or knowledge of TCM.

[6] Gao, X., Hu, J., Zhang, X., Zuo, Y., Wang, Y. and Zhu, S., 2020. Research progress of aconitine toxicity and forensic analysis of aconitine poisoning. *Forensic Sciences Research*, *5*(1), pp.25-31.
[7] Tai, Y.T., Lau, C.P., Young, K. and But, P.H., 1992. Cardiotoxicity after accidental herb-induced aconite poisoning. *The Lancet*, *340*(8830), pp.1254-1256.
[8] Nyirimigabo E, Xu Y, Li Y, Wang Y, Agyemang K, Zhang Y (2014) A review on phytochemistry, pharmacology and toxicology studies of Aconitum. J Pharm Pharmacol. 67(1):1-19.
[9] Chan TYK. (2009) Aconite poisoning. Clinical Toxicology, 47:279-285.
[10] Chan TYK. (2011) Causes and prevention of herb-induced aconite poisonings in Asia. Human and Experimental Toxicology. 30(12):2023–2026.
[11] Aboud NS, Osoro EK, Imbenzi PS (2015) A review on toxicity effects on Aconitum carmichaelii Debx (Chuanwu and Fuzi) and TCM processing approach 'Pao zhi' in reducing/ eliminating toxicity. Int J Pharma Sc. 5 (5), 1236-1241
[12] Gao, X., Hu, J., Zhang, X., Zuo, Y., Wang, Y. and Zhu, S., 2020. Research progress of aconitine toxicity and forensic analysis of aconitine poisoning. *Forensic Sciences Research*, *5*(1), pp.25-31.

3 Interim decisions on proposed amendments referred to the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #27, March 2021)

3.1 Interim decision in relation to kambo

Proposal

A Delegate of the Secretary of the Commonwealth Department of Health (the Delegate) proposed an amendment to include kambo in Schedule 9 of the Poisons Standard in response to concerns regarding its impact on public health.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the scheduling of kambo in the current Poisons Standard as follows:

Schedule 10 – New Entry

KAMBO

Index – New Entry

KAMBO
cross reference: Secretion of the South American Giant Leaf Frog or Giant Monkey Frog (*Phyllomedusa bicolor*)

Schedule 10

Materials considered

In making this interim decision, the Delegate considered the following material:

- An external expert evaluation on the properties of kambo;
- The 83 public submissions, including 23 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the meeting of the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #27);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard;
- A review by J Hesselink, Kambo and its Multitude of Biological Effects: Adverse Events or Pharmacological Effects? (2018);

- A case report by Pogorzelska and Łapiński, Toxic hepatitis caused by the excretions of the Phyllomedusa bicolor frog – a case report (2017);
- A case report by Gonzaga et al., Kambo Frog Poison as a Cause of Esophageal Rupture (2020);
- A case report by Roy et al., Can Overuse of Kambô Cause Psychosis? (2018);
- A case report by Aquila et al., The Biological Effects of Kambo: Is There a Relationship Between its Administration and Sudden Death? (2017); and
- A review by J Hesselink, Transformation and Migration of Healing Rituals from Indigenous Cultures to the West: Amphibian Secretions, the 'Frog Medicine and Toad Medicine' (2019).

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee advised that a new entry for kambo be created in Schedule 10 of the Poisons Standard as follows:

> **Schedule 10 – New Entry**
>
> KAMBO
>
> **Index – New Entry**
>
> **KAMBO**
> cross reference: Secretion of the South American Giant Leaf Frog or Giant Monkey Frog (*Phyllomedusa bicolor*)
>
> Schedule 10

The Committee also recommended an implementation date of **1 October 2021**.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Benefits:
  - Anecdotal claims of healing both physical and mental health conditions, through purging of toxins - vomiting, diarrhoea and involuntary urination. Vomiting can be severe and persistent and lead to esophageal rupture.
- Risks:
  - Reports of hyponatremia
  - Hypotension and tachycardia, reports of death from cardiac arrest

b) the purposes for which a substance is to be used and the extent of use of a substance

- Used in Traditional Indigenous ceremonies in South America and in non-traditional ceremonies in western countries.
- Extent of use in Australia is increasing.

c) the toxicity of a substance

- Serious acute adverse effects including nausea, vomiting, oesophageal rupture, diarrhoea, stomach pain, liver damage, burning sensation, lowered blood pressure and increased heart rate. There are also significant health risks for people with cardiovascular disease due to the significant cardiovascular effects. Deaths have also been reported.
- Potential for use of more toxic frog secretions.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- Dosage is variable, as secretions are dried onto sticks or bamboo slivers. Estimated dose is between 20-30mg per ritual. Estimated exposure of 1.4mg of active peptides.
- No standardized dosing of the preparations.

e) the potential for abuse of a substance

- Deltorphin and dermorphin may be present at very low levels.
- One case of abuse of Kambo ritual by a person who developed psychosis.

f) any other matters that the Secretary considers necessary to protect public health

- Issues with identifying the correct species of frogs, obtaining more toxic secretions and using it as kambo.
- Interactions with other medications not clear.
- The suitability of scheduling a complex mixture (kambo) instead of the active substances (for example caeruleins, tachykinins, bradykinins, sauvagine and opioid receptors agonists like deltorphin and dermorphin).

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision to create a new entry for kambo in Schedule 10 of the Poisons Standard.

I agree with the Committee's findings that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are: (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

In my view, the relevant parts of the Scheduling Policy Framework (SPF 2018) are the scheduling factors for Schedule 10:

- Kambo poses such a high public health risk that its sale, supply or use requires very strict control.
- The public health risks, particularly relating to kambo ceremonies, substantially outweigh any public health benefits.
- The potential health risk does not include a potential for dependency or abuse that would warrant inclusion in Schedule 9.

I note that kambo is a preparation obtained from dried secretions of the South American frog species *Phyllomedusa bicolor,* and is used in traditional indigenous ceremonies in South America. These rituals are now also occurring in non-indigenous communities in Australia, administered

by kambo "practitioners" with therapeutic claims of purification, healing and wellness. The ritual ceremony involves burning the participant's skin, followed by direct application of kambo to the burned region – leading to a wide range of adverse symptoms that are considered by kambo practitioners to be "cleansing". Kambo use as part of these ceremonies has led to several serious adverse events in Australia. A number of deaths from Kambo use have been reported in non-indigenous communities outside of Australia. I am of the firm view that the substance presents major risks to public health in Australia, and requires control through scheduling.

