Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

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

21 October 2022

TGA Health Safety Regulation

Confidentiality
All submissions received will be placed on the TGA's Internet site, unless marked confidential. Any confidential material contained within your submission should be provided under a separate cover and clearly marked "IN CONFIDENCE". Reasons for a claim to confidentiality must be included in the space provided on the TGA submission form. For submission made by individuals, all personal details, other than your name, will be removed from your submission before it is published on the TGA's Internet site. In addition, a list of parties making submissions will be published. If you do not wish to be identified with your submission you must specifically request this in the space provided on the submission form.

Contents

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

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

- the interim decisions made by a delegate[1] of the Secretary of the Department of Health and Aged Care (the **Delegate**) under regulation 42ZCZN in relation to proposed amendments to the current Poisons Standard which were referred to an expert advisory committee[2] under subdivision 3D.2 of the Regulations in June 2022;
- the proposed date of effect of the proposed amendments (in circumstances where the interim decision proposes an amendment to the current Poisons Standard).

In accordance with regulation 42ZCZP, interested persons (including the applicant requesting the amendment) are invited to make submissions to the Secretary in relation to these interim decisions on or before **24 November 2022**.

Please note that there are two consultations hubs relating to this notice:

- Submissions relating to the decisions regarding **psilocybine and/or MDMA** should be provided through the consultation hub for psilocybine and MDMA; and
- Submissions relating to **any other substance in the notice** should be provided through the second consultation hub.

Submissions will be considered by the Delegate in making the final decision.

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

[1] For the purposes of s 52D of the *Therapeutic Goods Act 1989* (Cth).
[2] Established under sections 52B and 52C of the *Therapeutic Goods Act 1989* (Cth).

2. Interim decisions on proposed amendments referred to the Advisory Committee on Medicines Scheduling (ACMS #38, June 2022)

2.1 Interim decision in relation to cetirizine

Proposal

The applicant proposed an amendment to the current Schedule 2 entry for cetirizine to lower the maximum age of patients for whom the substance is indicated, from 12 years and over to 6 years and over, when not scheduled in the Poisons Standard (the **Proposal**). The amended entry would allow access to certain oral preparations of cetirizine for the treatment of seasonal allergic rhinitis from outlets such as supermarkets for individuals aged 6 years and over.

Interim decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (Cth) (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made an interim decision to amend the current Poisons Standard substantially in line with the Proposal as follows:

Schedule 4 – Amend entry

CETIRIZINE **except:**

a) when included in Schedule 2; or

b) in divided preparations for oral use for the treatment of seasonal allergic rhinitis in adults and children ~~12~~6 years of age and over when:

i) in a primary pack containing not more than 10 days' supply; and

ii) labelled with a recommended daily dose not exceeding 10 mg of cetirizine.

Schedule 2 – Amend entry

CETIRIZINE in preparations for oral use except in divided preparations for the treatment of seasonal allergic rhinitis in adults and children ~~12~~6 years of age and over when:

a) in a primary pack containing not more than 10 days' supply; and

b) labelled with a recommended daily dose not exceeding 10 mg of cetirizine.

Materials considered

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

- The application to amend the current Poisons Standard with respect to cetirizine (the **Application**);

[3] For the purposes of s 52D of the *Therapeutic Goods Act 1989* (Cth).

- The 3,148 public submissions,[4] including 6 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 38th Meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989* (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The Scheduling Policy Framework 2018 (the **SPF**); and
- The Scheduling handbook: Guidance for amending the Poisons Standard

Summary of Committee advice to the Delegate

The Committee recommended that the scheduling for cetirizine be amended in Schedules 2 and 4 in the Poisons Standard as follows:

Schedule 4 – Amend entry

CETIRIZINE **except:**

a) when included in Schedule 2; or

b) in divided preparations for oral use for the treatment of seasonal allergic rhinitis in adults and children ~~12~~6 years of age and over when:

i) in a primary pack containing not more than 10 days' supply; and

ii) labelled with a recommended daily dose not exceeding 10 mg of cetirizine.

Schedule 2 – Amend entry

CETIRIZINE in preparations for oral use except in divided preparations for the treatment of seasonal allergic rhinitis in adults and children ~~12~~6 years of age and over when:

a) in a primary pack containing not more than 10 days' supply; and

b) labelled with a recommended daily dose not exceeding 10 mg of cetirizine.

The Committee also recommended an implementation date of **1 February 2023**.

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

The reasons for the advice included:

[4] Through the consultation portal, interested parties were given the choice to select from options to indicate their support or opposition to the proposed amendment without providing a written component. These options appeared alongside options for the scheduling proposals for MDMA and psilocybine that were also being considered at the June 2022 meetings of the ACMS and ACCS. These proposals generated significant public interest and campaigning for members of the public to make a submission in support of those proposals. As a result, an unusually high number of responses were received in the portal for all substances on which submissions were sought prior to these meetings.

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

Risks

- Very low risk of overuse

Benefits

- Cetirizine is an effective first line treatment for the symptoms of seasonal allergic rhinitis (SAR) in children and adults. Effectiveness is established in the age group that is subject of the proposal.
- Safety profile is good – somnolence is the most common adverse event. Side effects can be recognised and managed by parents, with appropriate labelling.
- The symptoms of seasonal allergic rhinitis are common and easily identified by consumers. Treatment with cetirizine can be safely managed by consumers without the need for healthcare professional intervention.

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

- Treatment of SAR, particularly for children aged 6-12 years.
- The current indication for use will remain unchanged, but extent of use will increase with increased availability to consumers.
- Aligns scheduling with similar antihistamines such as loratadine and fexofenadine.

c) the toxicity of a substance:

- Toxicity and safety of cetirizine is well characterized. Considered acceptable for Schedule 2 use in children under 12 years. Children over 6 years of age show peak plasma levels and times to peak similar to adults, with slightly more rapid elimination supporting up to twice daily dosing.
- Over 20 years' experience in Australia as an OTC medicine. More recently, over 8 years' experience as a medicine available by general sale when limited to 5 days' supply, and more than 4 years' experience when limited to 10 days' supply, for use in SAR for adults and children 12 years and over. No medically confirmed safety issues reported and no known interactions.
- Certain preparations of cetirizine were unscheduled (removal from Schedule 2) in October 2012 on the basis of a well-established safety profile

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

- Divided preparations for the treatment of seasonal allergic rhinitis in adults and children 6 years of age and over.
- The product will be a chewable tablet presented in child resistant packaging. Proposal is 5 mg every 12 hours as needed
- The labelling is currently under evaluation by the TGA. All mandatory warning statements required by the TGA will be included and are expected to be the same as those applied to similar existing products.
- The current Schedule 2 product for this age group is a scored 10 mg tablet that must be divided by the responsible adult.

e) the potential for abuse of a substance:

- The use of the medicine is very unlikely to produce dependency. No evidence to suggest abuse potential.

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

I have made an interim decision to amend the current Poisons Standard in relation to cetirizine. The detailed reasons for my decision follow.

I agree with the Committee's findings on the relevant provisions of section 52E of the Act.

The Proposal would allow divided preparations of cetirizine for oral use to be made available for general sale when indicated for children aged 6 and up, in a primary pack containing not more than 10 days' supply and with a recommended daily dose not exceeding 10 mg of cetirizine. I note that this Application coincides with an application to the TGA for registration of a new 5 mg cetirizine chewable tablet product.

In considering paragraph 52E(1)(b) of the Act, I am of the view that the symptoms of SAR are easily recognised and able to be treated by the consumer without the requirement for medical intervention. This aspect of the medicine extends to the 6-11 years age group that is the subject of the Proposal.

With regards to paragraph 52E(1)(c) of the Act, I agree with the Committee that cetirizine has a well-established history of safe use, with the main side effect of concern being the sedating properties of the substance. However, I note that the incidence of somnolence associated with cetirizine use has been shown to be lower in children (1.8%, compared to 1.4% placebo) than other age groups.

Turning to paragraph 52E(1)(d) of the Act, I agree with the Committee that the proposed pack size limit of 10 days' supply is appropriate for a medicine available by general sale with these properties and intended use. The proposed limit on supply is consistent with those already in place for other age groups as well as other medicines in the same class as cetirizine, such as loratadine and fexofenadine. These medicines are already available by general sale when presented in a manner similar to that specified in the Proposal (10 days' supply for ages 6+).

In considering paragraph 52E(1)(e) of the Act, I note that overuse of the medicine is unlikely to be an issue, as there are several alternative treatments for SAR that are readily available. Any consumer finding that cetirizine is an ineffective treatment is likely to discontinue use of the medicine and/or seek medical advice. I also note that there are no significant health risks associated with long-term use of the medicine, which is pertinent to paragraph 52E(1)(a) of the Act.

In view of paragraph 52E(1)(a) of the Act, I agree with the Committee that allowing the general sale of cetirizine for the 6-11 year age group would enhance health outcomes by facilitating access outside of normal pharmacy trading hours. This would allow timely treatment of symptoms via retailers with extended trading hours such as supermarkets, while also easing the burden on parents or guardians who may wish to purchase regular use medicines with other household needs.

