



**Australian Government**

**Department of Health**

Therapeutic Goods Administration

# Consultation: Proposed amendments to the Poisons Standard – ACMS, ACCS and Joint ACMS/ACCS Meetings, March 2021

24 December 2020

**TGA** Health Safety  
Regulation

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## Contents

1	Proposed amendments referred for scheduling advice to ACMS #33	4
1.1	Metoclopramide	4
1.2	Chloramphenicol	8
1.3	Prochlorperazine	13
1.4	Processed Aconitum carmichaelii	17
2	Proposed amendments referred for scheduling advice to ACCS #30	21
2.1	Lead (in paint)	21
2.2	Cyflumetofen	25
2.3	Isocycloseram	27
2.4	1,4-Benzenediamine, 2-(methoxymethyl)	29
3	Proposed amendments referred for scheduling advice to the Joint ACMS-ACCS #27	33
3.1	Kambo	33
3.2	Lidocaine	36
3.3	Nitrous oxide	41
3.4	Hemp seed oil	44
4	How to respond	47
5	What will happen	47

# 1 Proposed amendments referred for scheduling advice to ACMS #33

## 1.1 Metoclopramide

### Proposal

Inclusion of a new entry for metoclopramide in Appendix H of the Poisons Standard to allow direct-to-consumer advertising of products containing the substance.

### CAS Number:

364-62-5

### Alternative names

4-Amino-5-chloro-*N*-[(2-diethylamino)ethyl]-2-methoxybenzamide, 4-amino-5-chloro-*N*-[2-(diethylamino)ethyl]-*o*-anisamide; 4-amino-5-chloro-2-methoxy-*N*-( $\beta$ -diethylaminoethyl)benzamide

### Applicant

Private applicant

### Current scheduling

Metoclopramide is currently listed in Schedules 3 and 4 of the Poisons Standard as follows:

#### Schedule 4

METOCLOPRAMIDE **except** when included in Schedule 3.

#### Schedule 3

METOCLOPRAMIDE when combined with paracetamol in divided preparations, packed and labelled only for the treatment of nausea associated with migraine, in packs containing not more than 10 dosage units.

### Proposed scheduling

#### Schedule 4

METOCLOPRAMIDE **except** when included in Schedule 3.

#### Schedule 3

METOCLOPRAMIDE when combined with paracetamol in divided preparations, packed and labelled only for the treatment of nausea associated with migraine, in packs containing not more than 10 dosage units.

### Appendix H – New Entry

**METOCLOPRAMIDE**

## Index – Amend Entry

### METOCLOPRAMIDE

Schedule 4

Schedule 3

Appendix H

## Key uses / expected use

Medicine used to treat nausea and vomiting

## Application summary - reasons for proposal

- The application proposes the inclusion of metoclopramide, when classified as a Schedule 3 (S3) medicine, in Appendix H of the Poisons Standard to permit advertising to the public.
  - Metoclopramide is a Schedule 3 medicine when combined with paracetamol in divided preparations, packed and labelled only for the treatment of nausea associated with migraine, in packs containing not more than 10 dosage units.
- Metoclopramide is an antiemetic used for the treatment of nausea, vomiting and migraine headaches.
- In May 2018, the TGA conducted a public consultation on [Substances proposed to be added to Appendix H of the Poisons Standard](#), to allow them to be advertised. After taking into consideration the potential impact on public health of direct to consumer advertising of each product, the TGA proposed several S3 substances, including metoclopramide, to be added to Appendix H.
- Following public consultation regarding the proposal, the Delegate decided against including metoclopramide in Appendix H, based on its sedative properties that are similar to other excluded substances and potential for misuse. The applicant contends that metoclopramide itself does not have sedative properties. A review of the [TGA Database of Adverse Event Notifications](#) identified three cases of sedation, with only one of those assessed as being solely due to metoclopramide.
- A recent paper ([Najjar et al 2017](#))<sup>1</sup> describes the use of metoclopramide to treat migraines in place of opioids to avoid development of drug dependency, as metoclopramide is not a drug of abuse. The TGA Database of Adverse Event Notifications identifies only one case of 'intentional product misuse' and one case of 'product in unapproved indication'.
- The sale of S3 products requires availability of professional advice from a pharmacist, which mitigates potential for misuse and adverse influence by advertising.
- Further risk mitigation is achieved through limiting pack sizes.
- It would be advantageous for the consumers to be aware, through advertising, that metoclopramide is available from their pharmacy for the symptomatic relief of headache, nausea and vomiting associated with migraine.

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<sup>1</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5438233/>



- The [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>6</sup> requires the following warning statements pertaining to Metoclopramide to be included on the labelling:

Substance	Conditions	Required Statement(s)
Metoclopramide	In medicines for oral use	Do not use in children and adolescents aged under 18 years.  Tell your doctor or pharmacist before use if you are taking other medicines.  Do not use if you have epilepsy [(seizures)/(fits)].

- Since January 2010, there have been 459 reports of adverse events for products containing metoclopramide as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),<sup>7</sup> with 302 reports where metoclopramide was the single suspected medicine.
- As of November 2020, there were three entries regarding metoclopramide listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>8</sup> These include an entry for the active constituent, and two prescription-only veterinary medicines (tablets and injections).
- In 2009-2019 the following adverse experiences were recorded for metoclopramide in the [APVMA Adverse Experience Reporting Program database \(AERP\)](#):<sup>9</sup>
  - One report of a possible incident classified as related to animal health (2014).

## International regulations

- Metoclopramide is included in the [WHO Model List of Essential Medicines 2019](#).
- Evidence of increased risks of neurological (brain and nerve) side effects associated with use of the substance and correlation with dosage and length of treatment prompted the [European Medicines Agency](#)<sup>10</sup> to recommend changes to the use of metoclopramide in 2013. These changes included short-term prescriptions, dose limitations, and age restrictions.
- The [Health Products Regulatory Authority of Ireland](#)<sup>11</sup> regulates 10mg tablets and 5mg/mL solutions for injection of metoclopramide as prescription-only medicines. Advertising to consumers is not permitted, however the products can be advertised to healthcare professionals.
- The [United States Food and Drug Administration Approved Drug Products Database](#)<sup>12</sup> approve use of metoclopramide as a prescription medicine.

<sup>6</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019  
<https://www.legislation.gov.au/Details/F2019L00213>

<sup>7</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>8</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>9</sup> APVMA Adverse Experience Reporting Program [database \(AERP\)](#) <https://apvma.gov.au/node/10946>

<sup>10</sup> EMA recommends changes to the use of metoclopramide  
[https://www.ema.europa.eu/en/documents/press-release/european-medicines-agency-recommends-changes-use-metoclopramide\\_en.pdf](https://www.ema.europa.eu/en/documents/press-release/european-medicines-agency-recommends-changes-use-metoclopramide_en.pdf)

<sup>11</sup> Health Products Regulatory Authority <https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?query=Metoclopramide+hydrochloride&field=ACTIVESUBSTANCES>

<sup>12</sup> Food and Drugs Administration Approved Drugs Database:  
<https://www.accessdata.fda.gov/scripts/cder/daf/>

- Metoclopramide is approved for use as a prescription medicine according to the [Canadian \(Health Canada\) Drug Product Database](#).<sup>13</sup>
- According to the [New Zealand Medicines and Medical Devices Safety Authority \(Medsafe\)](#)<sup>14</sup> metoclopramide is available as follows:

Ingredient	Conditions	Classification
Metoclopramide	<b>except</b> when specified elsewhere in this schedule	Prescription
Metoclopramide	when compounded with paracetamol in packs of not more than 10 tablets or capsules for the treatment of nausea associated with migraine	Restricted <sup>15</sup>

## 1.2 Chloramphenicol

### Proposal

Inclusion of a new entry for chloramphenicol in Appendix H of the Poisons Standard to allow direct-to-consumer advertising of products containing the substance.

### CAS Number:

56-75-7

### Alternative names

2,2-Dichloro-*N*-[(1*R*,2*R*)-2-hydroxy-1-(hydroxymethyl)-2-(4-nitrophenyl)ethyl]acetamide, *D*-*threo*-*N*-dichloroacetyl-1-*p*-nitrophenyl-2-amino-1,3-propanediol; *D*(-)-*threo*-2-dichloroacetamido-1-*p*-nitrophenyl-1,3-propanediol; *D*-*threo*-*N*-(1,1'-dihydroxy-1-*p*-nitrophenylisopropyl)dichloroacetamide

### Applicant

Private applicant

### Current scheduling

Chloramphenicol is currently listed in Schedules 3 and 4 of the Poisons Standard as follows:

#### Schedule 4

CHLORAMPHENICOL **except** when included in Schedule 3

#### Schedule 3

CHLORAMPHENICOL for ophthalmic use only.

<sup>13</sup> Health Canada Drug Product Database: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

<sup>14</sup> Medsafe Medicine Classification Database: <https://www.medsafe.govt.nz/profs/class/classintro.asp>

<sup>15</sup> Restricted medicines in NZ are also referred to as Pharmacist Only medicines. See <https://www.medsafe.govt.nz/Consumers/PharmOnly.asp> for details



## Proposed scheduling

### Schedule 4

CHLORAMPHENICOL **except** when included in Schedule 3

### Schedule 3

CHLORAMPHENICOL for ophthalmic use only.