I agree with the Committee's advice that the toxicity profile of kambo is not consistent with safe human use. The preparation contains a complex mixture of bioactive peptides, including caeruleins, tachykinins, bradykinins, opioid receptor agonists and hallucinogenic methoxyindole derivatives; many of these substances have significant pharmacological actions and warrant tight regulatory controls. The interactions between these substances are also unknown, and may amplify their individual effects. When taken by humans, the mixture causes the rapid development of significant hypotension, tachycardia, and psychological symptoms, which can each lead to serious adverse events in certain groups. Adverse clinical symptoms includes vomiting, diarrhoea and involuntary urination. In my view, kambo is a dangerous mixture of substances that requires a significant level of control. A Schedule 10 entry in the Poisons Standard for kambo is commensurate with its risks to human health and safety.

In considering the human health risks of the substance, I have also noted its use and toxicity in the specific context of kambo ceremonies. These ceremonies may be particularly dangerous for people with cardiovascular disease, hypotensive syndromes or severe mental health conditions[13]; the risk is greatest when these conditions are undiagnosed, as they are very unlikely to be identified by non-health practitioners in any pre-ceremony screening. A wide range of adverse events have already occurred at kambo ceremonies, identified and recorded in recent scientific/medical literature. Concerningly, these include reports of liver damage[14], oesophageal rupture[15], psychosis[16], and death[17]. There are also accounts that kambo is traditionally used to terminate pregnancies[18], and it is unclear whether its abortifacient properties are consistently recognised in the context of Western ceremonies. These findings do not lend support to arguments that any risks to human health and safety associated with the use of Kambo can be adequately mitigated by Kambo practitioners within or outside of Kambo ceremonies.

In making my decision, I have carefully considered all responses received during the pre-meeting consultation, noting that 20 out of 23 written submissions were against the proposed amendment. Opposing respondents included the International Association of Kambo Practitioners (IAKP) and several consumers of kambo. These argued that kambo is safe and beneficial when administered by practitioners with appropriate training – and that the proposed scheduling may push its use underground. However, I am of the firm view that kambo remains too dangerous to allow in any context in Australia, even if IAKP training may reduce the risks to some extent. I also note that these IAKP practitioners are not recognised by the Australian Health Practitioner Regulation Agency, and that the benefits and safety advertised within their communities are neither supported by scientific studies nor toxicity data. In contrast with the views expressed in the opposing submissions, I consider that the public health risks of kambo significantly outweigh the claimed benefits.

[13] https://dx.doi.org/10.23937/2572-3987.1510017
[14] https://dx.doi.org/10.5114%2Fceh.2017.65228
[15] https://doi.org/10.7759/cureus.10677
[16] https://dx.doi.org/10.7759%2Fcureus.2770
[17] https://doi.org/10.1111/1556-4029.13641
[18] https://www.jsmcentral.org/sm-psychiatry/fulltext_smjpmh-v4-1014.pdf

In making my decision, I have also considered the three written responses that were in favour of the scheduling proposal. I found the concerns raised in these submissions are highly pertinent:

- The Pharmacy Guild noted that the effects of kambo are induced by individual bioactive components/peptides rather than an overreaction of the immune system. This means that even a minimal dose may induce pharmacological effects that can pose a significant health risk.
- The Australian Medical Association outlined that the act of blistering the skin and applying kambo could lead to other health risks such as infection. The submission also raised concerns that using kambo may prevent patients from seeing a medical practitioner, and that there is currently insufficient evidence for its intended therapeutic effects.
- The NSW Poisons Information Centre described the three calls that they had received regarding kambo use since 2018. One patient had complications of infection at the burn sites of application; the second presented to hospital with melaena and persistent vomiting; and the third was diagnosed with oesophageal rupture that required surgical repair.

Having considered the significant risks to users and the lack of established therapeutic benefit, I am of the view that kambo should be included in Schedule 10 of the Poisons Standard.

I agree with the Committee's advice that, in order to provide a simple and enforceable definition, kambo should be regulated as a secretion rather than a list of its component substances. The new entry should include the specific frog species *P. bicolor* in the index as a cross reference.

Proposed implementation date

1 October 2021

3.2 Interim decision in relation to lidocaine

Proposal

The applicant proposed an amendment to expand the current Schedule 5 entry for lidocaine to include specifically targeted injectable solutions, at up to 2% concentration, for the pain relief of lambs or calves undergoing animal husbandry procedures.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the scheduling of lidocaine in the current Poisons Standard as follows:

Schedule 5 – Amend Entry

LIDOCAINE

a) in aqueous gel preparations containing 4.5 per cent or less of lidocaine, for the dermal spray-on administration to the wounds of animals; or

b) in injectable preparations containing 2 per cent or less of lidocaine when packaged in a bottle with a tamper resistant cartridge which can only be dispensed through a rubber ring applicator for tail docking and castration of lambs; or castration of calves.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to lidocaine;

- The 91 public submissions, including 29 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the meeting of the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #27);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee advised that the Schedule 5 entry for lidocaine be amended as follows:

Schedule 5 – Amend Entry

LIDOCAINE

a) in aqueous gel preparations containing 4.5 per cent or less of lidocaine, for the dermal spray-on administration to post-surgical wounds associated with 'mulesing' of sheep; tail docking and castration of lambs; or castration and disbudding/dehorning in calves[19]; or

b) in injectable preparations containing 2 per cent or less of lidocaine when packaged in a bottle with a tamper resistant cartridge which can only be dispensed through a rubber ring applicator for tail docking and castration of lambs; or castration of calves.

The Committee also recommended an implementation date of **1 October 2021**.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Significant benefit to animal welfare for routine animal husbandry measures. The improvement of animal welfare will also benefit the mental health and wellbeing of humans in contact with those animals.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Use is for pain relief for wounds associated with rubber ring applicator for tail docking and castration of lambs; castration of calves.

c) the toxicity of a substance

- Formulated product has low oral and dermal toxicity.

[19] Changes to the Schedule 5 entry for lidocaine were incorporated in the 1 February 2021Poisons Standard. These changes are reflected in the delegate's current interim decision.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- New packaging of an existing product that reduces the risk of inappropriate use.
- The injection of lidocaine can only occur during the application of a rubber ring, which prevents accidental injection or needle stick injury.
- If unintended exposure occurs, the dosage is metered, and is sufficiently low that it would not present a major health concern.

e) the potential for abuse of a substance

- Minimal potential for abuse; less risk than some existing products.

f) any other matters that the Secretary considers necessary to protect public health

- Nil

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision to amend the current Schedule 5 entry for lidocaine to include specifically targeted injectable solutions, at up to 2% concentration, for the pain relief of lambs or calves undergoing animal husbandry procedures.