I have considered the points raised in the 6 written submissions received in response to the Proposal, which expressed mixed opinions. I am of the view that the concerns regarding the new dosage form do not form a barrier to re-scheduling as these concerns will be assessed during the regulator's usual evaluation processes for the registration of a medicine on the Australian Register of Therapeutic Goods (ARTG), as previously outlined in the points relating to paragraph 52E(1)(d).

These submissions also raised the point of the similar treatments already available for general sale, such as loratadine and fexofenadine, which are less-sedating than cetirizine and already provide the consumer with adequate choices for treatment of SAR. Having already addressed the

issue of the sedation properties of the substance in the age group specified in the Proposal, I acknowledge these concerns but still consider the alignment of the scheduling of cetirizine with other antihistamines to be appropriate.

In summary, I have made my interim decision to amend the Poisons Standard because the benefits outweigh the risks of the Proposal, including the toxicity and potential for abuse of cetirizine.

Proposed implementation date

1 February 2023

2.2 Interim decision in relation to budesonide

Proposal

The applicant proposed the creation of a Schedule 3 entry for inhaled budesonide in single ingredient inhaler devices for the maintenance of asthma in people aged 12 years and older where the maximum daily dose does not exceed 800 micrograms (the **Proposal**). Inhaled formulations of budesonide are currently available only with a prescription.

Interim decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (Cth) (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made an interim decision to not amend the current Poisons Standard in relation to budesonide.

Materials considered

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

- The application to amend the current Poisons Standard with respect to budesonide (the **Application**);
- The 2,831 public submissions,[4] including 9 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 38th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989* (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health.
- The Scheduling Policy Framework 2018 (the **SPF**); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Committee advice to the Delegate

The Committee recommended that the current Poisons Standard entry for budesonide remains appropriate.

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

The reasons for the advice included:

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

Risks

- The risks for over-use or inappropriate use with availability of multiple strengths as over-the-counter medicines are high and may lead to confusion and potential harm for patients.
- Risk of increased non-compliance for treatment as it could result in decreased health professional oversight. High risk of worsening of disease state for patients.
- Risk for increased inappropriate usage if there are more dosages made accessible.

Benefits

- Increased accessibility, especially for patients in rural and remote areas.
- Safety profile established over a long period of time.

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

- Treatment of bronchial asthma.
- Prevention of chronic respiratory condition exacerbations.
- Can be used in replacement or to reduce oral steroid therapy.

c) the toxicity of a substance:

- In category A for pregnancy.
- Can be excreted through breastmilk, however, it is at a low enough level for safe use when breastfeeding.
- Habitual use can cause hypercorticism and hypothalamic pituitary adrenal suppression, though unlikely with inhaled use.

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

- Dry powder inhaler available in 3 doses at 100mcg, 200mcg and 400 mcg each with ~200 doses.
- Dosing instructions would need to be very clear and would vary between packs and strengths to ensure that any maximum doses are not exceeded.

e) the potential for abuse of a substance:

- No evidence that budesonide has an abuse liability, evidence of inappropriate use for non-asthma indications already exists.

f) any other matters considered necessary to protect public health:

- The risks discussed outline the lack of clarity of the application rather than for the substance itself. There are other avenues to address continual supply in rural and remote areas.
- High risk of patient confusion between dosages and instructions compared to when substance is dispensed with a prescription.

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

I have made an interim decision to not amend the current Poisons Standard in relation to budesonide. The detailed reasons for my decision follow.

I agree with the Committee's findings on the relevant provisions of section 52E of the Act.

With reference to paragraph 52E(1)(a), I am of the view that the benefits of the Proposal do not outweigh the potential risks. Without the proper time and tools to assess a patient's symptoms and history, asthma can easily be misdiagnosed as it shares symptoms with several other respiratory conditions. In addition, the potential misdiagnosis of asthma in place of another respiratory condition such as croup, chronic obstructive pulmonary disease (COPD) or pneumonia increases the risk of a delay in seeking appropriate and timely medical assistance. I am concerned that self-managed treatment of asthma, which requires medical assessment and discussion of patient history, may lead to undesirable and potentially harmful patient outcomes.

I recognise that access to general practitioners has recently become a significant issue due to COVID-19 lockdowns, particular in rural and remote areas, which goes to the potential benefits of the Proposal for the purposes of paragraph 52E(1)(a). However, I agree with the Committee's view that amendment of the Poisons Standard is not in this instance an appropriate mechanism to address these concerns, as any changes to the scheduling of budesonide will affect all of Australia. The potential for adverse impacts of such changes on urban areas has not been quantified in the Application, and there are already other avenues to address accessibility issues to medicines for rural and remote areas. I note as well that access to general practitioners by telehealth is available.

Additionally, with reference to paragraph 52E(1)(a), I note that the assertion in the Application for increased access to inhaled corticosteroids to reduce over-use of short acting beta agonists (SABAs). I agree with the Committee's advice in reference to paragraph 52E(1)(f) that increasing the range of doses with minimal intervention from a health professional could cause confusion for patients, leading to a reduced quality of asthma management. I am of the view that there is significant potential for the substance to be misused or overused if availability increases, and likely to cause non-compliance with current treatment plans or worsening of disease-state should a patient be charged with the responsibility of their own treatment.

With reference to 52E(1)(b), I acknowledge budesonide's long-standing history of use in the treatment of bronchial asthma and established safety profile. As outlined above, I remain of the view that the oversight of medical professionals is essential in the diagnosis and ongoing treatment of the conditions which budesonide is used to treat and prevent.

In reference to paragraph 52E(1)(c), I acknowledge that adverse events associated with the use of corticosteroids, including adrenal insufficiency, fractures, and complications with pregnancies, are normally associated with systemic absorption and are less prevalent with inhaled preparations. While considered, this was not a significant factor in my decision regarding the Proposal and was outweighed by my concerns outlined above.

I have read and considered the Submissions, including those which expressed concerns regarding the impact of this proposal on the Quality Use of Medicines (QUM). The QUM is a national strategy which outlines the principles required to ensure medicines are prescribed appropriately in Australia. It is my view that the Proposal would contravene the QUM's approach to using medicines safely with respect to the use of budesonide. The addition of a Schedule 3

entry would also be inconsistent with international regulations, with the USA, Canada, Ireland and New Zealand all regulating inhalational budesonide products as prescription only medicines.

I have also noted the submissions from the Royal Australian College of General Practitioners, the Australian Medical Association, and Asthma Australia. All expressed their concerns in relation to the Proposal, citing the importance of appropriate diagnostic tools, monitoring of any disease progression and the ability to check patient history to properly diagnose asthma.

Having considered the need for medical practitioner oversight and the risks to consumers due to the lack of patient review and follow up, and the increased risk of inappropriate use, I have decided that the current scheduling of budesonide is appropriate.

2.3 Interim decisions in relation to psilocybine and MDMA

This section contains two independent interim decisions in respect to (i) psilocybine and (ii) MDMA (the **substances**). Given the current scheduling and the proposed amendments to the Poisons Standard in relation to the substances are identical, and their nature and intended uses provided by the proposed amendments are highly similar, the reasons for making the interim decision for each substance are substantially the same. As such, these reasons have been consolidated to assist the reader.

Proposals

Psilocybine

The applicant proposed the creation of a Schedule 8 entry for the use of psilocybine in combination with psychotherapy for treatment resistant mental illness in medically controlled environments in certain circumstances (the **current psilocybine proposal**). Psilocybine is currently included in Schedule 9, which limits its use to authorised research and analytical purposes only.

MDMA

The applicant has proposed the creation of a Schedule 8 entry for the use of MDMA in combination with psychotherapy for treatment resistant mental illness in medically controlled environments in certain circumstances (the **current MDMA proposal**). MDMA is currently included in Schedule 9, which limits use to authorised research and analytical purposes only.

Interim decisions

Pursuant to regulation 42ZCZN of the *Therapeutic Goods Regulations 1990* (Cth) (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made the following two interim decisions (the **present decisions**):

(i) to not amend the current Poisons Standard in relation to psilocybine.

(ii) to not amend the current Poisons Standard in relation to MDMA.

The Delegate's detailed reasons for the present decisions follow.

Materials considered

In making the present decisions, the Delegate considered the following material.

In relation to psilocybine:

- The application to amend the current Poisons Standard with respect to psilocybine (the **psilocybine application**);
- The 6,650 public submissions on the current psilocybine proposal, including 2,332 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **psilocybine submissions**);
- The advice concerning the Psilocybine Application received from the 38th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**); and
- The Delegate's final decision to not amend the Poisons Standard in relation to psilocybine on 15 December 2021 (the **previous psilocybine decision**) and the materials they considered in making those decisions.