### Appendix H – New Entry

CHLORAMPHENICOL

### Index – Amend Entry

CHLORAMPHENICOL

Schedule 4

Schedule 3

Appendix H

## Key uses / expected use

Medicines (antibacterial, antibiotic)

## Application summary - reasons for proposal

- The application proposes inclusion of chloramphenicol, when classified as a Schedule 3 (S3) medicine, in Appendix H of the Poisons Standard to permit advertising to the public.
  - Chloramphenicol is a S3 medicine for ophthalmic use only.
- Schedule 3 topical preparations of chloramphenicol are used for the treatment of bacterial conjunctivitis and, under medical supervision only, for other superficial ocular infections due to sensitive organisms. It is also used for the treatment of otitis externa due to sensitive organisms. As Schedule 4 medicine, chloramphenicol is used for the treatment of infections due to susceptible organisms such as bacterial meningitis, typhoid fever, rickettsial, intraocular and other serious infections.
- In May 2018, the TGA conducted a public consultation on [Substances proposed to be added to Appendix H of the Poisons Standard](#), to allow them to be advertised. After taking into consideration the potential impact on public health of direct to consumer advertising of each product, the TGA proposed several S3 substances, including chloramphenicol, to be added to Appendix H.
- Following public consultation regarding the proposal, the Delegate decided against including chloramphenicol in Appendix H, based on potential for promoting antibiotic resistance and the inherent difficulties in differentiating viral and bacterial conjunctivitis without professional medical advice.
- The applicant contends that chloramphenicol is regarded as a safe and highly effective treatment for bacterial conjunctivitis, a common and contagious eye disease. For such a condition, early treatment is important and direct to consumer advertising would inform consumers they can consult with a pharmacist for early treatment.
- There is an increased awareness among medical practitioners and consumers of improper use of antibiotics that could lead to antibiotic resistance. The product information includes guidance that treatment should be continued for at least 48 hours after the eye appears

normal and not to use for more than 5 days in total except on medical advice. These precautions will address the improper use of the product, if any, thus managing any effects that could contribute to antibiotic resistance.

- The applicant also states that the consultative feedback that overuse may result in increased antibiotic resistance is applicable to all antibiotics, and is not considered specific to chloramphenicol alone.
- Chloramphenicol is not sedating nor a drug of abuse. A review of the [TGA Database of Adverse Event Notifications](#) identified only one case of 'intentional product misuse' and one case of 'product use in unapproved indication', and no reports of 'drug interaction' or sedation. There are no reported drug-drug interactions with chloramphenicol in ophthalmic use.
- The sale of S3 products requires availability of professional advice from a pharmacist, which mitigates potential for misuse and adverse influence by advertising.
- Advertising would inform consumers they can see a pharmacist for early treatment and avoid potential for spreading the disease.
- Chloramphenicol is supplied as a 1% eye ointment tube (4 g) and a dilute solution of 5 mg/mL eye drop (10 mL) in plastic dropper bottles. Both ophthalmic presentations are for external use only and clear instructions are provided concerning amount and duration of use.

## Australian regulations

- According to the [TGA Ingredient Database](#),<sup>16</sup> chloramphenicol is
  - available for use as an active ingredient in biologicals, export only, over the counter and prescription medicines, and available for use as an excipient in biologicals, devices and prescription medicines;
  - available for use as an equivalent ingredient in prescription medicines;
  - available for use as an active ingredient or excipient in biologicals, export only and prescription medicines, as chloramphenicol sodium succinate;
  - available for use as an active ingredient in biologicals and prescription medicines, and as an excipient in biologicals, devices and prescription medicines, as chloramphenicol palmitate.
- As of November 2020, there were 19 active medicines on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>17</sup> that contained chloramphenicol as an active ingredient. These include 1 prescription and 18 non-prescription medicines. Non-prescription formulations include 5mg/mL eye drops and 10mg/gram eye ointment.
- Chloramphenicol is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>18</sup> No.3 of 2020.

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<sup>16</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>17</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>18</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20\\$LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20$LB$Permissible%20Ingredients$RB$%20Determination)

- The [TGA prescribing medicines in pregnancy database](#)<sup>19</sup> classifies chloramphenicol as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Chloramphenicol	A	Antimicrobials	Antibiotics	
Chloramphenicol (ophthalmic)	A	Ophthalmic drugs		

**Category A** – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

- The [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>20</sup> requires the following warning statements pertaining to chloramphenicol to be included on the labelling:

Substance	Conditions	Required Statement(s)
Chloramphenicol	In medicines for ophthalmic use	Contact lens wearers should not use this product except on the advice of a doctor or optometrist.  If your eye infection does not improve within 48 hours, seek immediate medical advice.  Do not use in children under 2 years of age except on medical advice.

- Since January 2010, there have been 56 reports of adverse events for products containing chloramphenicol as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),<sup>21</sup> with 44 reports where chloramphenicol was the single suspected medicine.
- As of November 2020, there were 12 entries regarding chloramphenicol listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>22</sup> These include three entries for active constituents, eight entries for ophthalmic preparations (all ointments), and one entry for a parenteral antibiotic liquid/solution/suspension.
- In 2009-19 the following adverse experiences were recorded for chloramphenicol in the [APVMA Adverse Experience Reporting Program database \(AERP\)](#):<sup>23</sup>
  - One report of a serious incident classified as related to animal health (2019-20).
  - One report of a possible incident classified as related to animal health (2015).
  - One report of a possible incident classified as related to animal health (2010).

<sup>19</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>20</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

<sup>21</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>22</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>23</sup> APVMA Adverse Experience Reporting Program database (AERP) <https://apvma.gov.au/node/10946>

- The Australian Commission on Safety and Quality in Health Care classifies chloramphenicol on its [Priority Antibacterial List for Antimicrobial Resistance Containment](#) as 'Access', that is a recommended first-line treatment for common infections. [Chloramphenicol is also listed as one of the five most prescribed antimicrobials in Australia](#), despite its status as a non-prescription medicine for ophthalmic use since 2010.

## International regulations

- Chloramphenicol is on the [WHO Model List of Essential Medicines](#).
- According to the [United States Food and Drug Administration Approved Drug Products Database](#)<sup>24</sup>, chloramphenicol is approved for use as a prescription medicine.
- According to the [Canadian \(Health Canada\) Drug Product Database](#)<sup>25</sup>, chloramphenicol is available as a prescription medicine.
- The [Health Products Regulatory Agency of Ireland](#)<sup>26</sup> regulate chloramphenicol eye drops (0.5% w/v) as a prescription-only medicine. Advertising to consumers is not permitted, however the products can be advertised to healthcare professionals.
- According to the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)<sup>27</sup>, chloramphenicol is available as follows:

Ingredient	Conditions	Classification
Chloramphenicol	except when sold in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board; except when specified elsewhere in this schedule	Prescription
Chloramphenicol	for ophthalmic use; <b>except</b> when sold in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board	Restricted <sup>28</sup>

<sup>24</sup> Food and Drug Administration Approved Drugs Database: <https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>25</sup> Health Canada Drug Product Database: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

<sup>26</sup> Health Products Regulatory Authority <https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?query=Chloramphenicol&field=ACTIVESUBSTANCES>

<sup>27</sup> Medsafe Medicine Classification Database: <https://www.medsafe.govt.nz/profs/class/classintro.asp>

<sup>28</sup> Restricted medicines in NZ are also referred to as Pharmacist Only medicines. See <https://www.medsafe.govt.nz/Consumers/PharmOnly.asp> for details

## 1.3 Prochlorperazine

### Proposal

Inclusion of a new entry for prochlorperazine in Appendix H of the Poisons Standard to allow direct-to-consumer advertising of products containing the substance.

### CAS Number:

58-38-8

### Alternative names

2-Chloro-10-[3-(4-methyl-1-piperazinyl)propyl]-10*H*-phenothiazine; 3-chloro-10-[3-(4-methyl-1-piperazinyl)propyl]phenothiazine; 2-chloro-10-[3-(1-methyl-4-piperazinyl)propyl]phenothiazine; *N*-[γ-(4'-methylpiperazinyl-1')propyl]-3-chlorophenothiazine; chlormeprazine; prochlorpemazine; proclorperazine

### Applicant

Private applicant

### Current scheduling

Prochlorperazine is currently listed in Schedules 3 and 4 of the Poisons Standard as follows:

#### Schedule 4

PROCHLORPERAZINE **except** when included in Schedule 3.

#### Schedule 3

PROCHLORPERAZINE in divided preparations for oral use in packs containing not more than 10 dosage units for the treatment of nausea associated with migraine.

#### Appendix K

PROCHLORPERAZINE

### Proposed scheduling

#### Schedule 4

PROCHLORPERAZINE **except** when included in Schedule 3.

#### Schedule 3

PROCHLORPERAZINE in divided preparations for oral use in packs containing not more than 10 dosage units for the treatment of nausea associated with migraine.