In considering the proposal, I have taken into account the 91 public submissions received in response to the pre-meeting consultation. I note that 29 written submissions were received, 27 fully supportive of the proposed amendment, one partially supportive and one opposed. Supporting submissions addressed the safety of the product, the benefits to animal welfare, and the need for increased access by farmers. I have considered each of these arguments in my interim decision to amend the Poisons Standard, and specifically addressed the opposing submission, as set out below.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are: (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance.

In my view, the relevant parts of the Scheduling Policy Framework (SPF 2018) are the scheduling factors for Schedule 5:

- Lidocaine, in the proposed formulation, has a low oral and dermal toxicity, and has a low potential for causing harm.
- Lidocaine presents a low hazard from repeated use and is unlikely to produce significant toxicity.
- The packaging of the product can appropriately mitigate the risks of injury in handling, storage and use. The product design specifically prevents needle-stick injury and accidental exposure.
- During use in castration and tail docking, lidocaine is capable of causing only minor adverse effects to humans (through accidental exposure).
- Lidocaine has a low potential for causing harm, demonstrated by its long history of safe veterinary use in Australia.

I note that lidocaine is a local anaesthetic with a low toxicity and a long history of safe use in Australian veterinary products. The current proposal relates to a new veterinary use of the substance – as a specifically targeted injectable solution for pain relief during animal husbandry procedures. Though this is a new method of administration, veterinary lidocaine products have

had only three reported adverse events[20,21] since the Australian Pesticides and Veterinary Medicines Authority approved the first product in 2005. These reports are consistent with the known low toxicity of lidocaine, which has been extensively covered in past decisions and committee meetings. The most recent decision on the substance, made in 2020, was to expand the Schedule 5 entry for topical lidocaine products, referencing a low toxicity and low risk to human health. In my view, lidocaine has a favourable safety profile that is consistent with its inclusion in Schedule 5.

While lidocaine does not require specific professional oversight in topical formulations, I acknowledge that injectable substances present a unique set of risks that depend on product packaging. These include a potential for needle-stick injury and accidental exposure that would usually necessitate the presence of a registered practitioner. I also note that the Joint ACMS-ACCS have previously expressed concern that bulk injectable lidocaine could be diverted for inappropriate use. I consider that the application adequately addressed each of these issues, with reference to a specific product design, noting the Committee's findings that:

- The cartridge size is small, and enclosed within a tamper-resistant device. Accessing the solution would take a complex deliberate effort, and require separate equipment for injecting the solution. The potential for diversion for inappropriate use is negligible.
- The injection of lidocaine can only occur during the application of a rubber ring, which precludes use in humans or at sites other than those targeted. The product presents a negligible risk of needle-stick injury or accidental exposure.
- The product dosage is metered. If an accidental human injection occurred, the dosage would be sufficiently low that it would not present a major health concern.

Having considered the applicant's product design against the SPF 2018, I have decided that certain injectable lidocaine products are appropriate for inclusion in Schedule 5. The intent of my interim decision is to capture products with the abovementioned safety features in Schedule 5, while keeping all other forms of injectable lidocaine in Schedule 4. As part of my decision, I have also decided to accept all minor amendments to the applicant's wording that were suggested by the Committee. I consider that these changes will give a more accurate description of the product and reduce ambiguity in interpretation of the schedule entry. In particular, I note that the product is better classified as 'tamper resistant' rather than 'tamper proof'.

I note concerns raised by the Australian Veterinary Association that the lack of tamper proofing, and potentially high availability, may allow inappropriate use that could cause harm to humans and animals. However, I consider that the product's tamper resistant packaging sufficiently mitigates risks of diversion, especially given the small cartridge size. I also reiterate that the decision relates to a specific product design with a different safety profile to other injectable anaesthetics. In light of the opposing public submission, I remain of the view that the risks of the substance and product are consistent with their inclusion Schedule 5.

In making my decision, I note that there are growing consumer expectations that farmers minimise animal suffering during castration and tail docking. The use of injectable anaesthetics may provide an effective solution, but currently requires the presence of a veterinarian. Since farmers or contractors tend to administer husbandry procedures themselves, this requirement may lead to increased costs and logistical difficulties that reduce uptake. These challenges may be especially complex for larger operations that castrate or dock hundreds of animals in a day, or for those that live in remote areas without access to well-resourced veterinary clinics. Allowing non-prescription access to injectable lidocaine could reduce these barriers and lead to a significant increase in animal welfare; in doing so, the change may help satisfy consumer

[20] According to: Adverse Experience Reporting Program annual reports | Australian Pesticides and Veterinary Medicines Authority (apvma.gov.au)
[21] The applicant noted that all of these adverse events appear to be caused by other substances in the product.

expectations and reduce the burden on farmers. In my view, expanding the Schedule 5 entry for lidocaine in this form may significantly benefit Australian farmers and their livestock.

Proposed implementation date

1 October 2021

3.3 Interim decision in relation to hemp seed oil

Proposal

The applicant proposed an amendment to the existing Schedule 9 entries for cannabis and tetrahydrocannabinols to exclude hemp seed oil for oral consumption from scheduling when compliant with the Food Standards Code.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the scheduling of hemp seed oil in the current Poisons Standard as follows:

CANNABIS

Schedule 9 – Amend Entry

CANNABIS (including seeds, extracts, resins, and the plant and any part of the plant when packed or prepared), **except**:

a) when separately specified in these Schedules; or

b) processed hemp fibre containing 0.1 per cent or less of tetrahydrocannabinols and hemp fibre products manufactured from such fibre; or

c) ~~when in~~ hemp seed oil ~~for purposes other than internal human use~~ containing ~~50~~ 75 mg/kg or less of cannabidiol ~~cannabinoids, including~~ and ~~20~~ 10 mg/kg or less of tetrahydrocannabinols.~~, when labelled with either of the following warning statements:~~

~~i) Not for internal use; or~~

~~ii) Not to be taken.~~

Schedule 8 – Amend Entry

CANNABIS (including seeds, extracts, resins and the plant, and any part of the plant) when prepared or packed for human therapeutic use, when:

a) cultivated or produced, or in products manufactured[1], in accordance with the *Narcotic Drugs Act 1967*; and/or

b) for use in products manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or

c) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or

d) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989*,

[1] "Cultivation", "production" and "manufacture" have the same meaning as in the *Narcotic Drugs Act 1967*

except ~~when~~:

i) when it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the *Therapeutic Goods Regulations 1990* applies; or

ii) when separately specified in the NABIXIMOLS entry in this Schedule; or

iii) when captured by the CANNABIDIOL entry in Schedule 4 or Schedule 3; or

iv) hemp seed oil containing 75 mg/kg or less cannabidiol and 10 mg/kg or less tetrahydrocannabinols.