In relation to MDMA:

- The application to amend the current Poisons Standard with respect to MDMA (the **MDMA application**);
- The 6,505 public submissions on the current MDMA proposal, including 2,068 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **MDMA submissions**);
- The advice concerning the MDMA Application received from the 38th meeting of the Committee; and
- The Delegate's final decision to not amend the Poisons Standard in relation to MDMA on 15 December 2021 (the **previous MDMA decision**) and the materials they considered in making that decision.

In relation to both Substances:

- The Independent expert panel report on *an evaluation of the therapeutic value, benefits and risks of methylenedioxymethamphetamine (MDMA) and psilocybin for the treatment of mental, behavioural or developmental disorders* (the **Expert Report**);
- The Royal Australian and New Zealand College of Psychiatrists' (RANZCP) clinical memorandum on the therapeutic use of psychedelic substances published in July 2022;
- The international regulatory status of the Substances and access pathways;
- Subsection 52E(1) of *the Therapeutic Goods Act 1989* (Cth) (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework for medicines and chemicals 2018 (the **SPF**); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Committee advice to the Delegate

The Committee individually considered the psilocybine application and the MDMA application and recommended that the current scheduling for each substance remains appropriate.

Members agreed that the matters under Section 52E(1) of the Act relevant to both substances are: (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is

to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health.

The Committee was of the view that there was insufficient additional evidence of the therapeutic value of either psilocybine or MDMA provided in the respective applications, compared to that considered in making the previous psilocybine or MDMA decisions, to now consider that the therapeutic value of either substance has been established. As such, the Committee considered that there was no basis on which to depart from its advice provided at its 36th meeting in November 2021 to not vary the scheduling of psilocybine and MDMA, and its reasons provided at that meeting are equally applicable to the present application.

Psilocybine

The reasons for the Committee's advice with respect to psilocybine included:

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

Risks:

- Can cause transient increase in blood pressure and tachycardia. Trials suggest some risk of suicidal ideation, although it is not clear at this stage if this is attributable to the treatment or illness. Some risk of psychosis in at-risk individuals.
- Extensive exclusion criteria for clinical trials limits generalisability to the wider population.

Benefits:

- The benefits include emerging evidence of efficacy in treating depression with demonstrated low risk of adverse events with short-term use in controlled settings.
- Possible, albeit less convincing, benefit in treating other mental health conditions.

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

- For use as an adjunct to psychotherapy (in psychedelic-assisted psychotherapy) for treatment-resistant depression.
- Clinical trials are underway for treatment of other conditions in similar settings.

c) the toxicity of a substance;

- based on animal studies, the lethal dose is extrapolated to 6 g in humans, equivalent to 300 times the typical therapeutic dosage.

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

- Trialled dosage includes 25 mg capsule (for patients up to 90 kg bw), 30 mg capsule (90 -115 kg) and 35 mg (>115 kg).
- Dosage forms are likely to be compounded by a pharmacist.
- It is unclear at this stage how the medication will be dispensed to a practitioner. No product for registration.

e) the potential for abuse of a substance;

- Low risk of addiction.

- Potential for diversion for recreation use. This is manageable in the clinical setting through Schedule 8 requirements, but concerns of diversion at other points throughout distribution still exist.

f) any other matters considered necessary to protect public health;

- Increased risk of use beyond the conditions for which there is clinical trial evidence of therapeutic benefit.
- Emerging evidence of therapeutic value, but not yet established as required by scheduling policy framework for Schedule 8.
- The risks and benefit of the substance not solely dependent on the substance but also on the skill of the therapist guiding patient through altered state of consciousness.
- Concerns with using down-scheduling as a mechanism to bypass the processes for clinical trials, by inserting specific requirements (to mirror a clinical trial environment) in the entry to allow it to fit a lower schedule.

MDMA

The reasons of the Committee with respect to MDMA included:

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

Risks:

- Acute effects include high blood pressure and pulse rate, faintness and panic attacks. In severe cases, MDMA can cause loss of consciousness and seizures.
- Secondary effects include involuntary jaw clenching, lack of appetite, depersonalisation, illogical or disorganised thoughts, restless legs, nausea, hot flashes or chills, headache, sweating and muscle/joint stiffness.
- Long-term use can result in sleep disturbances, difficulties with concentration, depression, heart disease, impulsivity and decreased cognitive function.

Benefits:

- There is limited but emerging evidence that MDMA-assisted psychotherapy may have therapeutic benefits in the treatment of PTSD in closely supervised clinical settings with intensive professional support. These benefits are currently under investigation in clinical trials.

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

- For use as an adjunct to psychotherapy (psychedelic-assisted psychotherapy) for post-traumatic stress disorder.
- MDMA-assisted psychotherapy sessions typically last 6 - 8 hours, relying on two trained specialists. The regime consists of 1 - 3 psychedelic-assisted therapy sessions, usually supplemented with 'integrative' therapy sessions where MDMA is not used.

c) the toxicity of a substance;

- The lethal dose is estimated at 10-20 mg/kg bw
- Due to the novel nature of the treatment, the adverse effects in the context of psychotherapy, outside of the acute effects, are largely unknown.

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

- Optimal dosages have not been established, especially outside of clinical trials for the treatment of PTSD.
- A typical dose in the context of psychotherapy ranges from 30-125 mg. This is often followed by an optional half-dose 1.5 to 2.5 hours into the session.

e) the potential for abuse of a substance;

- It is not clear whether MDMA causes dependence. However, it affects many of the same neurotransmitter systems in the brain that are targeted by drugs with an abuse and dependence liability, and some studies report symptoms of dependence in users.

f) any other matters considered necessary to protect public health;

- There remains significant doubt regarding the degree to which the psychedelic/psychotherapy interaction is dependent on the specific type of psychotherapy administered. This raises the question as to the stringency with which protocols need to be followed and the practicality for implementing these in clinical practice outside of the highly controlled clinical trial environment.
- There are currently no medicines containing MDMA proposed for inclusion or already included in the ARTG.
- There are significant benefits to waiting for the results of clinical trials. MDMA-assisted psychotherapy may prove to be safe and efficacious, but the evidence does not yet suggest this - especially for conditions outside of PTSD.
- It will take time to develop a curriculum and accredited training process for psychiatrists. To protect public health and prevent inappropriate use, MDMA should not be down-scheduled until all necessary safeguards have been established and implemented.
- A substantial evidence base will be required to inform a curriculum and accredited training process for psychiatrists. To protect public health and prevent inappropriate use, MDMA should not be down-scheduled until all necessary safeguards have been established and implemented.
- There is a high risk of diversion for misuse, even in conjunction with Schedule 8 controls.
- Scheduling is not an appropriate mechanism for establishing clinical governance of the therapeutic use of MDMA.

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

I have made the present decisions because I am of the view that retaining the current entries for these substances in Schedule 9 ensures appropriate control over their access. In reaching this view, I am satisfied that both psilocybine and MDMA meet the scheduling factors for Schedule 9 in the SPF, and the currently limited evidence of benefit for both substances is outweighed by the risks to patients and public health from any increased access. Insufficient new information or clinical evidence for either substance has been presented by the applicant since I made the previous psilocybine and MDMA decisions to depart from those decisions. The detailed reasons for my present decisions follow.

I agree with the Committee's findings on the relevant provisions of section 52E of the Act. Paragraph 52E(2)(a) provides that in exercising the power under subsection 52D(2), I must comply with the SPF.

The SPF sets out the factors to consider for Schedule 8, which are:

1. The substance is included in Schedule I or II of the *United Nations Single Convention on Narcotic Drugs 1961* or in Schedule II or III of the *United Nations Convention on Psychotropic Substances 1971*.

2. The substance has an established therapeutic value but its use, at established therapeutic dosage levels, is recognised to produce dependency and has a high propensity for misuse, abuse or illicit use. The substance has an established therapeutic value but by reason of its novelty or properties carries a substantially increased risk of producing dependence.

The factors to consider for Schedule 9 are:

1. The substance is included in either Schedule IV to the *United Nations Single Convention on Narcotic Drugs 1961* or in Schedule I of the *United Nations Convention on Psychotropic Substances 1971*.

2. The substance has no currently established therapeutic value and is likely to present a high risk of dependency, abuse, misuse or illicit use.

Pursuant to paragraph 52E(1)(a) and in view of the SPF, I note that my previous psilocybine and MDMA decisions turned in significant part on the lack of established therapeutic value of the substances, and by extension the uncertain benefit from their use in patients. I considered that these substances did not meet the Schedule 8 scheduling factors and the risks outweighed the benefits from down-scheduling them.

In this context, in relation to those completed studies that were before me in making my previous psilocybine and MDMA decisions, I am not persuaded by the applicant's arguments in the current psilocybine and MDMA applications that my concerns about the quality of these studies were unfounded. In this regard I have attached significant weight to the analysis and findings of the Expert Report.