#### Appendix H – New Entry

**PROCHLORPERAZINE**

#### Appendix K

PROCHLORPERAZINE

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## Index – Amend Entry

### PROCHLORPERAZINE

Schedule 4

Schedule 3

**Appendix H**

Appendix K

## Key uses / expected use

Medicines (antiemetic, antipsychotic)

## Application summary - reasons for proposal

- The application proposes inclusion of prochlorperazine, when classified as a Schedule 3 (S3) medicine, in Appendix H of the Poisons Standard to permit advertising to the public.
  - Prochlorperazine is a S3 medicine in divided preparations for oral use in packs containing not more than 10 dosage units for the treatment of nausea associated with migraine.
- Prochlorperazine as a Schedule 4 medicine is used for the treatment of nausea and vomiting due to various causes including migraine, Meniere's syndrome, labyrinthitis and other causes in adults and children. As a S3 medicine, it is indicated for the treatment of nausea associated with migraine.
- In May 2018, the TGA conducted a public consultation on [Substances proposed to be added to Appendix H of the Poisons Standard](#), to allow them to be advertised. After taking into consideration the potential impact on public health of direct to consumer advertising of each product, the TGA proposed several S3 substances to be added to Appendix H.
- The TGA Delegate recommended not adding prochlorperazine to Appendix H, due to the potential negative impact on health related to possible misuse, abuse or diversion.
- While prochlorperazine is mainly known for the treatment of nausea and vomiting, it has also been reported that it can alter mood and perception. However, the applicant contends it is not known to deliver the euphoria that is often delivered by more commonly abused drugs.
- The sale of S3 products requires availability of professional advice from a pharmacist, which mitigates potential for misuse and adverse influence by advertising. Further risk mitigation is achieved through limiting pack sizes.
- While cases of abuse and physical dependence have been reported on some medications listed in Appendix H of the SUSMP, the applicant suggests that prochlorperazine is not considered to pose risks above these medicines currently in Appendix H.
- A search of the [TGA Database of Adverse Event Notifications](#) showed no reports of drug abuse and only 1 report of off-label use, out of 1218 cases reported (to November 2020).

## Australian regulations

- According to the [TGA Ingredient Database](#),<sup>29</sup> prochlorperazine is:
  - available for use as an active ingredient or excipient in biologicals, prescription medicines and devices, and available for use as an equivalent ingredient in prescription medicines;
  - available for use as an active ingredient in biologicals, export only, over the counter, prescription medicines and devices, as well as an excipient in biologicals, prescription medicines and devices, as prochlorperazine mesilate;
  - available for use as an active ingredient in biologicals, export only, over the counter, and prescription medicines, as well as an excipient in biologicals, prescription medicines and devices, as prochlorperazine maleate;
  - available for use as an active ingredient in biologicals and prescription medicines, and as an excipient in biologicals, prescription medicines and devices, as prochlorperazine edisilate (edisylate).
- As of November 2020, there were 27 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>30</sup> that contain prochlorperazine as an active ingredient. These include 11 prescription, 15 non-prescription medicines and 1 export-only medicine. Non-prescription formulations include 5mg tablets.
- Prochlorperazine is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>31</sup> No.3 of 2020.
- The [TGA prescribing medicines in pregnancy database](#)<sup>32</sup> classifies prochlorperazine as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Prochlorperazine	C	Central Nervous System	Antiemetics, antinauseants	Phenothiazines
<p><b>Category C</b> – Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.</p>				

- Prochlorperazine is required to have a sedation warning on the label as it is listed in Appendix K of the Poisons Standard.
- There are no warning statements pertaining to prochlorperazine in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>33</sup>.

<sup>29</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>30</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>31</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB%20Determination)

<sup>32</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>33</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>



- Since January 2010, there have been 123 reports of adverse events for products containing prochlorperazine as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),<sup>34</sup> with 79 reports where prochlorperazine was the single suspected medicine. There were no reports of death associated with prochlorperazine use.
- Product information leaflets state that prochlorperazine may enhance the CNS depressant effects of alcohol and other depressant drugs, and potentiate the anticholinergic effects of atropinic agents and tricyclic antidepressants.
- As of November 2020, there were no products containing prochlorperazine listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>35</sup>

## International regulations

- According to the [United States Food and Drug Administration Approved Drug Products Database](#),<sup>36</sup> prochlorperazine is approved for use as a prescription medicine in the United States.
- Prochlorperazine is approved as a prescription medicine in Canada according to the [Canadian \(Health Canada\) Drug Product Database](#).<sup>37</sup>
- The [Health Products Regulatory Authority of Ireland](#)<sup>38</sup> regulates prochlorperazine maleate as a prescription only medicine in 5 mg tablets. Advertising to consumers is not permitted, however the products can be advertised to healthcare professionals.
- According to the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)<sup>39</sup>, prochlorperazine is regulated as follows:

Ingredient	Conditions	Classification
Prochlorperazine	<b>except</b> when specified elsewhere in this schedule; <b>except</b> when sold for the treatment of nausea associated with emergency contraception by pharmacists or nurses accredited to sell levonorgestrel for emergency contraception	Prescription
Prochlorperazine	in packs containing not more than 10 tablets or capsules for the treatment of nausea associated with migraine	Restricted <sup>40</sup>

<sup>34</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>35</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>36</sup> Food and Drug Administration Approved Drugs Database: <https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>37</sup> Health Canada Drug Product Database: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

<sup>38</sup> Health Products Regulatory Authority <https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results/item?pano=PA0540/127/005&t=Stemetil%205mg%20Tablets>

<sup>39</sup> Medsafe Medicines Classification Database: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

<sup>40</sup> Restricted medicines in NZ are also referred to as Pharmacist Only medicines. See <https://www.medsafe.govt.nz/Consumers/PharmOnly.asp> for details



## 1.4 Processed *Aconitum carmichaelii*

### Proposal

Amendment of the existing entries for *Aconitum* spp. in Schedules 2 and 4 of the Poisons Standard to recognise the reduced toxicity of the processed herb.

### CAS Number:

N/A

### Alternative names

N/A

### Applicant

Private applicant

### Current scheduling

*Aconitum* spp. is currently listed in Schedules 2 and 4 of the Poisons Standard as follows:

#### Schedule 4

ACONITUM spp. **except**:

- a) when included in Schedule 2;
- b) in preparations for oral use in adults in packs containing 0.02 mg or less of total alkaloids; or
- c) in preparations for dermal use in adults containing 0.02 per cent or less of total alkaloids in packs containing 0.02 mg or less of total alkaloids.

#### Schedule 2

ACONITUM spp. for therapeutic use in adults:

- a) in preparations for oral use in packs each containing 0.2 mg or less of total alkaloids **except** in packs containing 0.02 mg or less of total alkaloids; or
- b) in preparations for dermal use containing 0.02 per cent or less of total alkaloids, in packs each containing 0.2 mg or less of total alkaloids **except** in packs containing 0.02 mg or less of total alkaloids.

### Proposed scheduling

#### Schedule 4 –Amend Entry

ACONITUM spp. **except**:

- a) when included in Schedule 2;
- b) in preparations for oral use in adults in packs containing 0.02 mg or less of total alkaloids; or

- c) in preparations for dermal use in adults containing 0.02 per cent or less of total alkaloids in packs containing 0.02 mg or less of total alkaloids; or
- d) processed *Aconitum* spp. in preparations or manufactured dosage forms used in Traditional Chinese Medicine **except** when included in Schedule 2.

### Schedule 2 – Amend Entry

ACONITUM spp. for therapeutic use in adults:

- a) in preparations for oral use in packs each containing 0.2 mg or less of total alkaloids except in packs containing 0.02 mg or less of total alkaloids; or
- b) in preparations for dermal use containing 0.02 per cent or less of total alkaloids, in packs each containing 0.2 mg or less of total alkaloids except in packs containing 0.02 mg or less of total alkaloids; or
- c) processed *Aconitum* spp. in preparations or manufactured dosage forms used in Traditional Chinese Medicine:
- 1) for oral use in packs each containing 0.6mg or less for single dose or 3.0mg or less for daily dose, of total diester diterpenoid alkaloids, calculated as the total amount of aconitine, hypaconitine and mesaconitine; or
  - 2) for dermal use in packs each containing 0.6mg or less for single dose or 3.0mg or less for daily dose, of total diester diterpenoid alkaloids, calculated as the total amount of aconitine, hypaconitine and mesaconitine.

### Key uses / expected use

Medicines (Traditional Chinese and ayurvedic medicines)

### Application summary - reasons for proposal

- The application proposes amendment of the existing entries for *Aconitum* spp. in Schedules 2 and 4 of the Poisons Standard to set appropriate limits on the toxins identified in *Aconitum carmichaelii* after processing.
- Unprocessed *Aconitum* spp. contain toxic levels of diester diterpenoid alkaloids, namely aconitine, hypaconitine and mesaconitine, which are known neurotoxins and cardiotoxins. The applicant claims processing of the herb reduces the levels of these compounds, and is common practice for registered practitioners of Chinese herbal medicine.
- The constituents of the herb do not exhibit narcotic or psychotropic properties, and there is no documented history of abuse or dependence.
- The processed herb is commonly used in China and other parts of the world, with a range of claimed benefits for common conditions including digestive disorders and abdominal pain, anti-inflammatory and antimicrobial effects.
- The alkaloids that are the subject of the proposal are already used as markers for quality control by the Chinese Pharmacopoeia, which sets limits on the alkaloids that are at least as stringent as those currently imposed by the Poisons Standard.
- The International Organisation is currently developing an international standard for *Aconitum* in Traditional Chinese Medicines for Standardisation, which will include various control parameters extending beyond alkaloid content (heavy metals, pesticides, other marker compounds).

- International restrictions
  - According to the applicant, both Health Canada and the Chinese Pharmacopoeia set permissible limits on the total amount of the alkaloids aconitine, hyaconitine and mesaconitine at 0.02% w/w of the dry herb.