Appendix D, Item 1 (Poisons available only from or on the prescription or order of an authorised medical practitioner)

CANNABIS for human use.

Appendix K

CANNABIS **except** cannabidiol when included in Schedule 4 or Schedule 3

Index

CANNABIS
cross reference: CANNABIS SATIVA, HEMP, HEMP SEED OIL, TETRAHYDROCANNABINOLS

Schedule 9
Schedule 8
Appendix D, Item 1
Appendix K

TETRAHYDROCANNABINOLS

Schedule 9 – Amend Entry

TETRAHYDROCANNABINOLS and their alkyl homologues, **except**:

a) when included in Schedule 4 or Schedule 8; or

b) processed hemp fibre containing 0.1 per cent or less of tetrahydrocannabinols, and hemp fibre products manufactured from such fibre; or

c) in hemp seed oil at a concentration of 10 mg/kg or less. ~~in hemp seed oil for purposes other than internal human use containing 50 mg/kg or less of total cannabinoids, including 20 mg/kg or less of tetrahydrocannabinols, when labelled with either of the following warning statements:~~

~~i) Not for internal use; or~~

~~ii) Not to be taken.~~

Schedule 8 – Amend Entry

TETRAHYDROCANNABINOLS when extracted from cannabis for human therapeutic use, when:

a) included in products manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or

b) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or

c) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989,*

except when:

i) it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the *Therapeutic Goods Regulations 1990* applies; or

ii) separately specified in the NABIXIMOLS entry in this Schedule; or

iii) captured by the CANNABIDIOL entry in Schedule 4 or Schedule 3; or

iv) in hemp seed oil at a concentration of 10 mg/kg or less.

Appendix D, Item 1 (Poisons available only from or on the prescription or order of an authorised medical practitioner)

TETRAHYDROCANNABINOLS for human use.

Appendix K

TETRAHYDROCANNABINOLS **except** cannabidiol when included in Schedule 4 or Schedule 3

Index

TETRAHYDROCANNABINOLS
cross reference: CANNABIS, HEMP SEED OIL, NABIXIMOLS

Schedule 9
Schedule 8
Appendix D, Item 1
Appendix K

CANNABIDIOL

Schedule 4 – Amend entry

CANNABIDIOL in preparations for therapeutic use or analytical and scientific research where:

a) cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and

b) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation;

except when:

i) included in Schedule 3; or

ii) in hemp seed oil at a concentration of 75 mg/kg or less of the hemp seed oil.

Schedule 3

CANNABIDIOL in oral, oromucosal and sublingual preparations included in the Australian Register of Therapeutic Goods when:

a) the cannabidiol is either plant derived or, when synthetic, only contains the (-)-CBD enantiomer; and

b) the cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and

c) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation and of which tetrahydrocannabinol (THC) can only comprise 1 per cent of the total cannabinoid content; and

d) the maximum recommended daily dose is 150 mg or less of cannabidiol; and

e) packed in blister or strip packaging or in a container fitted with a child-resistant closure; and

f) in packs containing not more than 30 days' supply; and

g) for persons aged 18 years and over.

Appendix F, Part 3

Poison	Warning Statements	Safety Direction
CANNABIDIOL when included in Schedule 3.	67, 111	
67: Do not use if pregnant or likely to become pregnant. 111: Do not use if breastfeeding or planning to breastfeed		

Index

CANNABIDIOL
cross reference: NABIXIMOLS, CANNABIS, TETRAHYDROCANNABINOLS

Schedule 4
Schedule 3
Appendix F, Part 3

HEMP SEED OIL

Index – New Entry

HEMP SEED OIL
cross reference: CANNABIDIOL, CANNABIS, TETRAHYDROCANNABINOLS

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to hemp seed oil;
- The 101 public submissions, including 9 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the meeting of the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #27);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling,

packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;

- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee advised that an exception be included in the Schedule 9 and Schedule 8 entries for cannabis and THC, and the Schedule 4 entry for cannabidiol (CBD), as follows:

Schedule 9 – Amend entries

CANNABIS (including seeds, extracts, resins, and the plant and any part of the plant when packed or prepared), **except**:

a) when separately specified in these Schedules; or

b) processed hemp fibre containing 0.1 per cent or less of tetrahydrocannabinols and hemp fibre products manufactured from such fibre; or

c) ~~when in~~ hemp seed oil ~~for purposes other than internal human use~~ containing ~~50~~ 75 mg/kg or less of cannabidiol ~~cannabinoids, including~~ and ~~20~~ 10 mg/kg or less of tetrahydrocannabinols~~, when labelled with either of the following warning statements:~~

~~i) Not for internal use; or~~

~~ii) Not to be taken.~~

TETRAHYDROCANNABINOLS and their alkyl homologues, **except**:

a) when included in Schedule 4 or Schedule 8; or

b) processed hemp fibre containing 0.1 per cent or less of tetrahydrocannabinols, and hemp fibre products manufactured from such fibre; or

c) in hemp seed oil at a concentration of 10 mg/kg or less. ~~in hemp seed oil for purposes other than internal human use containing 50 mg/kg or less of total cannabinoids, including 20 mg/kg or less of tetrahydrocannabinols, when labelled with either of the following warning statements:~~

~~i) Not for internal use; or~~

~~ii) Not to be taken.~~

Schedule 8 – Amend entries

CANNABIS (including seeds, extracts, resins and the plant, and any part of the plant) when prepared or packed for human therapeutic use, when:

a) cultivated or produced, or in products manufactured[1], in accordance with the *Narcotic Drugs Act 1967*; and/or

b) for use in products manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or

[1] "Cultivation", "production" and "manufacture" have the same meaning as in the *Narcotic Drugs Act 1967*

c) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or

d) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989*,

except ~~when~~:

i) when it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the *Therapeutic Goods Regulations 1990* applies; or

ii) when separately specified in the NABIXIMOLS entry in this Schedule; or

iii) when captured by the CANNABIDIOL entry in Schedule 4 or Schedule 3; or

iv) hemp seed oil containing 75 mg/kg or less cannabidiol and 10 mg/kg or less tetrahydrocannabinols.