I note evidence has been presented in the current psilocybine and MDMA applications that is additional to what was before me, including in the previous applications by the same applicant, when I made the previous psilocybine and MDMA decisions. Before turning to my consideration of this evidence, I acknowledge the applicant's arguments about the definition of 'established' therapeutic value. I agree with the applicant that therapeutic value of a substance may be 'established' for the purposes of the SPF, despite there being insufficient efficacy evidence to support the inclusion of a product containing that substance in the Australian Register of Therapeutic Goods (ARTG). However, I am of the view that for the therapeutic value to be 'established' the evidence must, contrary to the applicant's arguments, go beyond the mere existence of completed clinical trials and an apprehension of therapeutic value based on a small number of promising trial results.

Turning to the additional evidence, in relation to psilocybine, one phase II trial[5] has been completed that has not yet completed its final analysis of all data and endpoints nor been peer reviewed or published. I acknowledge that this study indicates significant improvement in outcomes for patients with treatment resistant depression who were administered a dosage of 25 mg, but not for 1 mg or 10 mg, of psilocybine. The details of an additional published study were also included in the psilocybine application, which was a 12-month follow up of 24 patients who were given two doses of psilocybine at 25 mg or 30 mg two weeks apart with assisted psychotherapy. The results showed that two doses of psilocybine for major depressive disorder produced large and stable antidepressant effects throughout a 12-month follow-up period in a select number of patients. Specifically, that there was a decrease in the depression score (GRID-

[5] Compass Ph2b clinical trial results: https://ir.compasspathways.com/static-files/0f9fbce8-2619-438b-a6ba-5bbe2ba08cf6

Hamilton Depression Rating Scale (GRID-HAMD)). Further high and stable rates of response and remission occurred throughout the follow-up period.[6]

While these studies represent increasing evidence of the long-term benefits of even small doses of psilocybine in conjunction with psychotherapy, I remain of the view and agree with the Committee that this is insufficient to consider that the therapeutic value of psilocybine is *established*. I share the Committee's concerns regarding: the broadness of the indication (treatment-resistant mental illness) included in the current psilocybine proposal, as this appears to be much broader than the indications for which there is emerging evidence (such as treatment-resistant depression); the lack of phase III trials; and the problems associated with the translation from a clinical trial setting to clinical practice. All of these concerns raise significant doubt about the established therapeutic value of psilocybine and the benefits likely to be realised were the current psilocybine proposal to be adopted.

In relation to MDMA, a phase III trial (MAPP1) referenced by the applicant in the MDMA application had previously been considered in the Expert Report. A second phase III study, MAPP2,[7] is listed as active (not recruiting) at the time of the MDMA application, with results anticipated in March 2023. The MAPP2 study protocol is not yet publicly available. As such, I am of the view that there is no new evidence in the MDMA application compared to that before the Committee and myself in connection with the previous MDMA decision to now consider that the therapeutic value of MDMA is established.

In considering paragraph 52E(1)(a) of the Act, I agree that there seems to be emerging evidence of the benefits of MDMA-assisted psychotherapy in the treatment of post-traumatic stress disorder (PTSD). However, I remain of the view that further research is required in this area. As I have stated above in relation to psilocybine, I have concerns regarding the broadness of the indication (treatment-resistant mental illness) included in the current MDMA proposal, the lack of the further phase III trial results, and the problems associated with the translation from a clinical trial setting to clinical practice.

In relation to each substance, I have considered the Royal Australian and New Zealand College of Psychiatrists (RANZCP) updated clinical memorandum released in July 2022,[8] which states that:

> *There is limited but emerging evidence that psychedelic therapies may have therapeutic benefits in the treatment of a range of mental illnesses.*

The RANZCP memorandum also states that:

> *Further research is required to assess the efficacy, safety, and effectiveness of psychedelic therapies to inform future potential use in psychiatric practice.*
>
> *Clinical use of psychedelic substances should only occur under research trial conditions that include oversight by an institutional research ethics committee and careful monitoring and reporting of efficacy and safety outcomes.*

A principal factor against down-scheduling each of these substances is therefore still that they do not meet the Schedule 8 factor in the SPF for established therapeutic value, the corollary of

[6] Natalie Gukasyan, Alan K Davis, Frederick S Barrett, Mary P Cosimano, Nathan D Sepeda, Matthew W Johnson, Roland R Griffiths, 2022 (sagepub.com), Efficacy and safety of psilocybin-assisted treatment for major depressive disorder: Prospective 12-month follow-up.

[7] MAPS Second Phase 3 Trial of MDMA-Assisted Therapy for PTS: https://maps.org/2022/05/09/maps-completes-enrollment-as-planned-for-the-confirmatory-phase-3-trial-of-mdma-assisted-therapy-for-ptsd/

[8] RANZCP Clinical Memorandum on the therapeutic use of psychedelic substances https://www.ranzcp.org/files/resources/college_statements/clinical_memoranda/cm-therapeutic-use-of-psychedelics.aspx

which is limited therapeutic benefit to patients (there being evidence only of potential therapeutic value) for the purposes of paragraph 52E(1)(a) of the Act.

I note that the current psilocybine and MDMA proposals incorporate, in the schedule entry and in Appendix D, a number of proposed controls on the substances when in Schedule 8 that were not part of the amendments previously proposed by the applicant in relation to which I made the previous psilocybine and MDMA decisions. The applicant has proposed these controls in response to the concerns expressed by the Committee, myself as the Delegate, and the authors of the Expert Report in relation to the previous applications. These additional proposed controls include requiring certain practitioner expertise and training, and procedures and standards for treatment of patients with the substances.

These additional controls could theoretically ensure the benefit for treated patients is realised despite there only being evidence of potential therapeutic value, and mitigate safety and public health risks. The RANZCP memorandum highlighted the need for guidelines for preparing patients undergoing psychedelic therapy and addressing issues regarding accreditation of training programs prior to regulatory controls being explored. Considering paragraphs 52E(1)(b) and (f) of the Act, I am of the view that the suitability and control of the treatment setting (such as a clinic), led by researchers with appropriate psychiatric and psychotherapy training (including specific training in psychedelic psychotherapy), are crucially important to mitigate the risks associated with psychedelic therapy. These risks include the vulnerability under which patients are placed by psychedelic agents that alter one's state of consciousness, such as psilocybine and MDMA, which requires appropriate oversight before, during and following the administration of either substance.

However, I am not satisfied that these controls that are purported to support a favourable benefit-risk balance will have the desired effect and support the proposed down-scheduling of the substances. This is due to how they would potentially operate in practice under State and Territory legislation. The Poisons Standard is not implemented by the States and Territories in a manner that is intended to give effect to highly specialised restrictions on clinical practice in situations where therapeutic value of a substance in Schedule 8 has not been established. This is because regulation of Schedule 8 substances under State and Territory legislation aligns with the corresponding scheduling factors in the SPF.

I accept the Committee's view that States and Territories do not have established mechanisms to give effect to the controls in the current psilocybine and MDMA proposals relating to training, including accreditation by an appropriate body, or to oversee the requirement for review by two additional psychiatrists. As such, I am of the view that many of the additional requirements included in the current psilocybine and MDMA proposals are not reasonably able to be administered or enforced at State and Territory level. This particularly poses an issue in relation to preparations containing the substances that are not included in the ARTG. Substances of this nature should remain in Schedule 9, where therapeutic use is largely restricted to clinical trials, until adequate evidence of their therapeutic value has been demonstrated and there are appropriately accredited training programs for the personnel involved.

Turning to paragraphs 52E(1)(d), (e) and (f) of the Act, I recognise that the risk of diversion of the substances is low in a controlled medical environment, yet I remain of the view that there are significant risks of their diversion at other points in the supply chain. In addition, not dispensing the substances from a pharmacy due to the lack of registered products would bypass the nationally implemented real-time prescription monitoring system, hence limiting oversight and governance. These issues argue for both substances to remain in Schedule 9, consistent with the relevant scheduling factors in the SPF.

I agree with the applicant that the *United Nations Convention on Psychotropic Substances 1971* permits exemptions to be granted for limited medical use and therefore the inclusion of psilocybine and MDMA in the Convention is not a barrier to the current proposals. However, I agree with the Committee that the regulation of access to the substances for therapeutic use

abroad is consistent with the controls associated with Schedule 9 of the Poisons Standard. In the case of MDMA, expanded patient access schemes have been instituted in countries including the United States, Israel and Switzerland under compassionate grounds for the treatment of PTSD. These are analogous to the current use of the Special Access Scheme in Australia, which allows patient access to Schedule 9 substances with approval under particular circumstances. In the case of psilocybine, I note its "Breakthrough Therapy" status in the USA, designated by the Food and Drug Administration (FDA), relating to treatment-resistant depression (TRD) only and not the broader indication included in the current psilocybine proposal. Moreover, this status is not connected to controls over access, but rather pathways to promote research and to market products. There are still no approved therapeutic products containing either substance anywhere in the world.

I note that a very large number of psilocybine and MDMA submissions were received from members of the public with the majority in favour of the current proposals, citing a clinical need (in relation to PTSD in the case of MDMA) and low risk of diversion of the substances. However, I note that both the Australian Psychological Society (APS) and RANZCP were against the proposals to down-schedule psilocybine and MDMA.