## Australian regulations

- According to the [TGA Ingredient Database](#),<sup>41</sup> Aconitum carmichaelii is:
  - Available for use as an active ingredient in export only, listed and prescription medicines.
  - Available for use as a homeopathic ingredient in listed medicines.
- As of November 2020, there were 16 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>42</sup> that contain Aconitum spp. as an active ingredient, including two that contain Aconitum carmichaelii. Both products containing *A.carmichaelii* were listed medicines. Both formulations containing *A.carmichaelii* were pills.
- According to the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>43</sup> No.3 of 2020, Aconitum carmichaelii is permitted to be included in listed medicines as follows:

Item	Ingredient name	Purpose	Specific requirements
351	ACONITUM CARMICHAELII	A, H	Total alkaloids (of Aconitum spp.) is a mandatory component of Aconitum carmichaelii.  The maximum amount of total alkaloids(of Aconitum spp.) must be no more than 0.02 milligrams
<p>A = active ingredient for a medicine has the same meaning as in the Regulations            H = homoeopathic preparation ingredient meaning an ingredient that is a constituent of a homoeopathic preparation</p>			

- The [TGA prescribing medicines in pregnancy database](#)<sup>44</sup> does not include Aconitum carmichaelii.
- There are no warning statements pertaining to Aconitum carmichaelii in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>45</sup>
- As of November 2020, there were no reports of adverse events for products containing Aconitum carmichaelii as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#).<sup>46</sup>

<sup>41</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>42</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>43</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB$%20Determination)

<sup>44</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>45</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

<sup>46</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

- As of November 2020, there were no products containing *Aconitum carmichaelii* listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>47</sup>

## International regulations

- Aconitum* spp. are not listed on the [Food and Drugs Administration Approved Drugs Database](#)<sup>48</sup> or the [Health Canada Drug Product Database](#)<sup>49</sup>.
- According to the [Medsafe Medicine Classification Database](#)<sup>50</sup>, *Aconitum* spp. are regulated as:

Ingredient	Conditions	Classification
<i>Aconitum</i> spp.	<b>Except</b> when specified elsewhere in this schedule	Prescription
<i>Aconitum</i> spp.	For oral use in packs containing 0.2 milligrams or less and more than 0.02 milligrams of total alkaloids; for dermal use in concentrations of 0.02% or less and in packs containing 0.2 milligrams or less and more than 0.02 milligrams of total alkaloids	Pharmacy Only
<i>Aconitum</i> spp.	for oral use in packs containing 0.02 milligrams or less of total alkaloids; for dermal use in concentrations 0.02% or less and in packs containing 0.02 milligrams or less of total alkaloids	General Sale

<sup>47</sup> Public Chemical Registration Information System Search (PubCRIS)  
<https://portal.apvma.gov.au/pubcris>

<sup>48</sup> Food and Drugs Administration Approved Drugs Database  
<https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>49</sup> Health Canada Drug Product Database <https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>50</sup> Medsafe Medicines Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

## 2 Proposed amendments referred for scheduling advice to ACCS #30

### 2.1 Lead (in paint)

#### Proposal

Amend the Schedule 10 entry for lead in paint in the Poisons Standard (and any other relevant sections of the Poisons Standard) to reduce the permissible level from 0.1% to 0.009%.

#### CAS Number:

7439-92-1

#### Alternative names

N/A

#### Applicant

Private applicant

#### Current scheduling

Lead (in paint) is currently in Schedule 10 of the Poisons Standard as follows:

##### Schedule 10

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

#### Proposed scheduling

An application has been made to reduce the allowable limit for lead in paint from 0.1% (1000ppm) to 0.009% (90ppm).

##### 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).

#### Key uses / expected use

Domestic and industrial, animal and homeopathic uses

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## Application summary - reasons for proposal

- Lead is a known cumulative toxin which the [World Health Organisation](#) has identified as a major public health concern, and to which many regulatory agencies have taken action to limit exposure to the general public.
- [The United Nations Environment Program](#) endorses a limit of 90 parts per million (0.009% w/w) of lead in paint, based on the need to minimise exposure to lead while also ensuring that the limit is feasible for paint manufacturers.
- Lead compounds can be added to paint as pigments, driers and to provide corrosion resistance, resulting in a high lead content, which may be in the order of thousands of parts per million (ppm). While the paint remains intact, the lead content is not a hazard; however, as the paint ages, it starts to crumble and flake, releasing lead into household dust.
- Young children are vulnerable to lead exposure from contaminated dust and flaking paint. Ingestion of paint flakes or chips, particularly in children, is a direct pathway of exposure to the substance.
- Even low levels of exposure to lead have demonstrated harmful effects. Known health effects include anaemia, hypertension, kidney damage, reduced IQ and behavioural changes. Exposure in adults is associated with increased risk of cardiovascular disease, including hypertension and coronary heart disease.
- The Institute for Health Metrics and Evaluation estimated that, in 2017, lead exposure accounted for 1.06 million deaths and the loss of 24.4 million years of healthy life (disability-adjusted life years) worldwide. Lead is a well-documented ecotoxicant, posing threats to both aquatic and terrestrial ecosystems.
- Historically, lead compounds have been added to solvent-based paints to provide colour, speed up drying time, increase durability and resist moisture that causes corrosion. Today, however, it is entirely possible to formulate paint with the desired characteristics without using lead compounds.
- International restrictions
  - [A 90 ppm limit has already been adopted by several countries](#) for some or all types of paints and coatings, including Bangladesh, Cameroon, Canada, China, Ethiopia, India, Iraq, Israel, Jordan, Kenya, Nepal, Philippines and the USA.

## Australian regulations

- According to the [TGA Ingredient Database](#),<sup>51</sup> lead is:
  - Available for use as an active ingredient in biologicals, export only, listed medicines, over the counter and prescription medicines.
  - Available for use in listed medicines as a homeopathic ingredient only.
  - Available for use as an excipient ingredient in biologicals, devices and prescription medicines.
  - Available for use as an equivalent ingredient in listed medicines.

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<sup>51</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

- As of November 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>52</sup> that contain lead as an active ingredient.
- According to the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>53</sup> No.3 of 2020, lead is permitted to be included in listed medicines as follows:

Item	Ingredient name	Purpose	Specific requirements
2955	LEAD	H	Only for use as an active homoeopathic ingredient.  The concentration in the medicine must be no more than 0.001%.
2956	LEAD ACETATE	H	Only for use as an active homoeopathic ingredient.
4139 4140 4141 4142 4143 4144	PROPOLIS PROPOLIS BALSAM PROPOLIS DRY EXTRACT PROPOLIS LIQUID EXTRACT PROPOLIS RESIN PROPOLIS TINCTURE	A, E A, E A, E A, E A, E A, E	Lead is a mandatory component of (these preparations).  The concentration of lead in the medicine must be no more than 0.001%.  When used topically, the medicine requires the following warning statement on the medicine label:  (PROP1) 'WARNING: Propolis may cause skin irritation. Test before use'  When used for other than for topical, the medicine requires the following warning statement on the medicine label:  (PROP2) 'Warning: Propolis may cause allergic reactions. If irritation or swelling of the mouth or throat occurs, discontinue use.'
<p>A = active ingredient for a medicine has the same meaning as in the Regulations H = homoeopathic preparation ingredient meaning an ingredient that is a constituent of a homoeopathic preparation</p>			

- The [TGA prescribing medicines in pregnancy database](#)<sup>54</sup> does not have an entry for lead.
- There are no warning statements pertaining to lead in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>55</sup>.

<sup>52</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>53</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB%20Determination)

<sup>54</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>55</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

- As of November 2020, there were no reports of adverse events for products containing lead as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),<sup>56</sup>.
- As of November 2020, there were two products containing lead listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)<sup>57</sup> (as lead acetate). Lead acetate is listed as an approved active constituent, and listed as an active constituent in a dermatological veterinary medicine.
- In 2009-2019 no adverse experiences were recorded for lead in the [APVMA Adverse Experience Reporting Program database \(AERP\)](#).<sup>58</sup>

## International regulations

- Lead is not listed on the [Food and Drugs Administration Approved Drugs Database](#)<sup>59</sup> or the [Health Canada Drug Product Database](#)<sup>60</sup>.
- According to the [Medsafe Medicine Classification Database](#)<sup>61</sup>, lead is regulated as a prescription medicine.
- The [European Chemicals Agency](#)<sup>62</sup> (ECHA) lists lead as a 'substance of very high concern'. Hazard classifications include "may damage fertility or the unborn child, causes damage to organs through prolonged or repeated exposure, is very toxic to aquatic life with long lasting effects, may cause cancer, is very toxic to aquatic life and may cause harm to breast-fed children".
- The [Health and Safety Authority](#)<sup>63</sup> of Ireland enforces a ban on the use of lead carbons and lead sulphates in paint except for restoration and maintenance of art and historic buildings.
- The [Consumer Product Safety Commission](#)<sup>64</sup> in the United States regulates the lead content in household paint at a limit of 0.009% (90 parts per million), according to the Consumer Product Safety Improvement Act of 2008.

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<sup>56</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>57</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>58</sup> APVMA Adverse Experience Reporting Program database (AERP) <https://apvma.gov.au/node/10946>

<sup>59</sup> Food and Drugs Administration Approved Drugs Database <https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>60</sup> Health Canada Drug Product Database <https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>61</sup> Medsafe Medicines Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

<sup>62</sup> European Chemicals Agency <https://echa.europa.eu/substance-information/-/substanceinfo/100.028.273>

<sup>63</sup> Health Safety Authority [https://www.hsa.ie/eng/Topics/Business\\_Licensing\\_and\\_Notification\\_Requirements/Chemicals/](https://www.hsa.ie/eng/Topics/Business_Licensing_and_Notification_Requirements/Chemicals/)

<sup>64</sup> Consumer Product Safety Commission <https://www.cpsc.gov/Business--Manufacturing/Business-Education/Lead/Lead-in-Paint>



## 2.2 Cyflumetofen

### Proposal

New entry for the pesticide cyflumetofen in Schedule 6 of the Poisons Standard.