TETRAHYDROCANNABINOLS when extracted from cannabis for human therapeutic use, when:

a) included in products manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or

b) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or

c) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989,*

except when:

i) it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the *Therapeutic Goods Regulations 1990* applies; or

ii) separately specified in the NABIXIMOLS entry in this Schedule; or

iii) captured by the CANNABIDIOL entry in Schedule 4 or Schedule 3; or

iv) in hemp seed oil at a concentration of 10 mg/kg or less.

Schedule 4 – Amend entry

CANNABIDIOL in preparations for therapeutic use or analytical and scientific research where:

a) cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and

b) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation;

except when

i) included in Schedule 3; or

ii) in hemp seed oil at a concentration of 75 mg/kg or less.

Index – New Entry

Hemp Seed Oil

Schedule 9
Schedule 8
Schedule 4

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Hemp seeds do not naturally contain THC and CBD but can be present due to contamination, with the levels dependent on the quality of raw material and the processing. The overall risk associated with HSO is likely to be low.
- Hemp seed oil is currently used as a food, is considered to be of nutritional value, and is a useful source of omega-3 and omega-6 fatty acids.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Currently used as a food. Potential uses in medicines and cosmetic products. It may also have vet medicine or animal feed additive use.

c) the toxicity of a substance

- Hemp seed oil itself is not considered to be toxic. The same risk currently exists for hemp seed oil supplied as food in Australia. The can be managed through targeted surveillance of products on the market.
- Toxicity may result from products that are contaminated or adulterated.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- Currently hemp seed oil is allowed for oral use in food only. However, some products are packaged similarly to therapeutic goods in dosage forms such as capsules.
- There are no other specific products proposed at present. Any medicines would require assessment through the TGA and any vet medicines and animal feed additives would require controls through the APVMA.

e) the potential for abuse of a substance

- Nil

f) any other matters that the Secretary considers necessary to protect public health

- If permitted for use in therapeutic goods, consideration should be given to the name of the product, labelling claims and permitted statements, and special attention to compliance given the potential for consumers to be misled given the current focus on medicinal cannabis.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision to amend the current Schedule 9 and Schedule 8 entries for cannabis and tetrahydrocannabinols, and the Schedule 4 entry for cannabidiol, to exclude hemp

seed oil from scheduling when compliant with the compositional requirements stated in the proposed scheduling.

Hemp seed oil (HSO) is taken to mean the oil obtained by cold expression from the ripened fruits (seeds) of *Cannabis sativa*. Critically, I note that hemp seeds do not naturally contain already scheduled cannabinoids THC and CBD, however these can be present in trace amounts in the final HSO product due to cross-contamination from other parts of the cannabis plant. Seasonal variability in the plant itself can also affect cannabinoid content. Therefore, exemptions granted in the Poisons Standard for HSO must include provisions to limit the content of these cannabinoids in the final product.

Under the Food Standards Code, amended by FSANZ in 2017, HSO is a permitted ingredient in foods with a limit of 10 mg/kg placed on the THC content. HSO has considerable nutritional value, as it is a good source of omega-3 and omega-6 fatty acids. It also has potential for use in medicines, cosmetics, or as an additive in animal feeds when compliant with the imposed compositional requirements. I have determined that it is appropriate to include this maximum concentration limit on THC allowed by FSANZ as a reasonably safe amount. This concentration is used in the amended scheduling entries to allow for a conditional exemption for HSO from scheduling at the same maximum concentration limits.

With regards to CBD, I have noted that FSANZ did not deem an upper limit necessary to protect public health and safety, a maximum level of 75 mg/kg was set to ensure enforceability. I have decided it is appropriate to also include this limit in the proposed scheduling changes for HSO.

I have considered the public submissions on the proposal, including nine written submissions, which were received as part of the pre-meeting consultation. In particular, I have noted that all written submissions were either supportive or partially supportive of the proposal, and generally emphasised the nutritional benefits associated with use of the substance, and its associated safety profile. I have noted that a majority of the non-written responses were also in favour of the proposed changes.

I have noted that this application is likely the applicant's first step towards the approval of HSO in medicines, which may include applying for HSO to be included in the TGA Permissible Ingredients Determination for use in listed medicines. As per the Scheduling Handbook, medicinal preparations exempted from scheduling must be determined to be able to be supplied, with reasonable safety, without any access to health professional advice. 'Reasonable safety' indicates that:

- the consumer is able to identify and self-manage the condition for which the medicine is intended without health professional input
- the risk of the consumer confusing their condition with more serious diseases or conditions is very small
- the risks to health from the medicine are small and can be managed with packaging and labelling

Consideration of the FSANZ safety assessments for HSO suggests that there is negligible risk of exposure to significant levels of these cannabinoids from HSO, when produced to the required standards of manufacture as stated in these amendments. On this basis I consider that HSO could be supplied with 'reasonable safety' in medicines.

I agree that the amendments, as proposed by the Committee, are suitable for inclusion in the Poisons Standard. I would note that careful consideration should be given to labelling requirements of HSO products to ensure consumers are fully informed of the nature of these products, and able to differentiate the intended use of HSO from products containing cannabis and other cannabis-related substances.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

Proposed implementation date

1 October 2021

4 Interim decisions on proposed amendments referred to the Advisory Committee on Chemicals Scheduling (ACCS #30, March 2021)

4.1 Interim decision in relation to lead (in paint)

Proposal

Three similar scheduling proposals, from three separate private applicants, which sought to amend the Schedule 10 entry for Lead compounds to reduce the permissible level of those compounds in paints from 0.1% to 0.009%.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the current Poisons Standard in relation to lead as follows:

PART 2, SECTION SEVEN/Appendix I – Amend Section

(2) A person must not manufacture, sell, supply or use:

a) an anti-fouling or anti-corrosive paint containing more than 0.1% Lead (the proportion of Lead for the purposes of this section is calculated as a percentage of the element present in the non-volatile content of the paint);

b) a paint (other than an anti-fouling or anti-corrosive paint) or tinter containing more than ~~0.1~~ 0.009% Lead (the proportion of Lead for the purposes of this section is calculated as a percentage of the element present in the non-volatile content of the paint).

Schedule 10 – Amend Entry

LEAD COMPOUNDS:

a) in anti-fouling or anti-corrosive paints **except** in preparations containing 0.1 per cent or less of lead calculated on the non-volatile content of the paint;

b) in paints (other than anti-fouling or anti-corrosive paints), tinters, inks or ink additives **except** in preparations containing ~~0.1~~ 0.009 per cent or less of lead calculated on the non-volatile content of the paint, tinter, ink or ink additive.