The APS indicated that until additional evidence is available from phase III clinical randomised controlled trials, there is insufficient evidence to endorse widespread adoption of psychedelic-assisted therapy. In the view of the APS there was insufficient data regarding the efficacy, safety, potential for abuse and tolerability of both substances in vulnerable patient populations. The RANZCP stated that until further research is available to clearly determine the therapeutic value, benefits and risks, and the development of best practice frameworks for clinical use have been subsequently developed, down-scheduling psilocybine and MDMA should not occur.

In summary, insufficient new evidence has been provided in either the psilocybine or MDMA application to establish the therapeutic value and benefits of the substances in psychedelic-assisted therapy in clinical practice. As such, I am of the view that the current psilocybine and MDMA proposals are inconsistent with the SPF and pose an unfavourable balance of the risks and benefits to the public. I have therefore decided to not amend the existing scheduling for either psilocybine or MDMA in the Poisons Standard.

2.4 Interim decision in relation to apronal (allylisopropylacetylurea)

Proposal

A proposal was initiated by a delegate of the Secretary of the Department of Health and Aged Care (the **Delegate**) to clarify the appropriate scheduling for apronal and allylisopropylacetylurea, which are currently in Schedule 4 and Schedule 10 of the Poisons Standard respectively. These entries represent the same substance.

Interim Decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (Cth) (the **Regulations**), a delegate of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made an interim decision to amend the current Poisons Standard in line with their proposal as follows:

Schedule 4 – Delete entry

~~APRONAL~~

Index – Delete entry

~~**APRONAL**~~

~~Schedule 4~~

Schedule 10 – Amend entry

APRONAL ~~ALLYLISOPROPYLACETYLUREA~~ for therapeutic use

Index – Amend entry

APRONAL
cross reference: ALLYLISOPROPYLACETYLUREA

Schedule 10

Materials considered

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

- The delegate-initiated application to amend the current Poisons Standard with respect to apronal/allylisopropylacetylurea (the **Application**);
- The 2,748 public submissions,[4] including 3 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 38th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989* (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health.
- The Scheduling Policy Framework 2018 (the **SPF**); and
- The Scheduling handbook: Guidance for amending the Poisons Standard

Summary of Committee advice to the Delegate

The Committee agreed with the proposal and recommended that the scheduling for apronal/allylisopropylacetylurea be amended in the Poisons Standard as below:

Schedule 4 – Delete entry

~~APRONAL~~

Index – Delete entry

~~**APRONAL**~~

~~Schedule 4~~

Schedule 10 – Amend entry

APRONAL ~~ALLYLISOPROPYLACETYLUREA~~ for therapeutic use

Index – Amend entry

APRONAL
cross reference: ALLYLISOPROPYLACETYLUREA

The Committee also recommended an implementation date of **1 February 2023**.

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

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

Risks:

- Potential side effects such as thrombocytopenic purpura and porphyria
- Haemolytic reactions and potential CYP450 enzyme activity

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

- Currently no approved products listed with apronal as active substance in Australia, nor in many international markets including Canada, US, NZ or the European Union
- Japan has an OTC medicine containing apronal with paracetamol and caffeine.

c) the toxicity of a substance

- Safety profile is not consistent with any Schedule other than Schedule 10.

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

- N/A

e) the potential for abuse of a substance

- Barbiturate-like substance with potential for abuse and evidence of development of dependence.

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

- To reduce confusion and duplication in the Poisons Standard

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

I have made an interim decision to amend the current Poisons Standard in relation to apronal/allylisopropylacetylurea in the manner proposed. The detailed reasons for my decision follow.

I agree with the Committee's findings on the relevant provisions of section 52E of the Act.

With reference to paragraph 52E(1)(f), I am of the view that consolidating the names for this particular substance in the Poisons Standard will reduce confusion and provide clarity, particularly for customs and law enforcement officials. I agree with the Committee that apronal is the more widely used name for the substance. It is the most appropriate name for the listing as the substance does not currently have an International Non-proprietary Name (INN), and allylisopropylacetylurea is lesser known in the industry and public sectors. To ensure consistency, allylisopropylacetylurea will be entered in the index as a cross reference to apronal.

As to consolidating the existing entries into one entry in Schedule 10 rather than Schedule 4, I share the Committee's concerns regarding the barbiturate-like structure of apronal and the potential for its misuse due to hypnotic side effects. Further to this, I have taken into account the safety profile and opinions associated with apronal with regards to paragraphs 52E(1)(a) and (c) of the Act, including the potential risks of haemolytic reactions and haemorrhagic thrombocytopenic purpura, haemorrhagic effects in the eyes, brain, eyelids, mouth and/or body,

and porphyria. I am therefore satisfied that the public health risks presented by this substance substantially outweigh any benefit from its use to the extent that there is no appropriate level of public access to the substance, consistent with the Schedule 10 factors in the SPF.

With regards to paragraph 52E(1)(b) of the Act, I acknowledge that the substance is used in Japan in over-the-counter analgesic medicines when mixed with paracetamol and caffeine, however, the dosage used in those products is significantly lower than if the substance were to be used as a sedative. I note that the substance is not currently used in any products registered on the Australian Register of Therapeutic Goods (ARTG), which aligns with regulations in the EU, NZ, Canada and the USA.

I have read and considered the public submissions received in response to the pre-meeting notice and note that the majority supported the proposal. Of the 3 written submissions that were received, all supported the proposal.

Proposed implementation date

1 February 2023

3. Interim decisions on proposed amendments referred to the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #38, June 2022)

3.1 Interim decision in relation to helional

Proposal

The applicant has proposed the creation of new Schedule 6 and Schedule 10 entries for the substance helional, which is not currently scheduled (the **Proposal**). Helional is used as a fragrance and flavouring agent in foods, but may be used as a precursor in the manufacture of illicit substances and may also be toxic by ingestion. The proposal is to prohibit internal use of helional except in low concentrations in therapeutic and food preparations, and place labelling and storage requirements on helional in most other preparations for external use.

Interim decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made an interim decision to exclude helional from scheduling. In line with the Scheduling Policy Framework (the **SPF**), substances that have been considered for scheduling but have not met the requirements for any schedule may be placed in Appendix B to record the outcome. The interim decision to create an Appendix B entry for helional is as follows:

Appendix B – New Entry

Substance	Date of entry	Reason for listing	Area of use
HELIONAL	February 2023	a (Low Toxicity)	7 (General)

Index – New Entry

HELIONAL

Appendix B, Part 3

Materials considered

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

- The application to amend the current Poisons Standard with respect to helional (the **Application**);
- The 2,667 public submissions,[4] including 3 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 31st meeting of the Advisory Committees on Medicines and Chemicals Scheduling in joint session (the **Committee**);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989* (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and

the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health;

- The Scheduling Policy Framework 2018; and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Committee advice to the Delegate

The Committee advised that that helional does not meet the factors in the SPF for any Schedule in the Poisons Standard and should remain unscheduled.

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

The reasons for the advice included:

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

Risks:

- There is no major risk when used for appropriate purposes and little risk of direct diversion for personal use.
- Skin sensitisation and precursor for making MDA and MDMA

Benefits

- There are benefits to its use in flavouring, perfumery and in some industrial applications.

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

- Used as an excipient in therapeutic goods, including medicines, sunscreens, disinfectants, topical gels and shampoos. Predominantly a perfumery product.
- Also used in washing and cleaning products, polishes and waxes, air fragrances, perfumes, cosmetics and personal care products. Used as a food additive in the European Union and United States.

c) the toxicity of a substance:

- Low acute toxicity and irritant.
- Some skin sensitivity risks (low-moderate) based on mice studies – similar studies on humans returned contrasting results.
- No reported direct poisonings.

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

- Highly variable.
- Has both internal and external applications, also used in cleaning applications.
- Potential personal care and perfume products.

e) the potential for abuse of a substance:

- No suggestion of direct abuse.
- Can be used in the synthesis of illicit substances such as MDA (reasonably preferred agent) and MDMA (not preferred agent).
- Potential diversion for illicit uses – regulated under State and Territory-controlled precursor legislation.

f) any other matters considered necessary to protect public health:

- Use as a precursor for drugs already prohibited in most states and territories.
- Variable name of substance.
- Schedule 10 factors are not met for this substance. Insufficient evidence for Schedule 6 classification.

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

I agree with the Committee's findings regarding the relevant provisions of section 52E of the Act.

I have made an interim decision to amend the current Poisons Standard in relation to helional. As I find that helional does not meet the factors in the SPF for any schedule, the substance should be included in Appendix B of the Poisons Standard. The detailed reasons for my decision follow.

In consideration of paragraphs 52E(1)(a), (b) and (d) of the Act, I note that helional is currently used in food, sunscreens, disinfectants, topical gels, shampoos, and several other consumer products as a flavouring or fragrance. The benefits of the substance in these products outweigh the associated risks, including that of the substance being used for inappropriate reasons, and present limited risk of diversion.