### CAS Number:

400882-07-7

### Alternative names

Benzenepropanoic acid,  $\alpha$ -cyano- $\alpha$ -[4-(1,1-dimethylethyl)phenyl]- $\beta$ -oxo-2-(trifluoromethyl)-, 2-methoxyethyl ester;  $\alpha$ -cyano- $\alpha$ -[4-(1,1-dimethylethyl)phenyl]- $\beta$ -oxo-2-(trifluoromethyl)-2-methoxyethyl ester benzenepropanoic acid; 2-methoxyethyl 2-(4-*tert*-butylphenyl)-2-cyano-3-oxo-3-[2-(trifluoromethyl)phenyl]propanoate

### Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

### Current scheduling

Cyflumetofen is not specifically scheduled in the current Poisons Standard.

### Proposed scheduling

#### Schedule 6 – New Entry

**CYFLUMETOFEN**

#### Index – New Entry

**CYFLUMETOFEN**

**Schedule 6**

### Key uses / expected use

Agriculture (acaricide for control of mites and ticks)

### Application summary - reasons for proposal

- Cyflumetofen is an acaricide that is new to Australia, however it is already registered for use in Japan, Canada, the United States and the European Union.
- The substance is intended for use as a spray on various crops to control certain mite species. These uses are anticipated to result in limited occupational exposure, with appropriate packaging and labelling controls to be utilised for risk management.
- Cyflumetofen is of low acute toxicity via the oral, dermal and inhalation routes of exposure. It is not irritating to the skin, slightly irritating to the eye and it is a potential skin sensitiser.
- There was no evidence of carcinogenicity in mice. In rats, a marginal increase in the incidence of Leydig cell tumours was observed at the highest dose tested, while there was also a slight increase in the incidence of thyroid c-cell tumours in the 2-year rat study.

However, these observations were determined to be incidental. Overall, cyflumetofen is considered unlikely to be carcinogenic to humans under its expected conditions of use.

- Cyflumetofen was tested for genotoxicity in an adequate range of assays, both *in vitro* and *in vivo*. A mouse lymphoma gene mutation assay was positive with and without liver enzyme activation at concentrations close to those at which precipitation occurred. Cyflumetofen was not genotoxic in an Ames test or in an *in vitro* chromosomal aberration assay. There was no evidence of genotoxicity in an *in vivo* micronucleus assay or in an *in vivo* unscheduled DNA synthesis assay in rat liver. Overall, it was concluded that cyflumetofen is unlikely to be genotoxic *in vivo*.
- Cyflumetofen is not neurotoxic in acute or subchronic neurotoxicity studies in rats. Cyflumetofen is not immunotoxic.
- Three medical reports from monitoring of manufacturing plant personnel were submitted. No adverse health effects were noted in any of the reports.

### Australian regulations

- Cyflumetofen is not listed on the [TGA Ingredient Database](#).<sup>65</sup>
- As of November 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>66</sup> that contain cyflumetofen as an active ingredient.
- As of November 2020, there were no products containing cyflumetofen listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>67</sup>

### International regulations

- The [European Chemicals Agency](#)<sup>68</sup> lists cyflumetofen as a suspected carcinogen and a possible skin sensitiser.
- Cyflumetofen is a registered pesticide with the [United States Environmental Protection Agency](#)<sup>69</sup>.
- Cyflumetofen is not listed on the [New Zealand Inventory of Chemicals](#)<sup>70</sup>.
- The [European Union Pesticides Database](#)<sup>71</sup> lists cyflumetofen as an authorised substance in many member countries, including Belgium, Bulgaria, Cyprus, Czech Republic, Germany, Spain, France, Croatia, Italy, Netherlands, Poland and Portugal. It is stated that plant protection products containing cyflumetofen shall only be authorised for uses where the level of metabolite B3 in groundwater is expected to be below 0.1 µg/L.

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<sup>65</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>66</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>67</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>68</sup> European Chemicals Agency <https://echa.europa.eu/substance-information/-/substanceinfo/100.170.873>

<sup>69</sup> US Environmental Protection Agency [https://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:3:::1.3,31,7,12,25:P3\\_XCHEMICAL\\_ID:1490](https://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:3:::1.3,31,7,12,25:P3_XCHEMICAL_ID:1490)

<sup>70</sup> New Zealand Inventory of Chemicals <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/>

<sup>71</sup> EU Pesticides Database <https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=2082>

## 2.3 Isocycloseram

### Proposal

New entry for the pesticide isocycloseram in Schedule 6 of the Poisons Standard.

### CAS Number:

2061933-85-3

### Alternative names

4-[5-(3,5-dichloro-4-fluorophenyl)-5-(trifluoromethyl)-4,5-dihydro-1,2-oxazol-3-yl]-N-(2-ethyl-3-oxo-1,2-oxazolidin-4-yl)-2-methylbenzamide

### Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

### Current scheduling

Isocycloseram is not specifically scheduled in the current Poisons Standard.

### Proposed scheduling

#### Schedule 6 – New Entry

**ISOCYCLOSERAM**

#### Index – New Entry

**ISOCYCLOSERAM**

**Schedule 6**

### Key uses / expected use

Agriculture (pesticide)

### Application summary - reasons for proposal

- Isocycloseram belongs to the group of isoxazoline insecticides. It is a new active constituent which has not previously been approved in Australia, and has not yet been considered for scheduling.
- The Scheduling Delegate and the Advisory Committee on Chemicals Scheduling (ACCS) have previously considered in the related active constituents [afoxolaner](#), [fluralaner](#), [lotilaner](#) and [sarolaner](#). Afoxolaner, fluralaner and lotilaner are included in Schedule 5, while sarolaner is included in Schedule 6 with a cut-off to Schedule 5 for 120 mg or less of sarolaner per dosage unit.
- Isocycloseram has very low acute toxicity by oral routes, and low acute toxicity by dermal and inhalational routes. It is a slight eye irritant. It is a potential skin sensitiser. In laboratory animals repeat dose studies, most adverse effects were clinical signs consistent with

neurotoxicity at high doses, as well as histopathological findings in the adrenal glands, liver, duodenum and spleen of mice and rats and in the lymph nodes of mice.

- Chronic studies did not demonstrate carcinogenic potential and this is supported by negative results in an adequate range of *in vitro* and *in vivo* genotoxicity assays.
- The active substance is not a reproductive or developmental toxicant in a multigenerational study in rats. In a prenatal developmental toxicity study in the rat, an increased incidence of bifid sternum above historical control levels was observed. No signs of developmental toxicity was seen in the rabbit, with no observed effect at a level of 7.5 mg/kg/day. There was no evidence of neurotoxicity.
- *In vitro* eye irritation test indicated that isocycloseram was not classified as severe irritant, but not classified as non-irritant to the isolated chicken eye. An *in vivo* eye irritation study showed isocycloseram as slightly irritant to the eye of rabbit. It was not irritant to the skin of rabbit, but the local lymph node assay showed a potential for skin sensitisation.

## Australian regulations

- Isocycloseram is not included on the [TGA Ingredient Database](#).<sup>72</sup>
- As of November 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>73</sup> that contain isocycloseram as an active ingredient.
- As of November 2020, there were no products containing isocycloseram listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>74</sup>

## International regulations

- Isocycloseram is not currently approved overseas. [Secretariat note: This information is from the Applicant.]
- Isocycloseram is not registered with the [European Chemicals Agency \(ECHA\)](#)<sup>75</sup> or the [European Food Safety Authority \(EFSA\)](#)<sup>76</sup>.
- Isocycloseram is not registered with the [US Environmental Protection Agency \(EPA\), Office of Pesticides Programs](#),<sup>77</sup> [Canada's Pest Management Regulation Agency](#),<sup>78</sup> or with the [New Zealand Inventory of Chemicals \(NZIOC\)](#).<sup>79</sup>

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<sup>72</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>73</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>74</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>75</sup> [https://echa.europa.eu/search-for-chemicals?p\\_p\\_id=disssimplesearch\\_WAR\\_dissearchportlet&p\\_p\\_lifecycle=0&disssimplesearch\\_WAR\\_dissearchportlet\\_searchOccurred=true&disssimplesearch\\_WAR\\_dissearchportlet\\_sessionCriteriaId=dissSimpleSearchSessionParam101401563842726334](https://echa.europa.eu/search-for-chemicals?p_p_id=disssimplesearch_WAR_dissearchportlet&p_p_lifecycle=0&disssimplesearch_WAR_dissearchportlet_searchOccurred=true&disssimplesearch_WAR_dissearchportlet_sessionCriteriaId=dissSimpleSearchSessionParam101401563842726334)

<sup>76</sup> <https://www.efsa.europa.eu/en/search/site/bixlozone>

<sup>77</sup> Office of Pesticide Programs <https://iaspub.epa.gov/apex/pesticides/f?p=chemicalsearch:1>

<sup>78</sup> Pest Management Regulatory Agency <https://pesticide-registry.canada.ca/en/active-ingredient-search.html>

<sup>79</sup> New Zealand Inventory of Chemicals <https://epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=bizlozone&DatabaseType=NZIOC>

## 2.4 1,4-Benzenediamine, 2-(methoxymethyl)-

### Proposal

New entries for the hair dye chemical 1,4-benzenediamine, 2-(methoxymethyl)- in Schedule 6 (with labelling conditions and a cut-off limit) and Schedule 10 of the Poisons Standard.