Schedule 6

LEAD COMPOUNDS **except**:

a) when included in Schedule 4 or 5;

b) in paints, tinters, inks or ink additives;

c) in preparations for cosmetic use containing 100 mg/kg or less of lead;

d) in pencil cores, finger colours, showcard colours, pastels, crayons, poster paints/colours or coloured chalks containing 100 mg/kg or less of lead; or

e) in ceramic glazes when labelled with the warning statement:

CAUTION – Harmful if swallowed. Do not use on surfaces which contact food or drink.

written in letters not less than 1.5 mm in height.

Schedule 5

LEAD COMPOUNDS in preparations for use as hair cosmetics.

Schedule 4

LEAD for human therapeutic use.

Appendix E, Part 2

Poison	Standard Statements
Lead compounds	
• in hair cosmetics	A
• in other preparations	A, S1
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). **S1** – If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.	

Appendix F, Part 3

Poison	Warning Statements	Safety Direction
Glazing preparations containing LEAD COMPOUNDS.	**50** - Unless adequately fired, utensils glazed with this preparation must not be used as containers for food or beverages; to do so may cause lead poisoning.	
Lead compounds		
a) andin hair cosmetics.	**25** - Do not use on broken skin. Wash hands thoroughly after use.	
b) when in Schedule 6.		**1** - Avoid contact with eyes. **4** - Avoid contact with skin. **8** - Avoid breathing dust (or) vapour (or) spray mist.

Appendix B, Part 3

Substance	Date of entry	Reason for listing	Area of use
LEAD METALLIC	-	a – Low Toxicity	7.1 – Any use

Index

LEAD
cross reference: GLAZING PREPARATIONS, PRINTING INKS or INK ADDITIVES, SELENIUM

Schedule 4

LEAD COMPOUNDS
cross reference: GLAZING PREPARATIONS, PRINTING INKS or INK ADDITIVES, SELENIUM

Schedule 10
Schedule 6
Schedule 5
Appendix E, Part 2
Appendix F, Part 3
Appendix F, Part 3

LEAD METALLIC

Appendix B, Part 3

Materials considered

In making this interim decision, the Delegate considered the following material:

- The applicants' proposals to amend the current Poisons Standard with respect to lead;
- The 72 public submissions, including three written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Chemicals Scheduling (ACCS #30);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard; and
- *Global elimination of lead paint: why and how countries should take action - Technical brief*, World Health Organization 14 August 2020.

Summary of ACCS advice to the Delegate

The Committee advised that the Schedule 10 entry for lead compounds be amended as follows:

Schedule 10 – Amend Entry

LEAD COMPOUNDS in paints, tinters, inks or ink additives **except** in preparations containing ~~0.1~~ 0.009 per cent or less of lead calculated on the non-volatile content of the paint, tinter, ink or ink additive.

PART 2, SECTION SEVEN/Appendix I – Amend Section

(2) A person must not manufacture, sell, supply or use a paint or tinter containing more than ~~0.1~~ 0.009% Lead (the proportion of Lead for the purposes of this section is calculated as a percentage of the element present in the non-volatile content of the paint).

The Committee also recommended an implementation date of **1 October 2021** for paints other than those used for anti-corrosion or anti-fouling purposes. The Committee did not recommend a specific implementation date for anti-fouling and anti-corrosion paints but noted that a longer transition period would be needed for these products.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Risks:
  - Lead is a heavy metal and cumulative toxin.
  - Young children and pregnant women are of highest risk of neurotoxicity.
  - No level of exposure to lead is known to be without harmful effects.
- Benefits:
  - The Committee noted the inclusion of lead in the Therapeutic Goods (Permissible Ingredients) Determination No.1 of 2021, when only for use as an active homeopathic ingredient.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Lead has a long history of use in paint. It can be added to paint to provide colour, speed up drying time, increase durability and resist moisture that causes corrosion.
- Lead has anti-fouling properties and can be added to paints used on solid (e.g. ship hull) to control or prevent the attachment of unwanted organisms.
- Its current limit in paints and tinters is 0.1% (1000ppm) calculated on the non-volatile content of the paint.

c) the toxicity of a substance

- Acute or chronic exposure to lead can cause adverse health effects, including:
  - cardiovascular disease
  - hypertension

- kidney damage
- cancer
- effects on the nervous system, including difficulty concentrating, hearing loss, loss of balance, tremors
- behavioural changes like aggression, anxiety and depression
- anaemia
- reduced fertility, and
- birth defects and developmental delays in children

d) the dosage, formulation, labelling, packaging and presentation of a substance

– Not applicable.

e) the potential for abuse of a substance

– Nil.

f) any other matters that the Secretary considers necessary to protect public health

– There is an international effort to protect global health from exposure to lead. In Australia, leaded petrol was completely phased out after 1 Jan 2002. Its effort in limiting and lowering lead in paints and tinters began in 1979.

– Delayed implementation date with regard to anti-corrosive and anti-fouling paints.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision to amend the Schedule 10 entry for lead compounds, and the corresponding requirements listed in Part 2, Section 7 of the Poisons Standard, to decrease the permissible level of lead in paints.

I agree with the applicants and the advice of the ACCS that the reduction in the allowable limit of lead in paints, tinters, inks and ink additives is necessary to protect public health from the known adverse effects of lead exposure. Lead is a heavy metal with known cumulative toxic effects affecting multiple body systems, including increased risk of cardiovascular disease. There is no level of exposure to lead that is known to be without harmful effects, and these effects are particularly pronounced in pregnant women and young children.

I recognise that the proposed reduction of the permissible limit to 0.009 per cent lead in paints would align the Poisons Standard with international regulations, including those endorsed by the United Nations Environment Program, and the limits already adopted by several countries in some or all types of paints and coatings.

I have considered the written public submissions, which were in support for the proposal, and note in particular the response from the Australian Paint Manufacturers' Federation which indicates that lead is no longer part of the composition of paints used by trade painters and 'DIYers'. This was taken to mean individuals undertaking repairs in the domestic setting without the direct aid of professionals. I also acknowledge the Australian Paint Manufacturers concerns with the difficulties surrounding lead contamination of zinc and copper in anti-fouling and anti-corrosion paints.

I agree with the Committee's advice that the impact of this amendment on industrial and domestic users of paints (other than those for anti-corrosion and anti-fouling purposes) is minimal, and a long transition period is not warranted for these preparations.