With reference to paragraph 52E(1)(c) of the Act, I have considered the Committee's advice regarding the insufficient safety and toxicity data to support the inclusion of helional in Schedule 6 as proposed. As per the SPF, a substance in Schedule 6 should exhibit moderate to high acute oral toxicity or acute dermal toxicity, neither of which are met by helional based on the information provided. Additionally, there is no evidence of skin sensitisation associated with the substance to warrant placement in Schedule 6.

I agree with the Committee's advice that the substance also does not meet the SPF factors for Schedule 10. Toxicity data indicate that it is a low irritant and that there are no reports of poisoning resulting from the ingestion of the substance. The substance has shown some low to moderate skin sensitivities but none substantial enough to warrant a Schedule 10 entry. I am unable to perceive a circumstance in which helional presents *"such a danger to public health, as to warrant prohibition of sale, supply and use"* and have therefore decided that the substance remain unscheduled.

Regarding paragraph 52E(1)(e) of the Act, there is low to no direct potential for abuse of helional. The main risks in this regard are indirect, namely diversion for the manufacture of illicit substances.

Turning to paragraph 52E(1)(f) of the Act, I note the Committee's advice regarding other controlled precursor substances that are not included in Schedule 10. These include substances such as acetaldehyde (unscheduled) and piperidine which is listed in Schedule 4, despite being known precursors to illicit opioid derivatives. I observe that the potential of diversion for substances to be used as precursors in illicit substances is more appropriately addressed through the controlled substances legislation of each state and territory, which also allow for legitimate use of such substances. The regulation of precursors of illicit substances is better

regulated through state and territory legislation than the Poisons Standard, particularly as the substance's toxicity profile does not meet the SPF for any schedule in the Poisons Standard.

I have noted the Submissions, including the 3 written submissions which were all supportive of the proposal to schedule helional on the basis of its potential use as a precursor. However, in view of the pre-existing legislative controls on diversion and noting the low acute toxicity of helional, it is my view that the substance does not meet the factors for inclusion in a Schedule. In the interests of recording this decision and consistent with the SPF, helional will be entered in Appendix B.

Proposed implementation date

1 February 2023

3.2 Interim decision in relation to hydroxypinacolone retinoate

Proposal

The applicant presented two proposed amendments of the Schedule 4 entry for tretinoin to exclude its salts and derivatives and/or hydroxypinacolone retinoate (HPR) for use in topical preparations containing 0.5 per cent or less of the substance (the **Proposals**).

Interim decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (Cth) (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made an interim decision to amend the current Poisons Standard substantially in line with the proposal as follows:

> **Schedule 4 – Amend entry**
>
> TRETINOIN except the ester hydroxypinacolone retinoate in preparations for dermal use containing 0.5 per cent or less of hydroxypinacolone retinoate.

Materials considered

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

- The application to amend the current Poisons Standard with respect to hydroxypinacolone retinoate (the **Application**);
- The 2,373 public submissions,[4] including 4 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**).
- The advice received from the 31st meeting of the Advisory Committees on Medicines and Chemicals Scheduling in joint session (the **Committee**);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989* (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance;
- The Scheduling Policy Framework 2018 (the **SPF**); and

- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Committee advice to the Delegate

The Committee recommended that the current scheduling for tretinoin be amended in Schedule 4 of the Poisons Standard as outlined in the Delegate's decision.

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

The reasons for the advice included:

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

Risks

- As a self-administered dermal treatment, there is a slight risk of overuse.

Benefits

- Low risk when used as intended

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

- Dermal preparations with less than 0.5% HPR; no medical intervention

c) the toxicity of a substance:

- HPR not easily absorbed through the skin
- Low potential for causing harm as it is non-corrosive
- Low toxicity and low health hazard potential

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

- Dermal preparations with less than 0.5% HPR

e) the potential for abuse of a substance:

- Nil

f) any other matters considered necessary to protect public health:

- Nil

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

I have made an interim decision to amend the current Poisons Standard in relation to tretinoin by including an exemption for certain preparations containing the derivative HPR. The detailed reasons for my decision follow.

I agree with the Committee's findings regarding the relevant provisions of section 52E of the Act.

I have noted the two Proposals included in the Application:

Proposal A: Exemption from scheduling of HPR in topical preparations for cosmetic use at concentrations not exceeding 0.5%;

Proposal B: Exemption of all salts and derivatives of tretinoin in topical preparations at concentrations not exceeding 0.5%.

I agree with the Committee's observations that, considering the properties of the substance, HPR could currently be regarded as a derivative of tretinoin under the meaning provided in the Poisons Standard. I consider HPR as a Schedule 4 (prescription-only) substance in accordance with subclause (2)(c) of Part 1 of the current Poisons Standard.

I agree with the Committee's advice that any exemption from the Schedule 4 entry for tretinoin in this matter should apply only to HPR. The data provided in the application directly addressed this substance, and a new scheduling entry encompassing all derivatives of tretinoin may potentially result in undesirable outcomes. Therefore, my considerations regarding this Application are with reference to Proposal A, rather than Proposal B.

I have also considered the distinction between topical and dermal preparations, as defined in the Poisons Standard. I agree with the Committee that the exemption should be restricted to dermal preparations, i.e. those applied to the skin for localised effect, consistent with the data provided in the Application. I am of the view that restricting any exemption to dermal preparations also better addresses the use of the substance referred to in the Application, and the typical use of the substance in existing products that contain HPR.

In reference to paragraph 52E(1)(b) of the Act, HPR is a short chain ester of retinoic acid used in cosmetics to purportedly reduce the signs of ageing, such as wrinkles and decreasing skin elasticity.

Turning to paragraph 52E(1)(c), I note the similarities in the pharmacology of the substance to tretinoin, a prescription-only retinoid, but importantly with no evidence of mutagenic or teratogenic activity. This is the primary toxicological property of tretinoin that characterises it as a prescription-only medicine due to the risk presented to the embryo or foetus. I also note that there is little to no skin irritation associated with dermal use of HPR, which was developed as an alternative to retinoic acid for use in cosmetic dermal anti-ageing preparations and has a significant history of safe use.

I note that HPR is a synthetic ester of retinoic acid that does not readily bio-convert into all-trans retinoic acid (ATRA, known as tretinoin when used as a pharmaceutical), unlike other retinoids. Results from a stem cell development toxicity screening test demonstrate that conversion from HPR to ATRA is unlikely, and developmental toxicity for the dermal exposure is therefore unlikely to occur. Further, I note that dermal use of the substance was not found to increase plasma levels and ATRA in the blood was below detectable levels when using HPR.

In consideration of paragraph 52E(1)(d) of the Act, I acknowledge that is not likely to present a high risk of dependency, abuse, misuse, or illicit use. The data set included in the Application that demonstrates the safety of HPR up to concentrations of 1 per cent is noted. This is observed as consistent with the viewpoint in several international jurisdictions that retinol and its equivalents are generally regarded as safe up to 1 per cent for dermal administration. However, given the limit of 0.5 per cent included in the Proposal, my considerations in making this particular decision do not extend beyond this concentration.

I acknowledge and call attention to the Committee's advice that HPR is not listed on the Australian Inventory of Industrial Chemicals, and therefore cannot be used in cosmetic products unless all regulatory requirements are fulfilled. Therefore, it remains that all cosmetic products containing HPR will be subject to the approval of the Australian Industrial Chemicals Introduction Scheme (AICIS).

Proposed implementation date

1 February 2023

3.3 Interim decisions in relation to MDMA and MDA nomenclature

This section contains two independent interim decisions in respect to the nomenclature of (i) MDMA and (ii) MDA (the **Substances**). Given the current scheduling and the proposed amendments to the Poisons Standard in relation to the substances are similar, the reasons for making the interim decisions for both substances are substantially the same. As such these reasons have been consolidated to assist the reader.

Proposals

MDMA

The applicant proposed amendment of the current Schedule 9 entry for N,α-dimethyl-3,4-(methylenedioxy)phenylethylamine (MDMA) to reference the international non-proprietary name (INN) midomafetamine (the **MDMA Proposal**). The original name for the substance would be included as a cross-reference in the index entry for the substance.

MDA

The applicant proposed amendment of the current Schedule 9 entry for 3,4-methylendioxyamfetamine (MDA) to reference the INN tenamfetamine (the **MDA Proposal**). The original names for the substance would be included as a cross-reference in the index entry for the substance.

Interim Decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (Cth) (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made the following interim decisions:

(i) to not amend the current Schedule 9 listings for MDMA in the Poisons Standard.
(ii) to not amend the current Schedule 9 listings for MDA in the Poisons Standard.

Instead, the INNs for these substances are to be entered as cross references to MDMA and MDA in the index as follows:

> **Index - Amend Entry**
>
> **N, α -DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA).**
> cross reference: 3,4- METHYLENEDIOXY-N-α-DIMETHYLPHENYLETHYLAMINE, MDMA, MIDOMAFETAMINE
>
> **3,4-METHYLENEDIOXYAMFETAMINE *(MDA).**
> cross reference: 3,4-METHYLENEDIOXYAMPHETAMINE, MDA, TENAMFETAMINE.