### CAS Number:

337906-36-2

### Alternative names

2-(methoxymethyl)benzene-1,4-diamine; 2-Methoxymethyl-p-phenylenediamine, 2-(methoxymethyl)-1,4-Benzenediamine

### Applicant

Australian Industrial Chemicals Introduction Scheme (AICIS, formerly known as The National Industrial Chemicals Notification and Assessment Scheme (NICNAS)) New Chemicals Program

### Current scheduling

1,4-Benzenediamine, 2-(methoxymethyl)- is currently covered by the following group entry for phenylenediamines in Schedule 6.

#### Schedule 6

PHENYLENEDIAMINES including alkylated, arylated and nitro derivatives not elsewhere specified in these Schedules:

- a) in preparations packed and labelled for photographic purposes;
- b) in preparations packed and labelled for testing water except tablets containing 10 mg or less of diethyl- para-phenylenediamine or dimethyl-para-phenylenediamine in opaque strip packaging provided the directions for use include the statement, "Do not discard testing solutions into the pool";
- c) in hair dye preparations except when the immediate container and primary pack are labelled with the following statements:

KEEP OUT OF REACH OF CHILDREN, and

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

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

- d) in eyelash and eyebrow tinting products when the immediate container and primary pack are labelled with the following statement:

WARNING – This product contains ingredients which may cause skin irritation to certain individuals, and when used for eyelash and eyebrow tinting may cause injury to the eye. A preliminary test according to the accompanying directions should be made before use.

written in letters not less than 1.5 mm in height.

## Proposed scheduling

### Schedule 6 – New Entry

1,4-BENZENEDIAMINE, 2-(METHOXYMETHYL)- in oxidative hair dyes at up to 1.8 per cent on head concentration, **except** when the immediate container and primary pack are labelled with the following statements:

KEEP OUT OF REACH OF CHILDREN, and

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

written in letters not less than 1.5 mm in height;

### Schedule 10 – New Entry

1,4-BENZENEDIAMINE, 2-(METHOXYMETHYL)- **except** when included in Schedule 6.

### Index – New Entry

1,4-BENZENEDIAMINE, 2-(METHOXYMETHYL)-

Schedule 10

Schedule 6

## Key uses / expected use

Cosmetic (hair dye)

## Application summary - reasons for proposal

- The proposal would bring the Poisons Standard listing for this substance in hair dyes into line with the corresponding AICIS certificate, including institution of an upper content limit.
- The chemical is used as an oxidative hair dye in Australia at on head concentrations up to 1.8% under a chemical certificate previously issued by NICNAS.
- The chemical has an acute dermal LD50 of 400 mg/kg bw in rats safety data sheet (SDS).
- It has acute inhalation LC50 of 1300 mg/m<sup>3</sup>/4-h exposure in rats (SDS).
- The chemical is a skin sensitiser (estimated EC3 = 4.3%).
- The sulfate salt of the chemical has an acute oral LD50 of 150-200 mg/kg bw in rats.
- According to the SCCS opinion (2013) (Attachment B) 1,4-benzenediamine, 2-(methoxymethyl)- is considered to be safe when used up to 1.8% on head concentration in oxidative hair dyes, apart from its sensitising potential.

## Australian regulations

- 1,4-Benzenediamine, (2-methoxymethyl)- is not listed on the [TGA Ingredient Database](#).<sup>80</sup>
- As of November 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>81</sup> that contain 1,4-Benzenediamine, (2-methoxymethyl)- as an active ingredient.
- 1,4-Benzenediamine, (2-methoxymethyl)- is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>82</sup> No.3 of 2020.
- 1,4-Benzenediamine, (2-methoxymethyl)- is not listed on the [TGA prescribing medicines in pregnancy database](#)<sup>83</sup>.
- There are no warning statements pertaining to 1,4-Benzenediamine, (2-methoxymethyl)- in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>84</sup>.
- As of November 2020, there were no reports of adverse events for products containing 1,4-Benzenediamine, (2-methoxymethyl)- as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)<sup>85</sup>.
- As of November 2020, there were no products containing 1,4-Benzenediamine, (2-methoxymethyl)- listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>86</sup>

## International regulations

- [According to the European Chemicals Agency](#)<sup>87</sup>, 1,4-Benzenediamine, 2-(methoxymethyl)- is a skin sensitizer. The substance is toxic if swallowed, is toxic in contact with skin, toxic to aquatic life with long lasting effects, causes serious eye irritation, is harmful if inhaled and may cause an allergic skin reaction.
- [The European Commission's database for information on cosmetic substances and ingredients](#)<sup>88</sup> (CosIng) includes a listing for 1,4-Benzenediamine, 2-(methoxymethyl)- as a "hair dye substance in oxidative hair dye products". The entry with regards to oxidative hair dye products includes wording of conditions of use and warnings:

To be printed on the label:

The mixing ratio.

"Hair colorants can cause severe allergic reactions.

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<sup>80</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>81</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>82</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB$%20Determination)

<sup>83</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>84</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

<sup>85</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>86</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>87</sup> European Chemicals Agency <https://echa.europa.eu/substance-information/-/substanceinfo/100.204.505>

<sup>88</sup> European Commission's CosIng [https://ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.details\\_v2&id=93725](https://ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.details_v2&id=93725)

Read and follow instructions.

This product is not intended for use on persons under the age of 16. Temporary “black henna” tattoos may increase your risk of allergy.

Do not colour your hair if:

- you have a rash on your face or sensitive, irritated and damaged scalp,
- you have ever experienced any reaction after colouring your hair,
- you have experienced a reaction to a temporary “black henna” tattoo in the past.”

The entry also specifies that after mixing under oxidative conditions the maximum concentration applied to hair or eyelashes must not exceed 1.8% (calculated as free base).

- 1,4-Benzenediamine, 2-(methoxymethyl)- is not listed on the [New Zealand Inventory of Chemicals \(NZIoC\)](#)<sup>89</sup>.

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<sup>89</sup> New Zealand Inventory of Chemicals <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/>



## 3 Proposed amendments referred for scheduling advice to the Joint ACMS-ACCS #27

### 3.1 Kambo

#### Proposal

Delegate-initiated discussion regarding the scheduling of kambo to mitigate its possible impact on public health, including toxicity and potential for abuse.

#### CAS Number:

N/A

#### Alternative names

Sapo ('frog' in Portuguese), dried secretion of the South American Giant Leaf Frog or Giant Monkey Frog (*Phyllomedusa bicolor*)

#### Applicant

Delegate-initiated

#### Current scheduling

Kambo is not specifically scheduled on the current Poisons Standard.

#### Proposed scheduling

This proposal has been initiated for committee discussion at the request of the Delegate. Advice from an external evaluator suggests a new entry in Schedule 9 referring to 'secretions of Phyllomedusa frog species'.

##### Schedule 9 - New Entry

Secretion of the South American Giant Leaf Frog or Giant Monkey Frog (*Phyllomedusa bicolor*)

#### Key uses / expected use

Medicines (purgative)

#### Reasons for proposal

- Kambo is a preparation obtained from the dried secretion of the South American Giant Leaf Frog or Giant Monkey Frog (*Phyllomedusa bicolor*). It is used in traditional indigenous ceremonies in South America.
- Reports of adoption of the ritual and use of kambo in non-indigenous communities, including Australia, have been noted.
- Kambo is a complex mixture with multiple bioactive components which cannot be separated at the source, it is therefore proposed that this substance should be regulated as the secretion rather than the component substances.

- The use and effects of kambo have received sporadic media coverage over a number of years, with some concern raised over its effects and potential for abuse.
- Use of kambo typically forms part of a ritualistic ceremony, involving burning of the participant's skin followed by direct application of the substance to the burned regions.
- Kambo use in the absence of medically trained supervision represents a significant health risk, especially for people with cardiovascular disease due to the significant cardiovascular effects.
- Although rare, deaths have also been reported from kambo use.
- The significant adverse effects from the topical application of kambo to scarified or burnt areas of skin include:
  - nausea
  - vomiting
  - oesophageal rupture
  - diarrhoea
  - stomach pain
  - liver damage
  - burning sensation
  - lowered blood pressure (hypotension)
  - increased heart rate (tachycardia)
- These effects are seen as part of the spiritual purification/healing process, however, there is no clinical evidence of kambo having any beneficial medical effect.
- Onset of clinical signs and symptoms is rapid, and there have been reports of altered mental state, agitation, paranoia, delusions and general psychosis. There is insufficient information to characterise the risk from long-term repeated use of kambo.

## Australian regulations

- Kambo is not included as an ingredient on the [TGA Ingredient Database](#),<sup>90</sup> nor are any of its constituent peptides (e.g. dermorphin, deltorphin, caerulein).
- As of November 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>91</sup> that contain kambo as an active ingredient, nor any of its constituent peptides.
- Kambo is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>92</sup> No.3 of 2020.

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<sup>90</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>91</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>92</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB$%20Determination)

- The [TGA prescribing medicines in pregnancy database](#)<sup>93</sup> does not include kambo as a substance.
- There are no warning statements pertaining to kambo in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>94</sup>.
- As of November 2020, there were no reports of adverse events for products containing kambo, nor any of its constituent peptides, as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)<sup>95</sup>.
- As of November 2020, there were no products containing kambo listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>96</sup>

### International regulations

- Kambo is not regulated by the [Food and Drug Administration](#) in the United States, [Health Canada](#), [Medsafe](#) in New Zealand or the [Health Products Regulatory Authority](#) in Ireland.
- Neither the [United States Environmental Protection Agency](#) nor the [European Chemicals Agency](#) list kambo on any of their publicly available databases.

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<sup>93</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>94</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

<sup>95</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>96</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

## 3.2 Lidocaine

### Proposal

Amendment of the existing Schedule 5 entry for lidocaine to include injections for veterinary use under special circumstances.

### CAS Number:

137-58-6

### Alternative names

2-(Diethylamino)-*N*-(2,6-dimethylphenyl)acetamide, 2-diethylamino-2',6'-acetoxylidide;  $\omega$ -diethylamino-2,6-dimethylacetanilide; lignocaine

### Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

### Current scheduling

Lidocaine is currently listed in Schedules 2, 4 and 5 of the Poisons Standard as follows:

#### Schedule 4

LIDOCAINE **except:**

- a) when included in Schedules 2 or 5;
- b) in dermal preparations containing 2 per cent or less of total local anaesthetic substances per dosage unit; or
- c) in lozenges containing 30 mg or less of total anaesthetic substances per dosage unit.

#### Schedule 2

LIDOCAINE in preparations for topical use other than eye drops:

- a) containing 10 per cent or less of total local anaesthetic substances, except:
  - i) in dermal preparations containing 2 per cent or less of total local anaesthetic substances; or
  - ii) in aqueous sprays for oromucosal use containing 0.6 per cent or less of total local anaesthetic substances; or
- b) in divided preparations containing 200 mg or less of total local anaesthetic substances, except in lozenges containing 30 mg or less of total local anaesthetic substances per dosage unit.

#### Schedule 5

LIDOCAINE 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.

## Proposed scheduling

### Schedule 4

LIDOCAINE **except:**

- a) when included in Schedules 2 or 5;
- b) in dermal preparations containing 2 per cent or less of total local anaesthetic substances per dosage unit; or
- c) in lozenges containing 30 mg or less of total anaesthetic substances per dosage unit.

### Schedule 2

LIDOCAINE in preparations for topical use other than eye drops:

- a) containing 10 per cent or less of total local anaesthetic substances, except:
  - i) in dermal preparations containing 2 per cent or less of total local anaesthetic substances; or
  - ii) in aqueous sprays for oromucosal use containing 0.6 per cent or less of total local anaesthetic substances; or
- b) in divided preparations containing 200 mg or less of total local anaesthetic substances, except in lozenges containing 30 mg or less of total local anaesthetic substances per dosage unit.

### 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;  
or
- b) in injectable preparations containing 2 percent or less of lidocaine when packaged in a bottle with a tamper proof cartridge for use in conjunction with a rubber ring applicator for tail docking and castration of lambs; or castration of calves.

## Key uses / expected use

Veterinary (local anaesthetic)

## Application summary - reasons for proposal

- This amendment relates to a new presentation for lidocaine, registered for the use in sheep and cattle as an injectable local anaesthetic (2% lidocaine), specifically for lambs and calves for pain management following tail docking and castration. The proposal includes use of a specialised applicator in conjunction with a rubber ring.
- The previously considered toxicity of lidocaine and the formulation remains unchanged from that associated with the registration of the product currently included in Schedule 4, and the exposure of human handlers to the active constituent is expected to be no greater than currently approved uses.

- Numerous products containing lidocaine are available in Australia for both human and veterinary use for administration through both topical and parental routes. Some of these products are exempt from Scheduling based on presentation and/or concentration.
- The intention is that providing the injectable lidocaine in Schedule 5 will contribute to improved animal welfare following procedures known to be painful, through allowing general access to the substance in a similar manner to the devices used for the procedures. The relevant [Australian Animal Welfare Standards and Guidelines](#) cover these procedures, and veterinary attendance is not required.
- Ready access of the Schedule 5 product through livestock stores would increase the likelihood of anaesthetic agents being used and the associated benefits.

## Australian regulations

- According to the [TGA Ingredient Database](#),<sup>97</sup> lidocaine is:
  - Available for use as an active ingredient in biologicals, export only, over the counter and prescription medicines, as anhydrous, hydrochloride and hydrochloride monohydrate;
  - Available for use as an excipient in biologicals, devices and prescription medicines, as anhydrous, hydrochloride and hydrochloride monohydrate;
  - Available as an equivalent ingredient as anhydrous or hydrochloride.
- As of November 2020, there were 192 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>98</sup> that contain lidocaine as an active ingredient. These include 53 prescription and 82 non-prescription medicines, 36 devices, and 21 products for export only. Formulations include injections in 0.5%, 1% and 2% strengths (with and without adrenaline), gels in 2%, 2.5% and 5% strengths, ointments in 5% and 10% strengths, creams in 4% and 5% strengths, lotions, oral liquids, jellies, paints, sprays/aerosols, pellets, dermal patches, eye drops and lozenges.
- Lidocaine is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>99</sup> No.3 of 2020.
- The [TGA prescribing medicines in pregnancy database](#)<sup>100</sup> classifies lidocaine as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Lidocaine	A	Cardiovascular System	Antiarrhythmics	
Lidocaine	A	Drugs Used in Anaesthesia	Local anaesthetics	

<sup>97</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>98</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>99</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB%20Determination)

<sup>100</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Lignocaine (lidocaine)	A	Cardiovascular System	Antiarrhythmics	
Lignocaine (lidocaine)	A	Drugs Used in Anaesthesia	Local anaesthetics	
Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.				

- The [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>101</sup> requires the following warning statements pertaining to lidocaine to be included on the labelling:

Substance	Conditions	Required Statement(s)
Lidocaine (lignocaine) (Entry 1 of 3)	In dermal preparations containing MORE THAN 2 per cent of total local anaesthetic substances	Do not apply to large areas of the body, except on the advice of a healthcare practitioner.  If skin irritation occurs, discontinue use and seek advice from your doctor or pharmacist.
Lidocaine (lignocaine) (Entry 2 of 3)	In dermal preparations containing 2 per cent OR LESS of total local anaesthetic substances	If skin irritation occurs, discontinue use and seek advice from your doctor or pharmacist.
Lidocaine (lignocaine) (Entry 3 of 3)	In lozenges	Do not take hot food or drink if the mouth feels numb after taking this product as it may burn the mouth.  Do not give to children under 6 years of age, unless recommended by a doctor, pharmacist or dentist.

- Since January 2010, there have been 261 reports of adverse events for products containing lidocaine as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),<sup>102</sup> with 144 reports where lidocaine was the single suspected medicine.
- As of November 2020, there were no products containing lidocaine listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>103</sup>

<sup>101</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019  
<https://www.legislation.gov.au/Details/F2019L00213>

<sup>102</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>103</sup> Public Chemical Registration Information System Search (PubCRIS)  
<https://portal.apvma.gov.au/pubcris>

## International regulations

- According to the [United States Food and Drug Administration Approved Drug Products Database](#)<sup>104</sup>, lidocaine is approved for use as a prescription medicine in the United States.
- [Lidocaine is approved as an over the counter and prescription medicine in Canada according to the Canadian \(Health Canada\) Drug Product Database](#)<sup>105</sup>.
- The [Health Products Regulatory Authority of Ireland](#)<sup>106</sup> lists lidocaine as a prescription only medicine in most formulations, although some preparations (e.g. creams of not more than 5% lidocaine) are available over the counter.
- According to the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)<sup>107</sup>, lidocaine (as lignocaine) is regulated as follows:

Ingredient	Conditions	Classification
Lignocaine	for injection <b>except</b> when used as a local anaesthetic in practice by a nurse whose scope of practice permits the performance of general nursing functions or by a podiatrist registered with the Podiatry Board or by a dental therapist or oral health therapist registered with the Dental Council; for ophthalmic use <b>except</b> when used in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board; for oral use <b>except</b> in throat lozenges in medicines containing 30 milligrams or less per dose form; for external use in medicines containing more than 10%; <b>except</b> in throat sprays in medicines containing 2% or less; <b>except</b> when specified elsewhere in this schedule	Prescription
Lignocaine	for urethral use; for external use in medicines containing 10% or less and more than 2%	Pharmacy Only
Lignocaine	in throat lozenges in medicines containing 30 milligrams or less per dose form; for external use in medicines containing 2% or less; in throat sprays in medicines containing 2% or less	General Sale

<sup>104</sup> Food and Drug Administration Approved Drugs Database:  
<https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>105</sup> Health Canada Drug Product Database: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

<sup>106</sup> Health Products Regulatory Authority <https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?page=1&field=ACTIVESUBSTANCES&query=Lidocaine>

<sup>107</sup> Medsafe Medicine Classification Database: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>



### 3.3 Nitrous oxide

#### Proposal

A new Schedule 10 entry for nitrous oxide when not included in Schedule 4 for therapeutic use.

#### CAS Number:

10024-97-2

#### Alternative names

Nitrogen oxide; dinitrogen monoxide; laughing gas; hyponitrous acid anhydride; factitious air

#### Applicant

Private applicant

#### Current scheduling

Nitrous oxide is currently in Schedule 4 of the Poisons Standard as follows:

##### Schedule 4

NITROUS OXIDE for human therapeutic use.

#### Proposed scheduling

An application has been made to create a new Schedule 10 entry for nitrous oxide for non-therapeutic purposes.

##### Schedule 10 – New Entry

##### NITROUS OXIDE **except:**

- a) when included in Schedule 4; or
- b) supplied in containers greater than 50 cm<sup>3</sup>; or
- c) supplied in a gaseous preparation alone in 10g or greater quantity.