However, I acknowledge the concerns raised by both the Committee and the Australian Paint Manufacturers' Federation regarding reductions in the lead content of paints used for anti-corrosion and anti-fouling purposes, where lead may be present as an impurity of the copper and/or zinc substitutes in these preparations. I also note that the significantly reduced exposure pathways for anti-fouling and anti-corrosive paints may be a mitigating factor in a longer transition period in comparison to other paints. This is reflected in the exemption of anti-corrosive and anti-fouling paints from this amendment, with a view to removing the exemption on **1 October 2023**.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

Proposed implementation date

1 October 2021

4.2 Interim decision in relation to cyflumetofen

Proposal

The applicant proposed a new entry for cyflumetofen in Schedule 6 of the Poisons Standard.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the current Poisons Standard in relation to cyflumetofen as follows:

Schedule 5 – New Entry

CYFLUMETOFEN

Index – New Entry

CYFLUMETOFEN

Schedule 5

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to cyflumetofen;
- The 54 public submissions, including no written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Chemicals Scheduling (ACCS #30);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance;

- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACCS advice to the Delegate

The Committee advised that a new entry for cyflumetofen be created in Schedule 5 of the Poisons Standard as follows:

Schedule 5 – New Entry

CYFLUMETOFEN

Index – New Entry

CYFLUMETOFEN

Schedule 5

The Committee also recommended an implementation date of **1 October 2021**.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- This is a new miticide product on market. Overuse of other miticides has created resistance in mite species which are considered to be consistent pests in deciduous fruit trees in WA.

b) the purposes for which a substance is to be used and the extent of use of a substance

- From the information provided the product is for occupational use on crops. No indication of domestic use.

c) the toxicity of a substance

- Low acute toxicity, non-skin irritant, slight eye irritant but it is a skin sensitiser.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- APVMA approved labels will be affixed to products. Advisory to wear appropriate PPE is to be included.

e) the potential for abuse of a substance

- Nil.

f) any other matters that the Secretary considers necessary to protect public health

- Nil.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision to create a new entry for cyflumetofen in Schedule 5 of the Poisons Standard. This decision is made noting that the application proposed a Schedule 6 entry for the substance.

Cyflumetofen is a novel acaricide that works by interfering with energy production (inhibition of complex II in mitochondria) on contact with spider mites only. It is an effective acaricide at all developmental stages of the spider mite. It has no effect on insects, crustaceans or vertebrates under conditions of practical use, and is effective at very low concentrations. It is not expected to be used in a domestic setting.

I note that cyflumetofen is approved for use as a pesticide in several countries including, US, Japan, EU and Canada, although there are currently no products containing cyflumetofen marketed in Australia.

I agree with the Committee's advice that the low toxicological profile of cyflumetofen is aligned with the Schedule 5 factors of the Scheduling Policy Framework. There is no current evidence of genotoxicity, neurotoxicity, immunotoxicity or carcinogenicity associated with the substance which provides weight to this advice. Medical reports from manufacturing plants for the substance indicate personnel have suffered no adverse health effects from the substance.

I have noted that a number of toxicological properties of cyflumetofen are consistent with the Schedule 5 scheduling factors, including:

- Oral median LD_{50} >2000 mg/kg bw in rats
- Acute dermal toxicity 5000 mg/kg bw in rats
- Inhalational LC_{50} >2650 mg/m^3
- It is not a skin irritant, but a slight eye irritant.
- The metabolites of cyflumetofen also have low acute toxicity.

I agree with the Committee's advice that the substance may be a skin sensitiser. However, as noted by the Committee, this was based on a positive result in a guinea pig maximisation test following intradermal induction with 1% cyflumetofen, but not following topical induction with 50% cyflumetofen. Further studies may assist with clarifying the sensitisation potential of the substance, however I am satisfied that reasonably foreseeable harm to users can be reduced through label warnings and safety directions consistent with a Schedule 5 poison.

I have noted that no written public submissions were received but consultation through the web portal indicated two individuals who were supportive, four partially supportive and two were opposed to the proposals. These respondents did not provide reasons for their support or opposition. As a result, the extent of my consideration is limited to noting that the submissions were balanced in terms of support or opposition to the proposal. The respondents are invited to submit reasons to clarify their position in the current consultation.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance.

Proposed implementation date

1 October 2021

4.3 Interim decision in relation to isocycloseram

Proposal

The applicant proposed a new entry for isocycloseram in Schedule 6 of the Poisons Standard.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the current Poisons Standard in relation to isocycloseram as follows:

Schedule 6 – New Entry

ISOCYCLOSERAM

Index – New Entry

ISOCYCLOSERAM

Schedule 6

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to isocycloseram;
- The 53 public submissions (no written submissions) received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Chemicals Scheduling (ACCS #30);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACCS advice to the Delegate

The Committee advised that a new entry for isocycloseram be created in Schedule 6 of the Poisons Standard as follows:

Schedule 6 – New Entry

ISOCYCLOSERAM

Index – New Entry

ISOCYCLOSERAM

Schedule 6

The Committee also recommended an implementation date of **1 October 2021**.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- Benefits:
  - Residual insecticide
  - Low toxicity of compound and limited exposure when used appropriately.
- Risks:
  - Incidental exposure.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Used in agricultural settings.
- Insecticidal treatment in horticulture and for pre-sowing seed treatment of canola in broadacre production systems.

c) the toxicity of a substance

- Potential for irreversible systemic toxicity at comparatively low doses.
- Generally low toxicity.
- Potential for developmental toxicity (per APVMA).

d) the dosage, formulation, labelling, packaging and presentation of a substance

- 1-20 litre containers for spray on, 1-1000 litre container for seed treatment formulation.

e) the potential for abuse of a substance

- Nil.

f) any other matters that the Secretary considers necessary to protect public health

- Nil.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision to create a new entry for isocycloseram in Schedule 6 of the Poisons Standard, as proposed by the applicant.

I have taken into account the purpose for which isocycloseram is to be used, i.e. an insecticidal treatment in horticulture and for pre-sowing seed treatment of canola in broadacre production systems. It is not expected to be used in the domestic setting.