Materials considered

In making these interim decisions, the Delegate considered the following material:

- The applications to amend the current Poisons Standard with respect to the nomenclature of MDMA and MDA (the **Applications**);

- The 5,350 public submissions,[4] including 2 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 31st meeting of the Advisory Committees on Medicines and Chemicals Scheduling in joint session (the **Committee**); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Committee advice to the Delegate

The Committee recommended that no change be made regarding the existing scheduling entries for MDMA and MDA, however agreed that the INNs for each substance should be included as cross-references in the respective index entries.

In making this recommendation the Committee members considered the main issues regarding the renaming of MDMA and MDA to be familiarity and recognition of the current names, as they are known to many organisations, industry, and the wider community.

The Committee acknowledged that at this time the substances MDMA and MDA are only listed in Schedule 9, and the names in Schedule 9 are the names that law enforcement and other agencies use, therefore including the INNs in the index as cross-references may avoid confusion.

Regarding the implications for State and Territory drug and poisons legislation, the Committee considered the fact that amending the index by adding the INNs as cross references to the existing entries would not adversely affect their legislative instruments.

Inconsistencies in international treaties and legislative documents with reference to these substances' nomenclature was also considered by the Committee.

The Committee also recommended an implementation date of **1 February 2023**.

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

I have made interim decisions to retain the names for MDMA and MDA as presently listed in the Poisons Standard. However, I have decided to include the INNs midomafetamine and tenamfetamine in the index as cross-references for MDMA and MDA respectively. The detailed reasons for my decision follow.

I note that the current Poisons Standard conventionally uses INNs in the absence of a name approved by an appropriate authority such as the TGA, and there are no registered products containing MDMA or MDA in Australia. In making this decision I have considered the Committee's advice regarding the inconsistencies in international treaties and legislative documents with reference to these substances. For example, I recognise the inconsistent naming of these substances in the United Nations Convention on Psychotropic Substances 1971, which uses the chemical name for MDMA as is listed in the Poisons Standard, but conversely, uses the INN for MDA (tenamfetamine). Additionally, it has been noted that the United States Food and Drug Administration (FDA) uses the INNs for both substances in the FDA's Global Substance Registration System.[9]

The current nomenclature for MDMA and MDA as used in Schedule 9 of the Poisons Standard is familiar to stakeholders such as law enforcement and customs officials, as well as the general public. I recognise that changing the nomenclature in the Schedule 9 entries may cause confusion for these bodies, and I agree with the Committee that including the INNs in the index as cross-references may be preferable. I also acknowledge the Committee's advice that

[9] FDA Global Substance Registration System https://precision.fda.gov/uniisearch

amending the index by adding the INNs as cross references to the existing entries would not adversely affect the relevant legislative instruments of the States and Territories.

I have also taken into consideration the two written submissions on the Proposal. In particular, the submission received from the Royal Australian & New Zealand College of Psychiatrists opposed the proposal, citing that clear communication would need to be provided to all sectors involved to avoid any confusion regarding these substances. The other written submission was by the Pharmacy Guild of Australia who supported the Applications, however I note that no reasons were provided.

The matters listed in section 52E of the *Therapeutic Goods Act 1989* were not considered in making these interim decisions, as the MDMA Proposal and MDA Proposal involved consideration of the nomenclature of the substances only and no other factors.

Proposed implementation date

1 February 2023

4. Interim decisions on proposed amendments referred to the Advisory Committee on Chemicals Scheduling (ACCS #31 June 2022)

4.1 Interim decision in relation to dichloromethane

Proposal

The applicant has proposed the deletion of the existing Schedule 5 entry in the Poisons Standard for dichloromethane (also known as methylene chloride), to be replaced by a new entry in Schedule 10 (the **Proposal**). This amendment would effectively prohibit any use of dichloromethane.

Interim decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (Cth) (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made an interim decision to not amend the current Poisons Standard in relation to dichloromethane.

Materials considered

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

- The application to amend the current Poisons Standard with respect to dichloromethane (the **Application**);
- The 2,812 public submissions,[4] including 22 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 34th Meeting of the Advisory Committee on Chemicals Scheduling (the **Committee**);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989* (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health;
- The Scheduling Policy Framework 2018 (the **SPF**), pursuant to paragraph 52E(2)(a) of the Act;
- A report regarding deaths associated with dichloromethane in Australia (2010-2019) provided by the National Coronial Information System;
- A summary of poisoning incidents involving products containing methylene chloride 2014-2022, provided by the New South Wales Poisons Information Centre; and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Committee advice to the Delegate

The Committee recommended that the current Poisons Standard entry for dichloromethane remains appropriate.

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

The reasons for the advice included:

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

Risks

- Accidental poisoning (particularly in occupational use in poorly ventilated settings) due to the substance's highly volatility and poor mixing with air. Toxicity arises from exposure to high concentrations of the chemical vapour and is dependent on duration of exposure. Prolonged exposure causes acute neurotoxic effects (such as dizziness, headache, drowsiness, poor concentration and loss of consciousness), and sometimes death.

Benefits

- Highly effective as a paint stripper with few comparable alternatives for this purpose.
- Useful as a mine marker paint – non-flammable and evaporates quickly.

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

- Paint stripper.
- Solvent in manufacturing of pharmaceuticals.
- Paints used in the mining industry.
- Wide use in domestic, commercial and industrial settings.

c) the toxicity of a substance:

- Toxic by ingestion and can penetrate the skin. Main risk is inhalational toxicity which can be life threatening in acute exposures (>50,000 ppm). This is increased in poorly ventilated settings or when concentrated in low lying areas, e.g. bathtubs.

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

- Varied formulations including liquids, foams and aerosols.

e) the potential for abuse of a substance:

- Can have narcotic effects, however potential for abuse is small due to risks of toxicity at similar doses.

f) any other matters considered necessary to protect public health:

- Specialised personal protective equipment is required for safe use of high strength products (respirators, suitable gloves, etc). Risks in workplace settings are addressed by other frameworks, e.g. work health and safety laws.
- Dichloromethane is present in many products, e.g. pharmaceuticals at residual concentrations that are unlikely to cause harm. The risk will be from use of concentrated products.
- A Schedule 7 classification may present a significant burden on users in some jurisdictions.

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

I have made an interim decision to not amend the current Poisons Standard in relation to dichloromethane.

I agree with the Committee's findings on the relevant provisions of section 52E of the Act.

In weighing up the benefits and risks, I have considered the 22 written public submissions received during the pre-meeting consultation period. I note that 17 were opposed to the proposed amendment to the Poisons Standard with regards to dichloromethane, 4 were partially supportive and one was supportive.

Interested parties were also given the choice to indicate their support or opposition to the Proposal without providing a written response. Of the 2,790 responses received, 2,384 were in support, 296 were partially supportive, and 132 were opposed to the Proposal. These respondents did not provide reasons for their support or opposition and as a result, the extent of my consideration is limited to noting that these submissions were generally supportive of the Proposal.

In relation to paragraph 52E(1)(a), I note that the Application identifies the inhalational hazards associated with the use of dichloromethane, particularly in domestic settings, as the primary driver for the proposed Schedule 10 entry. In addition, I note the neurotoxic effects associated with prolonged exposure to high concentrations of dichloromethane vapour, which present a particular hazard in domestic settings and other enclosed areas with poor ventilation. However, these risks are balanced against the chemical's properties and usefulness in a variety of industrial and commercial fields, which necessitate careful consideration of any additional controls that may be placed on the supply of dichloromethane.

In relation to paragraph 52E(1)(b), I note that dichloromethane is a volatile organic solvent that has applications in a variety of settings, primarily as a paint stripping agent and degreaser. It is also used in paints found in the mining industry, as an active ingredient in industrial and commercial cleaning products, as an aerosol propellant, as a process solvent in manufacturing, and in the printing industry. I also observe that there is an allowance in many pharmaceutical medicines for the presence of dichloromethane as a residual solvent.

With regards to paragraph 52E(1)(c), the toxicity of dichloromethane has been well characterised and documented. The relatively low acute toxicity of dichloromethane is consistent with the SPF factors for the existing Schedule 5 classification. However, I agree with the Committee that these data are not the focus of the Application, and the primary concern is the inhalational risk, particularly when used in inadequately ventilated areas which has resulted in hospitalisations and deaths. An increasing trend in these events has led the United States Food and Drug Administration (FDA) to ban the use of the substance in consumer products in 2019. I also note that the European Union and Health Canada place restrictions on the use of dichloromethane in paint strippers, cosmetics and aerosols.

With these international regulations in mind, I have reviewed data from the National Coronial Information System (NCIS) and the New South Wales Poisons Information Centre (PIC) regarding adverse events associated with dichloromethane in Australia. I find that the trend in adverse events associated with dichloromethane observed in the US has not been replicated in Australia. The NCIS reviewed all coronial reports from 2010-2019 and found that two deaths associated with dichloromethane had occurred in that time, both associated with use in a poorly ventilated, domestic setting with inadequate protective equipment. The PIC data, while demonstrating the hazards associated with the use of paint strippers in particular, did not indicate an increasing trend of adverse health events associated with exposure to the substance. The reasons for the lack of correlation of the frequency and severity of these events in Australia compared to other countries are unknown. Based primarily on these two sources of information, I am of the view that the key driver for the Proposal cannot be demonstrated within Australia to a degree that necessitates an amendment to the Poisons Standard.

In support of this view, I also note the human health tier II assessment[10] of the health and environmental impacts of dichloromethane, as published by the National Industrial Chemical Notification and Assessment Scheme (NICNAS, now known as AICIS) in 2014. This assessment concluded that "products containing the chemical should be labelled in accordance with state and territory legislation", which correlates with the existing Schedule 5 classification.

In making my decision to retain the current scheduling of dichloromethane in the Poisons Standard, I would like to make particular reference to paragraph 52E(2)(f) of the Act as it pertains to this substance. The material I have considered regarding the use of this substance in consumer products indicates a very low level of risk associated with professional use. This correlates with the use of appropriate personal protective equipment, such as chemical-resistant gloves,[11] breathing apparatus where required, and use of forced ventilation systems in enclosed workspaces. It is likely that many of the adverse events experienced from the use of products containing this substance occurred in the absence of such equipment. I consider that the warning statements that are already included in the Poisons Standard for dichloromethane, including those associated with exposure to the eyes, skin, and respiratory system, to be adequate in informing users of the potential hazards when using products containing this substance.

The diverse applications of dichloromethane are reflected in the written submissions, which were largely opposed to the Proposal. In particular, I note submissions from stakeholders of a wide range of industries, including manufacturers of paints and degreasers, aerosol marking products, adhesives, pharmaceuticals and cosmetics. These submissions opposed the Proposal largely based on the practical and, in some cases, irreplaceable properties of the substance within the products in each industry. I therefore find that prohibition of the use of dichloromethane, via creation of a Schedule 10 entry as proposed, would be unduly detrimental to the operations of many industries.

I have considered other options for increasing the controls on dichloromethane, such as a Schedule 7 entry for paint stripping products that contain high concentrations of dichloromethane. These preparations have been demonstrated to be of the highest risk to users. However, I agree with the Committee's advice that such a classification would place an undue burden on industrial and commercial users, who have almost invariably been shown to use these products in a safe manner compliant with labelled warnings and work health and safety regulations.

I would like to highlight the various labelling requirements for dichloromethane (methylene chloride) as indicated in Appendix E (First Aid Instructions) and F (Warning Statement and General Safety Directions), that would indicate that significant risk mitigations are currently in place for users of products containing this substance.

For general use:

A	For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once).
G3	If swallowed, do NOT induce vomiting.

[10] https://www.industrialchemicals.gov.au/sites/default/files/Methane%2C%20dichloro-_Human%20health%20tier%20II%20assessment.pdf

[11] It is important to note that no glove is chemical-proof or non-permeable but may be chemical resistant to particular chemicals over a period of time. Users of chemical-resistant gloves and other PPE should inform themselves of the most appropriate equipment for use with the chemical(s) they are using. Various manufacturers of gloves will have information about the suitability of different glove materials e.g. latex, PVC, nitrile, etc, to resist penetration/break-through to chemicals, including dichloromethane (methylene chloride).

G5	Avoid giving milk or oils.
E1	If in eyes wash out immediately with water.
R1	If inhaled, remove from contaminated area. Apply artificial respiration if not breathing.
S1	If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.

In pressurised spray packs:

A	For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once).
G6	If sprayed in mouth, rinse mouth with water.
S1	If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.

When present 'in paint or lacquer removers':

12	Vapour is harmful to health on prolonged exposure.
16	Forms dangerous gas near radiators or naked flames.
1	Avoid contact with eyes.
4	Avoid contact with skin.
8	Avoid breathing dust (or) vapour (or) spray mist.
11	No smoking.

When present in 'other than in paint or lacquer removers':

1	Avoid contact with eyes.
4	Avoid contact with skin.
8	Avoid breathing dust (or) vapour (or) spray mist.
25	Avoid contact with food.

In conclusion, I consider there to be insufficient evidence of adverse events associated with dichloromethane in Australia to justify a change to the scheduling of this substance. The conditions already applied to the use of dichloromethane in consumer products through the Schedule 5 classification, such as the above labelled warning statements, are deemed sufficient to advise consumers of the risks of using this substance, which are far outweighed by the benefits it provides in a considerable number of applications.

4.2 Interim decision in relation to ipflufenoquin

Proposal

The applicant, the Australian Pesticides and Veterinary Medicines Authority (APVMA), proposed to enter a new fungicide, ipflufenoquin, into Appendix B of the Poisons Standard (the **Proposal**). Appendix B of the Poisons Standard contains a list of substances for which the available information indicates that inclusion in the Poisons Standard is not necessary or not the most appropriate means of controlling the risk to public health.

Interim Decision

Pursuant to regulation 42ZCZN of the Therapeutic Goods Regulations 1990 (Cth) (the **Regulations**), a delegate[3] of the Secretary of the Department of Health and Aged Care (the **Delegate**) has made an interim decision to amend the current Poisons Standard substantially in line with the Proposal as follows:

Appendix B – New Entry

Substance	Date of entry	Reason for listing	Area for use
IPFLUFENOQUIN	September 2022	a	1.3, 1.3.1

Index – New entry

IPFLUFENOQUIN

Appendix B, Part 3

Materials considered

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

- The application to amend the current Poisons Standard with respect to ipflufenoquin (the **Application**);
- The 2,703 public submissions,[4] with one including a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 34th meeting of the Advisory Committee on Chemicals Scheduling (the **Committee**);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989* (the **Act**), in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;

- The Scheduling Policy Framework 2018 (the **SPF**), pursuant to paragraph 52E(2)(a) of the Act; and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Committee advice to the Delegate

The Committee advised that ipflufenoquin does not meet the scheduling factors listed in the SPF for any Schedule in the Poisons Standard.

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

The reasons for the advice included:

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

Risks:

- Low risk of toxicity.

Benefits:

- New broad-spectrum quinoline fungicide with a potentially new fungicidal mode of action and low resistance.

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

- Broad-spectrum fungicide for professional use on berries and fruit.
- The extent for which this substance can be used has not yet been identified as the details for a formulated product were not included in the application.

c) the toxicity of a substance

- Generally low toxicity. Observed acute toxicity in rats was at levels well above expected intake levels. Slight eye irritant in rabbits.

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

- No formulated products included in application.

e) the potential for abuse of a substance

- Nil.

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

- This application raises issues about the meaning of Appendix B. Appendix B is not a Schedule and should not be considered a “positive list” of safer chemicals.
- The majority of the Committee agree that inclusion in a Schedule is not required for this substance.

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

I have made an interim decision to amend the current Poisons Standard by creating a new entry in Appendix B for ipflufenoquin, excluding the substance from the controls included in the Poisons Standard. The detailed reasons for my decision follow.

I agree with the Committee's findings on the relevant provisions of section 52E of the Act.

Ipflufenoquin is a fungicide that is intended to be used on berries and pome fruits such as apples and pears. With reference to paragraph 52E(1)(c) of the Act, the submitted toxicity data showed low levels of acute oral, dermal, and inhalational toxicity in rats. I note that the information provided by the applicant showed that the substance produced no evidence of immunological toxicity, was not carcinogenic in animal lifetime studies and was not teratogenic or a reproductive toxicant in developmental studies. In addition, the substance was not shown to be a skin irritant in rabbits or a skin sensitiser in mice.

The substance was first approved in Japan in 2020 for agricultural use and has since been submitted for registration in several other countries including South Korea, the USA and the EU.

While some concerns were raised by Committee members for fruit pickers and farmers who will have a higher risk of over exposure than the average consumers, the information that was provided supported my view that the overall risk profile of the substance is low enough to warrant exemption from scheduling in the Poisons Standard. As the substance will only be used in professional and agricultural settings, I agree with the Committee regarding the low potential of the substance to cause harm.

I have noted the single written submission received which opposed the proposal to exempt ipflufenoquin from scheduling controls, stating that there was insignificant safety data to support exempting the substance from the Poisons Standard. However, I agree with the Committee that sufficient data have been provided to support the Proposal.

I have noted the Committee’s advice that ipflufenoquin does not meet any factors for inclusion in any Schedule in the Poisons Standard. As stated in the SPF, substances may be placed into Appendix B when they have been considered for scheduling but found not to meet the factors for inclusion in the Schedules of the Poisons Standard. It is also considered that there is a public benefit by adding an entry to Appendix B to record the outcome.

Proposed implementation date

1 February 2022