##### Schedule 4

NITROUS OXIDE for human therapeutic use

##### Index – Amend Entry

NITROUS OXIDE

##### Schedule 10

Schedule 4

#### Key uses / expected use

Medicines (inhalant anaesthetic), industrial use

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## Application summary - reasons for proposal

- Nitrous oxide is a non-flammable gas that is used as an anaesthetic during surgery and dentistry, but also has non-therapeutic applications in food and engineering. Small canisters are used as a propellant for the purposes of preparing whipped cream, and are legally available for purchase in person or online. Nitrous oxide has superior properties for this purpose compared to other substances.
- The availability and anaesthetic properties of nitrous oxide lend it to notable misuse, with heavy users capable of consuming the contents of hundreds of canisters per session.
- Nitrous oxide deactivates vitamin B12. Chronic repeated use can cause neurogenic symptoms of B12 deficiency, including peripheral neuropathy, spinal cord degeneration, dizziness, dissociation, loss of balance, impaired memory and cognition, and lower limb weakness. Prolonged exposure can lead to permanent disability, and the risk of asphyxiation has resulted in fatalities associated with nitrous oxide abuse.
- [The National Drug and Alcohol Research Centre](#) perform an annual survey of regular psychostimulant users. The proportion of respondents that reported nitrous oxide misuse increased from 23% in 2014 to 53% in 2019.
- International restrictions
  - Possession of nitrous oxide in the United States is legal under federal law, however prosecution is possible under the [Food Drug and Cosmetics Act](#) for sale or distribution for human consumption. Some individual states regulate the sale and possession of nitrous oxide.

## Australian regulations

- According to the [TGA Ingredient Database](#),<sup>108</sup> nitrous oxide is:
  - Available for use as an active ingredient in biologicals, export only and prescription medicines.
  - Available for use as an excipient in biologicals, devices, prescription medicines.
- As of November 2020, there were seven medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>109</sup> that contain nitrous oxide as an active ingredient. These include seven prescription medicines (gas for medicinal use).
- Nitrous oxide is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>110</sup> No.3 of 2020.

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<sup>108</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>109</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>110</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB$%20Determination)

- The [TGA prescribing medicines in pregnancy database](#)<sup>111</sup> classifies nitrous oxide as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Nitrous oxide	A	Drugs Used in Anaesthesia	General anaesthetics	
Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.				

- There are no warning statements pertaining to nitrous oxide in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>112</sup>.
- Since January 2010, there have been 29 reports of adverse events for products containing nitrous oxide as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)<sup>113</sup> with 14 reports where nitrous oxide was the single suspected medicine. There were five reports of deaths associated with nitrous oxide use (these reports of death may or may not have been the result of taking the medicine).
- As of November 2020, there were no products containing nitrous oxide listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)<sup>114</sup>.

## International regulations

- According to the [Food and Drugs Administration Approved Drugs Database](#)<sup>115</sup>, nitrous oxide is a prescription medicine.
- The [Health Canada Drug Product Database](#)<sup>116</sup> lists nitrous oxide as an ethical medicine, i.e. an unscheduled non-prescription product for professional use.
- According to the [Medsafe Medicines Classification Database](#)<sup>117</sup>, nitrous oxide is regulated as a prescription medicine when supplied for inhalation.

The [Health Products Regulatory Authority](#)<sup>118</sup> of Ireland regulates nitrous oxide as a prescription only medicine.

<sup>111</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>112</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

<sup>113</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>114</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>115</sup> Food and Drugs Administration Approved Drugs Database <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>

<sup>116</sup> Health Canada Drug Product Database <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

<sup>117</sup> Medsafe Medicines Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

<sup>118</sup> Health Products Regulatory Authority <https://www.hpra.ie/homepage/medicines>

## 3.4 Hemp seed oil

### Proposal

Amendment of the existing Schedule 9 entries for CANNABIS and TETRAHYDROCANNABINOLS to exclude hemp seed oil for oral consumption from scheduling when compliant with the Food and Standards Code.

### CAS Number:

N/A

### Alternative names

N/A

### Applicant

Private applicant

### Current scheduling

Hemp seed oil is currently included in the following Schedule 9 entries of the Poisons Standard (with exceptions):

#### Schedule 9

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 mg/kg or less of 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.

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 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.

## Proposed scheduling

### 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 mg/kg or less of 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.; **or**
- d) **when in hemp seed oil preparations extracted from the seed of low THC *Cannabis sativa* for oral use containing levels of cannabinoids permitted for oral consumption as a food for sale or an ingredient in a food for sale by the Australia New Zealand Food Standards Code (as amended from time to time).**

### 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 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.; **or**
- d) **when in hemp seed oil preparations extracted from the seed of low THC *Cannabis sativa* for oral use containing levels of cannabinoids permitted for oral consumption as a food for sale or an ingredient in a food for sale by the Australia New Zealand Food Standards Code (as amended from time to time).**

## Key uses / expected use

Food

## Application summary - reasons for proposal

- The Poisons Standard defines hemp seed oil (HSO) as being “obtained by cold expression from the ripened fruits (seeds) of *Cannabis sativa*”. Unlike other parts of the *Cannabis sativa* plant, hemp seeds do not naturally contain cannabinoids such as cannabidiol (CBD) or tetrahydrocannabinol (THC), though trace amounts may be present due to cross-contamination of the seed hull with cannabinoid-containing resins in bracts and leaves during maturation, harvesting and processing.

- Whilst being naturally low in CBD and THC, HSO is considered to be of particular importance and nutritional value due to its balance of omega-3 and omega-6 fatty acids.
- [The Office of Drug Control](#) allows importation of HSO without a licence or permit under the Prohibited Import Regulations, provided that the substance meets specified content criteria.
- The oral consumption of hemp seed foods, including hemp seed oil, was endorsed by [Food Standards Australia New Zealand \(FSANZ\)](#) in 2017 as being safe for human consumption.
- Removal of HSO from the Poisons Standard would enable consideration for inclusion as a therapeutic good, however such use would still be subject to additional regulatory requirements and approvals.

## Australian regulations

- The [TGA Ingredient Database](#)<sup>119</sup> [does not include](#) hemp seed oil.
- As of November 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)<sup>120</sup> that contain hemp seed oil as an active ingredient.
- Hemp seed oil is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)<sup>121</sup> No.3 of 2020.
- The [TGA prescribing medicines in pregnancy database](#)<sup>122</sup> does not include an entry for hemp seed oil.
- There are no warning statements pertaining to hemp seed oil in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)<sup>123</sup>.
- As of November 2020, there were no reports of adverse events for products containing hemp seed oil as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#).<sup>124</sup>
- As of November 2020, there were no products containing hemp seed oil listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).<sup>125</sup>
- Hemp seed oil is permitted for import without permission by the [Office for Drug Control](#)<sup>126</sup> provided the total cannabidiol (CBD) content is not more than 0.0075% by weight, and the total tetrahydrocannabinol (THC) content is not more than 0.005% by weight.

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<sup>119</sup> TGA Ingredient Database <https://www.ebs.tga.gov.au/>

<sup>120</sup> ARTG database <https://www.tga.gov.au/artg>

<sup>121</sup> Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20Ingredients$RB%20Determination)

<sup>122</sup> TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

<sup>123</sup> Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

<sup>124</sup> Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

<sup>125</sup> Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

<sup>126</sup> ODC page on hemp seed product regulation <https://www.odc.gov.au/hemp-products>

## International regulations

- There is no entry for hemp seed oil on the [Food and Drug Administration Approved Drugs Database](#)<sup>127</sup>, the [Health Canada Drug Product Database](#)<sup>128</sup>, or the [Medsafe Medicines Classification Database](#)<sup>129</sup>.
- The [Australia New Zealand Food Standards Code](#) was amended in 2017 to permit low-tetrahydrocannabinol hemp seed to be a food.
- [Hemp seed oil is permitted to be marketed in Canada](#)<sup>130</sup> as a food, cosmetic and health product, provided it does not contain more than 10 parts per million of tetrahydrocannabinol.
- [In 2018, the Food and Drug Administration evaluated hemp seed oil](#)<sup>131</sup> as “generally regarded as safe” (GRAS) for use as an ingredient in food.

## 4 How to respond

Submissions must be provided by the closing date of **27 January 2021** through our [consultation hub](#). Any submission about any of the proposals to amend the Poisons Standard will be considered at the next meeting of the [Advisory Committee on Medicines Scheduling \(ACMS\)](#), meeting of the [Advisory Committee on Chemicals Scheduling \(ACCS\)](#), or a joint meeting of these two committees.

## 5 What will happen

All public submissions will be published on the TGA website at [Public submissions on scheduling matters](#), unless marked confidential or indicated otherwise in the submission coversheet (see [Privacy information](#)).

Following consideration of public submissions received before the closing date and advice from the expert advisory committee/s, decisions on the proposed amendments will be published as interim decisions on the TGA website: [Scheduling delegate's interim decisions & invitations for further comment](#) on **3 June 2021**.

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<sup>127</sup> Food and Drugs Administration Approved Drugs Database  
<https://www.accessdata.fda.gov/scripts/cder/daf/>

<sup>128</sup> Health Canada Drug Product Database <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

<sup>129</sup> Medsafe Medicines Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

<sup>130</sup> Health Canada statement regarding CBD and hemp seed oil <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/about/cannabidiol.html#a9>

<sup>131</sup> FDA evaluation of hemp seed oil as a food ingredient <https://www.fda.gov/food/cfsan-constituent-updates/fda-responds-three-gras-notice-hemp-seed-derived-ingredients-use-human-food>