Based on my assessment of the evidence below, the potential risk of irreversible toxicity is consistent with Schedule 6 and it was a key determinant in my decision to include isocycloseram in Schedule 6 of the Poisons Standard:

- The key toxicity data are found in the repeat dose toxicity reports. Primary targets appeared to be adrenals and liver, and tubular degeneration of the testes. These effects were reproducible across a number of different time period studies and generally seen at doses of

the order of 10 mg/kg bw/day in rats (11.2 mg/kg in a 90 day study and 12 mg/kg in a 2 generation study);

- There was also limited evidence of developmental toxicity, with the rare defect of bifid sternum seen in two foetuses from different rat litters at 15 mg/kg bw/day in a gestational developmental study;
- In both a one generation and a two generation reproductive study, the developmental effects were not seen, nor any change in reproductive performance associated with testicular toxicity. However similar effects to those seen in repeat dose studies were seen at similar doses, including the tubular degeneration of the testes;
- Clinical signs of systemic toxicity, including lymphatic and non-lymphatic plasmacytosis, after repeat dosing in mice, were observed;
- Isocycloseram is rapidly absorbed through gastrointestinal tract and it is extensively metabolised and excreted within 72 hours. However, some residues can be found 7 days after dosing; and
- Neurological effects were observed at high doses.

On the balance of evidence, my view is that isocycloseram presents a moderate hazard from repeated use and moderate risk of producing irreversible toxicity based on clinical signs of systemic toxicity after repeated dose and the observation of reproducible histopathological effects at comparatively low doses, particularly those in the testes.

I have considered that some of the toxicological properties of isocycloseram are consistent with Schedule 5, these included oral LD_{50}, dermal LD%, inhalational LC_{50} and eye irritation characteristics. The Schedule 5 factors of the Scheduling Policy Framework (SPF) also require a substance to present a low hazard from repeated use and be unlikely to produce irreversible toxicity. It is on that basis that I have decided that isocycloseram does not meet the Schedule 5 factors of the SPF.

I am satisfied that reasonably foreseeable harm to users can be reduced through strong label warnings and extensive safety directions as outlined by the pesticide regulator (APVMA). The potential risk of tubular degeneration of the testes can be mitigated through warning statements which informs the consumer about the known dangers. The potential harm associated with incidental exposure is reduced through labelling which informs the consumer about the safety measures to apply during handling and use. No further label statements are deemed necessary under the Poisons Standard, other that those required with a Schedule 6 substance.

I note that no written public submissions were received but consultation through the web portal indicated 2 supportive, 1 partially supportive and 4 individuals who were opposed to the proposal. These respondents did not provide reasons for their support or opposition. As a result, the extent of my consideration is limited to noting that the majority of submissions opposed the proposal. The respondents are invited to submit reasons to clarify their position in the current consultation.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance.

Proposed implementation date

1 October 2021

4.4 Interim decision in relation to 1,4-benzenediamine, 2-(methoxymethyl)-

Proposal

A proposal to create specific entries for 1,4-benzenediamine, 2-(methoxymethyl)- in Schedule 6 for use in hair dyes with labelling conditions and a cut-off limit, and Schedule 10 of the Poisons Standard, The substance is currently captured by group entries for phenylenediamines in Schedule 6 and Schedule 10.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision not to amend the current Poisons Standard in relation to 1,4-benzenediamine, 2-(methoxymethyl)-.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to 1,4-benzenediamine, 2-(methoxymethyl)-;
- The public report on the substance, compiled by NICNAS in August 2018;
- The 58 public submissions, including one written submission, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Chemicals Scheduling (ACCS #30);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACCS advice to the Delegate

The Committee advised that the current scheduling for 1,4-benzenediamine, 2-(methoxymethyl)- remains appropriate.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance;

The reasons for the advice included:

a) the risks and benefits of the use of a substance

- 1,4-benzenediamine, 2-(methoxymethyl)- is a potential skin sensitizer in hair dyes.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Used in hair dyes and eyebrow/eyelash tinting preparations.

c) the toxicity of a substance

- Acutely toxic with an acute LD50 of 400 mg/kg bw in rats (SDS), acute inhalation LC50 of 1300 mg/m^3/4-h exposure in rats (SDS); and the sulfate salt of the chemical has an acute oral LD50 of 150-200 mg/kg bw in rats.
- Eye irritant, but not below concentration of 6.1%, based on in vitro isolated chicken eye test.
- Skin sensitizer: EC3 of 4.3% was estimated based on an LLNA for the sulfate salt, EC3 of 7.11%.
- No evidence that the substance is a carcinogen, mutagen or reproductive toxicant.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- The Applicant's proposal is to limit the concentration of the substance to 1.8% on head concentration in oxidative hair dyes

e) the potential for abuse of a substance

- Nil.

f) any other matters that the Secretary considers necessary to protect public health

- Nil.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision not to amend the scheduling of 1,4-benzenediamine, 2-(methoxymethyl)- in the current Poisons Standard, and maintain the scheduling of the substance under the current group entries for phenylenediamines in Schedule 6 and Schedule 10.

This substance is used in oxidative hair dyes and eyebrow/eyelash tinting preparations, and is covered in the current Poisons Standard by the general Schedule 6 and 10 entries for phenylenediamines. It is a known skin sensitiser and the proposed new scheduling entries would align the Poisons Standard with European Union (EU) controls for the substance when used in hair or eyelash products.

I note that in the EU, use of the substance is restricted to concentrations up to 1.8% after mixing and when applied to the head or eyelashes in oxidative hair dyes. It is an eye irritant and skin sensitiser at concentrations above the proposed Schedule 6 cut-off of 1.8%, but is not known to possess any carcinogenic or mutagenic activity. It is not a reproductive toxicant.

I agree with the Committee's advice that the toxicological data for the substance meets the Schedule 6 factors of the Scheduling Policy Framework, including:

- It is acutely toxic with an acute LD_{50} of 400 mg/kg bw in rats (SDS), acute inhalation LC_{50} of 1300 mg/m^3/4-h exposure in rats (SDS); and the sulfate salt of the chemical has an acute oral LD_{50} of 150-200 mg/kg bw in rats.
- It is an eye irritant, but not below concentration of 6.1%, based on in vitro isolated chicken eye test.
- It is a skin sensitizer: EC3 of 4.3% was estimated based on an LLNA for the sulfate salt, EC3 of 7.11%.

I have noted the one written submission on the proposal from Accord Australia, which was supportive of aligning the controls for the substance with those for cosmetics in the EU, but opposed the proposed Schedule 10 entry on the grounds of lack of information for other uses of

the substance. This is consistent with the Committee advice that, considering the low risk to public health associated with use of the substance, the Schedule 10 factors are not met.

Given that the substance meets the Schedule 6 scheduling factors and is already captured by the group entry for phenylenediamines in Schedule 6, I have decided that no amendments to the Poisons Standard are necessary for the substance at this time.

I agree with the Committee's finding that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance.