Australian Government
Department of Health
Therapeutic Goods Administration

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

3 February 2021

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 of the Secretary under regulation 42ZCZN in relation to proposed amendments to the current Poisons Standard which were referred to an expert advisory committee under subdivision 3D.2 of the Regulations in November 2020;
- 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 **4 March 2021**.

We have changed the way to make submissions.

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

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

2 Interim decisions on proposed amendments referred to the Advisory Committee on Medicines Scheduling (ACMS #32, November 2020)

2.1 Interim decision in relation to amygdalin and hydrocyanic acid

Interim decision

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

Materials considered

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

- The application to amend the current Poisons Standard with respect to amygdalin and hydrocyanic acid;
- The 129 public submissions, including two written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #32);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard; and
- An external expert evaluation of the private application.

Summary of ACMS advice to the Delegate

The Committee recommended that the current scheduling for amygdalin and hydrocyanic acid remains appropriate.

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

The reasons for the advice included:

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

- Risks
  - High risk of cyanide toxicity with high variability.
- Benefits
  - Limited evidence of benefit, other than increased access.

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

- Amygdalin and hydrocyanic acid (released by the natural degradation of amygdalin by enzymes in the plant preparation) occur naturally in plants used in traditional Chinese medicines for health conditions described within the philosophy (theory, pathology, diagnosis, treatment and herbal pharmacology principles) of traditional Chinese medicine. Legitimate purpose of use not well defined.
- The substance is currently prohibited and the extent of use is unknown.

c) the toxicity of a substance:

- The toxicity of the substance is well established. Amygdalin exhibits considerable toxicity due to the production of hydrocyanic acid following hydrolysis.
- Complete degradation of 1g amygdalin releases 59mg of hydrocyanic acid (5mg amygdalin would be equivalent to 0.3mg HCN). Cyanide is readily absorbed reaching maximum blood levels within minutes and is distributed to all organs. The primary mode of action by which cyanide exerts acute toxicity is the inhibition of oxidative phosphorylation.
- In humans, the lethal oral dose of HCN is reported to be 0.5–3.5 mg/kg body weight. A level of 0.5 mg/L (approximately 20 micromolar) of cyanide in blood is cited in the literature as a toxicity threshold in humans. A series of poisoning cases are reported from ingestion of preparations containing amygdalin and bitter apricot kernels. In adults, 20 or more kernels were reported to be toxic while the corresponding number in children was five.
- Toxicity is dose-related but also exhibits considerable inter-individual variability.
- The independent evaluation report requested by the delegate includes 5 case reports of toxicity in adults with daily oral amygdalin/laetrile doses ranging from approximately 420mg to 1.5g.

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

- Traditional Chinese medicines uses various oral dose forms; no specific products were described in the application.
- Limiting amygdalin to being a natural component of traditional Chinese medicines for oral use by adults does not provide sufficient regulatory safety.

e) the potential for abuse of a substance:

- Amygdalin has been inappropriately promoted and used as an alternative cancer treatment. Claims for use in treating or preventing cancer are unproven.

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

I have made an interim decision to retain the scheduling of amygdalin and hydrocyanic acid in the current Poisons Standard. This decision is to not down-schedule amygdalin as a natural component in Traditional Chinese Medicines (TCM) for oral use in adults from Schedule 10 to Schedule 4, make amygdalin unscheduled when the maximum recommended daily dose is ≤5 mg amygdalin; nor to make hydrocyanic acid unscheduled for therapeutic use when present as a natural component of amygdalin in TCM for oral use in adults. The detailed reasons for my interim decision are set out below.

Amygdalin is a naturally occurring cyanogenic glycoside compound converted into hydrocyanic acid in the gut. Hydrocyanic acid (cyanide) halts cellular respiration leading to nausea, fever, headaches, insomnia, thirst, lethargy, nervousness, joint and muscle aches and pains, falling

blood pressure, and in some cases, death[1]. The toxicity of amygdalin is highly variable and influenced by numerous factors, including other ingested plants or nutrients (e.g. plant enzymes or ascorbic acid), vitamin B12 and individual gut flora[2].

I consider that amygdalin should not be down-scheduled from its current listing in Schedule 10. The history of persistent misuse of amygdalin for the treatment of cancer is of relevance to my consideration[3]. Amygdalin has been prohibited since 1974 when it was supplied as Laetrile or vitamin B17, a purported treatment for cancer with serious toxicity and no clear evidence of therapeutic benefit[4,5]. I am concerned that the down-scheduling of amygdalin may contribute to excessive use of amygdalin, particularly where people who have or who have had cancer are seeking alternative treatments.

The applicant describes indications of amygdalin use as "cough and wheezing, profuse sputum, masses, lung abscess and intestinal abscess". I find these indications are likely to require medical diagnosis, management or monitoring by a trained medical practitioner. I note that a TCM practitioner does not have authority to prescribe Schedule 4 medicines, unless they are also registered as a medical practitioner. Having considered the findings of the external expert evaluation, which indicates there is less evidence for the safety of higher doses of amygdalin, I find that listing under Schedule 4 is not appropriate.

I have taken into consideration the two public submissions from the NSW Poisons Information Centre (NSW PIC) and the Australian Medical Association (AMA), whom both oppose this decision. The NSW PIC have documented 8 incidences over 6 years of amygdalin/cyanide poisoning resulting from intentional ingestion. There is serious concerns of the risks associated with deliberate self-poisonings and chronic overuse of these products.

I also do not support the down-scheduling of amygdalin at 5 mg or less to unscheduled, to align with the limits set by the Australian New Zealand Food Standards (FSANZ). The FSANZ food limits are based on the Acute Reference Dose (ARfD) for a safe level of one-off exposure, rather than regular and possibly chronic ingestion, which is the assumed practice for a TCM. The submission from the AMA raises similar concerns of serious risks associated with hydrocyanic acid accumulation in the body[6,7].

I note the conclusion of the external evaluation report, that exclusion from Schedule 10 for preparations containing a maximum daily dose not exceeding 5 mg amygdalin, may be appropriate. Notwithstanding the evidence that the risk of toxicity at this proposed cut-off may be low, I find there are factors which make it inappropriate for amygdalin to be available in a general sales environment. In particular, there is potential for use by children and use as an alternative cancer treatment. Fatalities have been recorded following doses of 0.5 to 2.5 grams of amygdalin, particularly in children. There is also significant inter-individual variability in the toxic response to amygdalin ingestion. For these reasons, I am of the view that such products cannot be supplied with reasonable safety with or without access to health professional advice.

The risks to public health and the toxicity of amygdalin associated hydrocyanic acid are evident[8] and significantly outweigh the benefit of increased access.

[1] https://emergency.cdc.gov/agent/cyanide/basics/facts.asp

[2] https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2016.4424

[3] https://www.hindawi.com/journals/criem/2017/4289527/

[4] https://www.cochrane.org/CD005476/GYNAECA_laetrile-treatment-cancer

[5] https://www.cancer.org.au/assets/pdf/submission-from-cancer-council-australia-to-fsanz-s-proposal-p1016-hydrocyanic-acid-in-apricot-kernels-other-foods

[6] https://pubs.acs.org/doi/pdf/10.1021/ja01605a006

[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6558459/

[8] https://www.publish.csiro.au/hc/pdf/HC15939

2.2 Interim decision in relation to bilastine

Interim decision

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

Schedule 4 - Amend Entry

BILASTINE except when included in Schedule 3.

Schedule 3 - New Entry

BILASTINE in divided oral preparations containing 20 mg or less in adults and adolescents 12 years of age and older.

Appendix H – New Entry

BILASTINE

Index – Amend Entry

BILASTINE

Schedule 4

Schedule 3

Appendix H

Materials considered

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

- The application to amend the current Poisons Standard with respect to bilastine;
- The 127 public submissions, including three written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #32);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance.
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACMS advice to the Delegate

The Committee advised that bilastine be entered in Schedule 4 and Schedule 3 in the Poisons Standard as follows:

Schedule 4 - New Entry

BILASTINE except when included in Schedule 3.

Schedule 3 - New Entry

BILASTINE in divided oral preparations containing 20 mg or less in adults and adolescents 12 years of age and older.

Appendix H – New Entry

BILASTINE

Index – Amend Entry

ANTIHISTAMINES
cross reference: ASTEMIZOLE, AZELASTINE, BILASTINE, DESLORATADINE, FEXOFENADINE, LORATADINE, TERFENADINE, CETIRIZINE

Schedule 4
Appendix F, Part 3

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

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included: (a) the risks and benefits of the use of a substance; (b) the 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

– Potential of substance to mask symptoms of common cold, or more serious dermatological conditions.

- Benefits

– Bilastine is a potent non-sedating antihistamine (second generation) with a high affinity for H1 receptors. It has a strong safety profile having been available internationally for over 10 years and is marketed in around 100 countries around the world, including in NZ where it has been marketed as a pharmacy medicine since 2018.

– Effective symptomatic treatment of allergic rhinitis and urticarial.

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

– Approved for the symptomatic treatment of allergic rhinoconjunctivitis (both seasonal and perennial) and urticarial which are common conditions that are considered to be suitable for self-management by consumers.

– Histamine has been shown to play a central role in most of the symptoms of allergic rhinitis primarily by its action at the H1-receptor site. Urticaria is also primarily mediated by the effects of histamine following degranulation of mast cells. Anti-histamines are first line treatment options for these common conditions. As another 2nd generation antihistamine in addition to those already available in pharmacies to consumers, bilastine offers another similar treatment option.

c) the toxicity of a substance:

– Risk profile relatively well understood with overseas safety data, wide therapeutic index.

– Certain drug interactions noted:

Ketoconazole and erythromycin increase bilastine concentration two-three fold.

Diltiazem increases bilastine concentration by 50%.

- Food interactions: interaction with grapefruit juice reduces bioavailability. Food reduces oral bioavailability by up to 30%.
- There are considerable data in support of the safety of bilastine from nonclinical and clinical trials. Clinical studies have demonstrated the safety and tolerability of bilastine with no statistically significant differences in adverse effects between the therapeutic dose (20 mg) and placebo.
- Headache, drowsiness, and lethargy are the most common adverse events reported by patients.

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

- 20mg immediate release tablet for once daily dosing, to be taken at least 1 hour before or 2 hours after food, grapefruit or other fruit juices.
- Proposed packaging size 4-60 tablets per pack size (blister pack).
- CMI to be included.
- Cautionary labelling in respect to indications, age (not for use in children) and seeking advice if pregnant.

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

I have made an interim decision to amend the Schedule 4 entry for bilastine and create a new Schedule 3 entry for bilastine in the current Poisons Standard. I note that effective 1 February 2021, a decision was made to list bilastine in Schedule 4 of the Poisons Standard. This decision was not published at the time of the November Committee meeting and I have made my decision based on the current listing of bilastine in the Poisons Standard.

My decision is to down-schedule bilastine from Schedule 4 to Schedule 3 when bilastine is divided in oral preparations containing 20 mg or less to adults and adolescents 12 years of age and over. I find that there is sufficient information to support the safety and lower toxicity of bilastine in these preparations. Bilastine has a well-defined safety and tolerability profile, with a wide therapeutic index. The daily dose of 20mg had been determined for adults and adolescents over the age of 12 years of age, noting that 10mg is reported as safe in children (6-11 years) with a body weight of at least 20kg.

Bilastine is a new second generation non-sedating antihistamine (NSAH). Bilastine belongs to the same pharmacological class as other Schedule 2 substances such as fexofenadine, loratadine and cetirizine, which are also used for the symptomatic treatment of allergic rhinitis and urticaria. My decision to down-schedule to Schedule 3, rather than Schedule 2, aims to ensure more appropriate support to Australian consumers, and to facilitate monitoring and reporting of pharmacovigilance factors through pharmacist interactions. As a newly registered product in Australia, bilastine does not have sufficient local experience or data on which to base a Schedule 2 entry. I am not satisfied bilastine can be supplied with reasonable safety without access to health professional advice. Self-selection without pharmacist input could lead to confusion and misuse, including a potential for doubling up on antihistamines. Additionally, drug-drug interactions have been documented, with considerable caution required for consumers with renal impairment using P-glycoprotein inhibitors. Future scheduling consideration may be warranted if further evidence of safety in the Australian context, is made available.

Having considered the matters set out in the *Guidelines for advertisements for medicines containing Schedule 3 substances*, I am satisfied that there are no foreseeable potential impacts

on public health that would preclude advertising bilastine directly to consumers through the provision of an Appendix H listing.

I have taken into account all of the public submissions, including those from the Australasian College of Dermatologists (ACD), the Australian Medical Association (AMA) and The Pharmacy Guild of Australia (PGA). Both the ACD and the AMA support the down-scheduling of bilastine to Schedule 2. However, I agree with the submission from the PGA, that bilastine is a new substance on the Australian market and as such, it requires a higher level of health professional input and oversight than is expected under Schedule 2.

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

Proposed implementation date

1 June 2021

2.3 Interim decision in relation to budesonide + formoterol

Interim decision

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

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 + formoterol;
- The 138 public submissions, including 12 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #32);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of the substance; (b) the purposes for which a substance is to be used and the extent of use of the substance; (c) the toxicity of the substance; (d) the dosage, formulation, labelling, packaging and presentation of the substance; (e) the potential for abuse of the substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard; and
- The Australian Asthma Handbook (AAH).

Summary of ACMS advice to the Delegate

The Committee recommended that the current scheduling of budesonide and formoterol remains appropriate.

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

- Benefit:

– Some benefit if patients at level 2, as defined by the Australian Asthma Handbook (AAH) have easier access to combination therapy.

– 'As-needed' low dose budesonide/formoterol reduces the risk of severe exacerbations by about two-thirds compared with SABA-only treatment and is non-inferior to daily low dose ICS for severe exacerbations

- Risk:

– Risk of inappropriate use (e.g. use for conditions other than asthma) and inadequate monitoring by non-asthmatics, AAH step 1 or step 3-4.

– Generally safe.

– Possible risk of adrenal suppression if ICS overused but not at usual therapeutic doses with regular medical review.

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

– Primary purpose is the relief of the symptoms of asthma but with a secondary benefit of reducing the risk of severe asthma exacerbations.

– This is a new indication and a significant change from previous guidance. Prescribers, dispensers and patients are all adapting to change. More evidence is needed on how the change in indication will affect usage in Australia.

– Potential for extensive use in population of patients who currently rely on SABA-only treatments, leading to improved asthma management.

c) the toxicity of a substance

– Established safety profile although there is a possible risk of adrenal suppression if ICS overused but not at usual therapeutic doses with regular medical review.

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

– Multiple dosages available for the same conditions with different scheduling proposed – may be confusing to consumer.

e) the potential for abuse of a substance

– Potential for overuse

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

– 'As-needed' low dose budesonide/formoterol without concomitant use of an inhaled corticosteroid (ICS)-based preventer is a recent change to asthma management in Australia and a period of adjustment/familiarisation may be required.

- Over-reliance on SABA, frequently in the context of poor compliance with prescribed ICS, is common.
- Patients are at risk of asthma-related death and urgent asthma-related healthcare if they are treated with SABA alone.

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

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

I acknowledge that recent updated clinical guidance has recommended the use of low dose beta agonist (LABA)/low dose inhaled corticosteroid (ICS) combined reliever medicines, as the primary medication in all but very mild asthma. However, the use of budesonide-formoterol fixed dose combination (FDC) as a PRN medication is very new to Australia and marks a significant change to asthma management. I am of the view that this proposal is premature and further evidence is required to support the use of this medicine in an over the counter (OTC) setting. Having considered the Scheduling Policy Framework 2018 (SPF 2018), I find that budesonide-formoterol FDC does not meet the Scheduling Factors under a Schedule 3 classification, as the limited clinical experience under the new guidelines, mean that the medicine would not be substantially safe with pharmacist intervention to ensure quality use.

I have considered the views expressed by the applicant and agree that there are potential benefits to OTC availability of budesonide-formoterol FDC as a PRN and that this may be a safer option than OTC use of short acting beta agonist (SABA). However, on balance, I find there is currently insufficient evidence of a net public health benefit from the wider availability of budesonide-formoterol FDC. In my opinion, there is a risk of inappropriate use for conditions outside of asthma and I am not confident that consumers could identify the ailments or symptoms that may be treated by this medicine.

I am of the view that increased availability could compromise medical management of asthma. Asthma is a serious chronic disease and good asthma management relies on accurate diagnosis, regular review and tailoring of treatment. Overlapping conditions and complex management decisions are common. I am concerned that these protections, in particular the provision of patient review and follow-up, would not be adequately in place under the care of a pharmacist. I find that the potential for harm in the absence of medical practitioner oversight carries more weight than the benefit of increased patient access.

I have considered the proposed risk mitigation strategies outlined in the Appendix M entry put forward by the applicant. I am concerned with the process, monitoring and audit of compliance with schedule M, including the feasibility for an asthma action plan to be uploaded to My Health Record (MyHR) for example, and for current, signed asthma management plans from a medical practitioner to be mandated as evidence. I note that previous prescriptions alone are inadequate as the same medications are used for a variety of respiratory conditions. I find that under the proposed Appendix M entry, it would be difficult to determine medically diagnosed asthma.

I have considered the public submissions received in response to the pre-meeting notice and note that the majority of submissions were in opposition to the proposal, including a number of asthma peak representative bodies (Asthma Australia and National Asthma Council). Furthermore, I note, that budesonide-formoterol FDC is currently a prescription only medicine in all other comparable international jurisdictions including the USA, UK, Canada and NZ.

Having considered the need for medical practitioner oversight and the risks to consumers with the lack of patient review and follow up in a pharmacy setting, I am of the view that the current scheduling of budesonide and formoterol under Schedule 4 is appropriate.

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

2.4 Interim decision in relation to psilocybin

Interim decision

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

Materials considered

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

- The application to amend the current Poisons Standard with respect to psilocybin;
- The 575 public submissions, including 357 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #32);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (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 (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard;
- The ClinicalTrials.gov database, provided by the U.S. National Library of Medicine;
- A review by *Reiff et al.,* Psychedelics and Psychedelic-Assisted Psychotherapy (2020);
- A review by *Gill et al.,* The emerging role of psilocybin and MDMA in the treatment of mental illness (2020);
- A review by *Vargas et al.,* Psilocybin as a New Approach to Treat Depression and Anxiety in the Context of Life-Threatening Diseases—A Systematic Review and Meta-Analysis of Clinical Trials (2020);
- A review by *Goldberg et al.*, The experimental effects of psilocybin on symptoms of anxiety and depression: A meta-analysis (2020); and
- A clinical memorandum by *the Royal Australian and New Zealand College of Psychiatrists*, Therapeutic use of psychedelic substances (2020).

Summary of ACMS advice to the Delegate

The Committee recommended that the current scheduling of psilocybin remains appropriate.

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

- Benefits:

– There is limited but emerging evidence that psychedelic therapies may have therapeutic benefits in the treatment of a range of mental illnesses. These benefits are currently under investigation in clinical trials.

- Risks:

– There remain many unknown factors and side effects, especially in the long term. The risks of developing psychosis, especially in vulnerable populations, must be established in a clinical trial setting.

– Can cause tachycardia and transient increases in blood pressure.

– Psilocybin, when misused, can caused psychosis.

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

– Psilocybin is taken in combination with psychotherapy for the treatment of depression, PTSD, anxiety, or end of life distress.

– Psilocybin-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 psilocybin is not used.

c) the toxicity of a substance

– The lethal dose is thought to be 6 g, although evidence around toxicity may be premature.

– The potential adverse effects, particularly relating to multi-drug toxicity, are unknown.

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

– A typical dose in the context of psychotherapy is 25 – 35 mg, depending on subject weight. An optimal therapeutic dosage has not been established.

e) the potential for abuse of a substance

– There is a high risk of diversion for misuse, even in conjunction with Schedule 8 controls.

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

– There are significant benefits to waiting for the results of clinical trials. Psilocybin-assisted psychotherapy may eventually prove to be safe and efficacious, but the evidence does not yet suggest this.

– It will take years to develop a curriculum and accredited training process for psychiatrists. To protect public health and prevent misuse, psilocybin should not be down-scheduled until all necessary safeguards have been established and implemented.

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

I have made an interim decision to retain the scheduling of psilocybin in the current Poisons Standard.

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

The Scheduling Policy Framework (SPF 2018) provides that substances included in Schedule I to the United Nations Convention on Psychotropic Substances 1971, and without an established therapeutic value, should be classified in Schedule 9. In my view, psilocybin fits these scheduling factors, and is not currently appropriate for listing as a Schedule 8 substance.

I note that psilocybin is an illicit drug with a high potential for misuse and an unknown safety profile. The medium and long-term effects of psilocybin-assisted psychotherapy are unknown, particularly in vulnerable populations, and the risk of developing psychosis may be high. Clinical trials will be essential to evaluating risks, but only three phase II trials have been completed. According to the ClinicalTrials.gov database, 11 phase II trials are currently either recruiting or underway, and no phase III trials have been registered. I note that St Vincent's Hospital Melbourne is currently undertaking Australia's first psychedelic clinical trial for terminally ill patients who are experiencing depression or anxiety. Given the emerging evidence base regarding safety and efficacy, I believe that down-scheduling is premature.

In forming this view, I have considered the findings of a recent review in *the American Journal of Psychiatry,* which concluded that, although research is promising, the overall database is insufficient for regulatory approval for clinical use. Several other reviews and meta-analyses published this year also draw similar conclusions, which describe promising results for early trials but advise that the current sample size is small (Gill et al., 2020; Vargas et al., 2020; Goldberg et al., 2020). After reviewing these papers, I affirm my conclusion that further research is required, with larger treatment populations and stringent placebo controls.

I also note the findings of a recent clinical memorandum on psychedelic therapies, published by the Royal Australian and New Zealand College of Psychiatrists (RANZCP), which found that evidence of safety and efficacy is limited but emerging. The memorandum highlights a number of potential risks, particularly the possibility that psilocybin can induce prolonged psychotic disorders in patients with a family history of psychosis. To minimise these risks, the RANZCP concluded that further research is required – much of which is already underway. I believe that these findings support my conclusion that current use of psilocybin should be limited to carefully monitored research trials.

In making my decision, I have taken into account the two 'Breakthrough Therapy Designations' that have been granted by the U.S. Food and Drug Administration. I note that, while these designations indicate that the therapy shows promise, they do not equate to FDA approval. Currently, no comparable country has down-scheduled psilocybin to a category equivalent to Schedule 8, and at present, there is no international framework for how to handle psychedelic-assisted therapies.

I have taken into account all 575 responses that were received during the pre-meeting consultation, noting that 553 were supportive of the proposed amendment, 11 partially supportive and 11 opposed. While the submissions indicate significant public support for rescheduling, few submissions addressed the factors relevant to scheduling. I have read and considered all responses in making my interim decision.

I find that the points raised in public submissions from several peak bodies were highly pertinent, noting the following concerns and recommendations:

- The RANZCP advised that further research is required to assess the efficacy, safety, and effectiveness of psychedelic therapies, emphasising that appropriate treatment methodologies and training protocols do not yet exist.
- The Australian Medical Association advised that more high-quality research, using larger-scale studies, is required to establish the safety and efficacy of psychedelic therapies. The risk of psychosis and persistent hallucinations, especially in susceptible subpopulations, is likely to be high.
- Psychedelic Research in Science and Medicine advised that, to ensure safe and ethical use, any decision to downschedule should include an extensive three-year implementation plan. In addition, psilocybin-assisted psychotherapy has not yet commenced phase 3 trials, and will require several years of further research to establish efficacy.

Having considered the risks to consumers, the lack of training for physicians, and the current state of research, I am of the view that Schedule 9 remains appropriate for psilocybin. I note that my decision does not affect current access to psilocybin for use in a clinical trial setting. Pending the outcome of current clinical research, the scheduling of psilocybin could be reconsidered in future applications. It is also important to note that the supply of psilocybin outside approved clinical trial settings is a criminal offence.

I agree with the Committee's advice that the current spelling of the Schedule 9 entry remains appropriate, noting that the spelling "psilocybine" is consistent with the International Nonproprietary Name and British Approved Name of the substance.

2.5 Interim decision in relation to N, α-Dimethyl-3,4-(methylenedioxy)phenylethylamine (MDMA)

Interim decision

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

Materials considered

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

- The application to amend the current Poisons Standard with respect to MDMA;
- The 478 public submissions, including 254 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #32);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (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 (SPF 2018);

- The Scheduling handbook: Guidance for amending the Poisons Standard;
- The ClinicalTrials.gov database, provided by the U.S. National Library of Medicine;
- A review by *Illingworth et al.,* A comparison of MDMA-assisted psychotherapy to non-assisted psychotherapy in treatment-resistant PTSD: A systematic review and meta-analysis;
- A review by *Bahji et al.,* Efficacy of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for posttraumatic stress disorder: A systematic review and meta-analysis; and
- A clinical memorandum by *the Royal Australian and New Zealand College of Psychiatrists*, Therapeutic use of psychedelic substances (2020).

Summary of ACMS advice to the Delegate

The Committee recommended that the current scheduling of MDMA remains appropriate.

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

- Benefits:

– There is limited but emerging evidence that MDMA-assisted psychotherapy may have therapeutic benefits in the treatment of PTSD. These benefits are currently under investigation in clinical trials.

- 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.

– MDMA can reduce the ability to perceive and predict motion and can therefore result in accidents.

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

– MDMA is taken in combination with psychotherapy for the treatment of PTSD.

– 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 10 – 20 mg/kg.

– The potential adverse effects are unknown in the context of psychotherapy.

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

- Optimal dosages have not been established, especially outside of PTSD treatment.
- A typical dose in the context of psychotherapy is 1-2 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.
- There is a high risk of diversion for misuse, even in conjunction with Schedule 8 controls.

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

- 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.

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

I have made an interim decision to retain the scheduling of MDMA in the current Poisons Standard.

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

The Scheduling Policy Framework (SPF 2018) provides that substances included in Schedule I to the United Nations Convention on Psychotropic Substances 1971, and without an established therapeutic value, should be classified in Schedule 9. In my view, MDMA fits these scheduling factors, and is not currently appropriate for listing as a Schedule 8 substance.

I note that MDMA is an illicit drug with a high potential for misuse in the Australian community, resulting in significant harms including seizures and deaths. MDMA shows some evidence of causing dependence, and may additionally lead to cognitive dysfunction in the medium or long term. Clinical trials will be essential to evaluating these risks. While several phase II trials have been completed, these lack appropriate sample sizes and control groups, and require rigorous follow-up in phase III. According to the ClinicalTrials.gov database, a single phase III trial has been registered, and completed, though its results are not yet publically available. Given the emerging evidence base regarding safety and efficacy, I believe that down-scheduling is premature.

In forming this view, I have also considered the findings of a recent systematic review and meta-analysis in the *Journal of Psychopharmacology,* which concluded that MDMA-assisted psychotherapy requires data from larger scale studies before approval for clinical use. The same sentiment was echoed in an earlier review, published in *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, which concluded that larger sample sizes and longer durations of treatment and follow-up were warranted. After reviewing these papers, I affirm my conclusion that further research is required.

I also note the findings of a recent clinical memorandum on psychedelic therapies, published by the Royal Australian and New Zealand College of Psychiatrists (RANZCP), which found that evidence of safety and efficacy is limited but emerging. The memorandum highlights a number of potential risks, particularly the possibility that MDMA can induce prolonged psychotic disorders in patients with a family history of psychosis. To minimise these risks, the RANZCP concluded that further research is required – much of which is already underway. I believe that these findings support my conclusion that current use of MDMA should be limited to carefully monitored research trials.

In making my decision, I have taken into account the 'Breakthrough Therapy Designation' that has been granted by U.S. Food and Drug Administration. I note that, while this designation indicates that the therapy shows promise, it does not equate to FDA approval. Currently, no comparable country has down-scheduled MDMA to an equivalent category to Schedule 8, and there is no international framework for how to handle psychedelic-assisted therapies.

I have taken into account all 478 responses that were received during the pre-meeting consultation, noting that 453 were supportive of the proposed amendment, 14 partially supportive and 11 opposed. While the submissions indicate significant public support for rescheduling, a significant fraction included no written justification, or directly paraphrased the sponsor, and few submissions were from practicing psychiatrists. I have read and considered all responses in making my interim decision.

I find that the points raised in public submissions from several peak bodies were highly pertinent, noting the following concerns and recommendations:

- The RANZCP advised that further research is required to assess the efficacy, safety, and effectiveness of psychedelic therapies, emphasising that appropriate treatment methodologies and training protocols do not yet exist.
- The Australian Medical Association advised that more high-quality research, using larger-scale studies, is required to establish the safety and efficacy of psychedelic therapies. The risk of psychosis and persistent hallucinations, especially in susceptible subpopulations, is likely to be high.
- Psychedelic Research in Science and Medicine advised that any decision to down-schedule should include an extensive two-year implementation plan. Only a limited number of Australian medical professionals are currently trained to provide MDMA-assisted psychotherapy, and premature down-scheduling may put patients at increased risk of harm.

Having considered the risks to consumers, the lack of training for physicians, and the current state of research, I am of the view that Schedule 9 remains appropriate for MDMA. I note that my decision does not affect current access to MDMA for use in a clinical trial setting. I would also like to note that the supply of MDMA outside of its use in approved clinical trials remains a criminal offence.

Pending the outcome of current clinical research, the scheduling of MDMA could be reconsidered in future applications.

3 Interim decisions on proposed amendments referred to the Advisory Committee on Chemicals Scheduling (ACCS #29, November 2020)

3.1 Interim decision in relation to azoxystrobin

Interim decision

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

Materials considered

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

- The application to amend the current Poisons Standard with respect to azoxystrobin;
- The 124 public submissions, which included no written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Chemicals Scheduling (ACCS #29);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACCS advice to the Delegate

The Committee recommended that the current scheduling for azoxystrobin remains appropriate.

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

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

- Fungicide used for the control of various fungal diseases in turf.
- Could be used up to 500 L in first two years of registration.
- Note: not currently intended for use in the home garden, by removing it from scheduling, there is a potential for similar products to become more attractive or marketed towards household users.

c) the toxicity of a substance:

- Acute oral toxicity >2000 mg /kg bw.
- Acute dermal toxicity >2000mg kg bw.
- Acute inhalational toxicity >2643 mg/m^3.
- Slight skin irritation and slight eye irritation.

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

- The amendment would see the commercial fungicide product no longer carrying the label 'CAUTION' but all other aspects of labelling required by APVMA would remain.
- Label specifies safety, warnings and first aid information.
- Packaging to be in 1-20L HDPE containers.

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

- A separate submission was considered to exempt triticonazole at a 20% cut-off. Acceptance of both proposals would result in a new product containing 10% azoxystrobin and 20% triticonazole being unscheduled.

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

I have made an interim decision to retain the scheduling of azoxystrobin in the current Poisons Standard. This decision is to not exempt azoxystrobin from scheduling, when suspension concentrate preparations contain azoxystrobin at a concentration of 10% or less. The reasons for my interim decision are set out below.

As a slight skin and eye irritant, I find that the current toxicology data for azoxystrobin remains consistent with the SPF 2018 Scheduling Factors for inclusion in Schedule 5. I find that the applicant has presented no compelling evidence to support the safety and reduced toxicity of preparations containing 10% or less azoxystrobin. Care should be taken in the use of products containing this substance to minimise exposure and I am concerned that the exemption of products at this cut-off, would remove the necessary label of 'CAUTION' from products containing ≤10% azoxystrobin.

I note no written public submissions were received in response to this application to amend the current Poisons Standard with regards to azoxystrobin.

With insufficient evidence of reduced toxicity and safety of products containing 10% or less azoxystrobin, I am unable to support the down scheduling of this substance.

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

3.2 Interim decision in relation to triticonazole

Interim decision

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

Materials considered

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

- The application to amend the current Poisons Standard with respect to triticonazole;
- The 124 public submissions, which included no written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Chemicals Scheduling (ACCS #29);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACCS advice to the Delegate

The Committee recommended that the current scheduling for triticonazole remains appropriate.

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

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

- Fungicide used for the control of various fungal diseases in turf.
- Could be used up to 500 L in first two years of registration.
- Note: not currently intended for use in the home garden, by removing it from scheduling, there is a potential for similar products to become more attractive or marketed towards household users.

c) the toxicity of a substance:

– Acute dermal toxicity > 2000 mg/kg bw.

– Acute inhalational toxicity >1400 mg/m^3.

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

– The amendment would see the commercial fungicide product no longer carrying the label 'CAUTION' but all other aspects of labelling required by APVMA would remain.

– Label specifies safety, warnings and first aid information.

– Packaging to be in 1-20L HDPE containers.

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

– A separate submission was considered to exempt azoxystrobin at a 10% cut-off. Acceptance of both proposals would result in a new product containing 10% azoxystrobin and 20% triticonazole being unscheduled.

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

I have made an interim decision to retain the scheduling of triticonazole in the current Poisons Standard. This decision is to not exempt triticonazole from scheduling when suspension concentrate preparations contain triticonazole at a concentration of 20% or less. The reasons for my interim decision are set out below.

The toxicology data for triticonazole remains consistent with the Scheduling Factors for inclusion in Schedule 5, having acute dermal and inhalational toxicity (SPF, 2018). I find that the applicant has presented no compelling evidence to support the safety and reduced toxicity of preparations containing of 20% or less triticonazole. Care should be taken in the use of products containing this substance to minimise exposure and I am concerned that the exemption of products at this cut-off, would remove the necessary label of 'CAUTION' from products containing ≤20% triticonazole.

I note no written public submissions were received in response to this application to amend the current Poisons Standard with regards to triticonazole.

With insufficient evidence of reduced toxicity and safety of products containing 20% or less triticonazole, I am unable to support the down scheduling of this substance.

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

4 Interim decisions on proposed amendments referred to the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #26, November 2020)

4.1 Interim decision in relation to azelaic acid

Interim decision

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

Materials considered

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

- The application to amend the current Poisons Standard with respect to azelaic acid;
- The 129 public submissions, including seven written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #26);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee recommended that the current scheduling of azelaic acid remains appropriate.

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

The reasons for the advice included:

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

- Risks
  - Reported adverse reactions including burning/stinging, pruritus, scaling, erythema, contact dermatitis, oedema and hypopigmentation;
  - Self-diagnosis and treatment for dermatological conditions which require medical assessment.

- Benefits

– Effective treatment of mild-to-moderate acne and papulopustular rosacea.

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

– Use in cosmetics and topical creams for the treatment of mild-to-moderate acne and papulopustular rosacea.

c) the toxicity of a substance:

– The toxicity of the substance is low, producing some eye, skin and mucous membrane irritation.

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

– Azelaic acid cosmeceuticals are marketed online to Australians by international brands without the restrictions imposed by Scheduling. These overseas products also promote therapeutic claims of these cosmetics.

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

I have made an interim decision to retain the scheduling of azelaic acid in the current Poisons Standard, specifically not to accept the proposal to down-schedule azelaic acid to general sales level (unscheduled) in topical preparations containing azelaic acid at a concentration of 10% or less, and up-schedule therapeutic and cosmetic preparations with a concentration greater than 10% to Schedule 5. The detailed reasons for my interim decision are set out below.

I find that there is insufficient evidence to support a 10% cut-off to exempt azelaic acid from scheduling. I am not satisfied that at this cut-off azelaic acid can be supplied at the general sales level with reasonable safety and without any access to health professional advice. While azelaic acid has low toxicity, eye, skin and mucous membrane irritation can occur with reported adverse reactions of burning/stinging, pruritus, scaling, erythema, contact dermatitis, oedema and hypopigmentation. Due to uncertainty of adverse effects, I find that the risks cannot be managed with packaging and labelling in the absence of pharmacist advice.

Reasonable safety, as defined in the Scheduling Handbook[9], requires that the consumer is able to identify and self-manage the condition for which the medicine is intended without health professional input and that the risk of the consumer confusing their condition with more serious diseases or conditions is very small. Misdiagnosis of papulopustular rosacea can occur with more serious chronic inflammatory conditions[10], such as systemic lupus erythematosus (SLE)[11], dermatomyositis[12], Carcinoid syndrome[13] and cutaneous lymphoma[14]. I am of the view that dermatological conditions such as mild-to-moderate acne and papulopustular rosacea require the availability of pharmacist advice. I am concerned that access to azelaic acid at the general sales level, without pharmacist input, may result in self-managed treatment of dermatological conditions which require medical assessment, and for which more appropriate medications are available.

I considered the applicant's statement that the down-scheduling of azelaic acid would increase the availability of superior products widely used in the UK, US and EU in cosmetic and cosmeceuticals. At present there are two Schedule 2 products on the ARTG available in Australia containing azelaic acid at concentrations of 15% and 20%. The proposed amendment to the current Poisons Standard would up-schedule the currently available products from Pharmacy

[9] https://www.tga.gov.au/publication/scheduling-handbook-guidance-amending-poisons-standard
[10] https://pubmed.ncbi.nlm.nih.gov/25101343/
[11] https://pubmed.ncbi.nlm.nih.gov/23053047/
[12] https://pubmed.ncbi.nlm.nih.gov/18827482/
[13] https://pubmed.ncbi.nlm.nih.gov/15656803/
[14] https://pubmed.ncbi.nlm.nih.gov/22508769/

Medicines (Schedule 2) to Schedule 5, reducing the availability for the consumer. In New Zealand, azelaic acid is classified as a 'Pharmacy Only' medicine for dermal use and otherwise, it is a 'Prescription Only' medicine. The European Chemicals agency requires a hazard/warning label for products containing azelaic acid.

I have taken into account the public submissions from Ego Pharmaceuticals, The Australian Medical Association, The Australasian College of Dermatologists, The Pharmaceutical Society of Australia, Accord Australasia, and The Pharmacy Guild of Australia. These submissions noted that the application as proposed would hinder consumer availability of existing Schedule 2 products. I note, a number of these public submissions would support the down-scheduling of azelaic acid if evidence was made available to support a 10% cut-off.

Any future applications to exempt topical azelaic acid at low concentrations, should include evidence to support the cut-off concentrations. I do note that the Australian Industrial Chemical Induction Scheme (AICIS) is currently assessing azelaic acid, which may provide useful safety evidence for future consideration of this substance.

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

4.2 Interim decision in relation to 2-hydroxyethyl methacrylate (2-HEMA)

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the current Poisons Standard in relation to 2-hydroxyethyl methacrylate as follows:

Schedule 5 – Amended entry

2-HYDROXYETHYL METHACRYLATE **except:**

a) when included in dental restorative preparations for therapeutic use; or

b) in nail preparations when labelled "Avoid contact with skin"; or

c) in other preparations containing 0.1 per cent or less of 2-hydroxyethyl methacrylate when labelled "Avoid contact with skin".

Appendix E, Part 2

2-HYDROXYETHYL METHACRYLATE

POISON	STANDARD STATEMENTS
2-HYDROXYETHYL METHACRYLATE	**A (**For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)). **E1 (**If in eyes wash out immediately with water.)**, S1** (If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.)

Appendix F, Part 3

POISON	WARNING STATEMENTS	SAFETY DIRECTION
2-HYDROXYETHYL METHACRYLATE	**28** ((Over) (Repeated) exposure may cause sensitisation	**4** (Avoid contact with skin.)

Index

2-HYDROXYETHYL METHACRYLATE

Schedule 5
Appendix E, Part 2
Appendix F, 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 2-hydroxyethyl methacrylate;
- The 122 public submissions, which included no written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #26);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee recommended that the current Schedule 5 entry for 2-hydroxyethyl methacrylate be amended as follows:

Schedule 5 – Amended entry

2-HYDROXYETHYL METHACRYLATE **except:**

a) when included in dental restorative preparations for therapeutic use; or

b) in nail preparations when labelled "Avoid contact with skin"; or

c) in other preparations containing 0.1 per cent or less of 2-hydroxyethyl methacrylate when labelled "Avoid contact with skin".

Appendix E, Part 2

2-HYDROXYETHYL METHACRYLATE

POISON	STANDARD STATEMENTS
2-HYDROXYETHYL METHACRYLATE	**A (**For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)). **E1 (**If in eyes wash out immediately with water.)**, S1** (If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.)

Appendix F, Part 3

POISON	WARNING STATEMENTS	SAFETY DIRECTION
2-HYDROXYETHYL METHACRYLATE	**28** ((Over) (Repeated) exposure may cause sensitisation	**4** (Avoid contact with skin.)

Index

2-HYDROXYETHYL METHACRYLATE

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

The Committee also advised an implementation date of **1 June 2021.**

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

The reasons for the advice included:

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

– The risk associated with 2-HEMA is likely to be low due to its low concentration.

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

– Proposed novel use in a children's toy.

c) the toxicity of a substance

– At low concentrations, 2-HEMA is not expected to be an irritant.

– The main toxicity concern, sensitisation, is reduced at concentration below 1%, and will be very low.

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

– Proposed product contains 0.09% of the poison and is labelled with appropriate warnings

e) the potential for abuse of a substance

Nil

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

– The Committee raised concerns that the product, if accidentally applied to the skin and exposed to sunlight, may cause burns. Members recommended that delegate consider additional label warnings regarding this.

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

I have made an interim decision to amend the Schedule 5 entry for 2-hydroxyethyl methacrylate (2HEMA) and exclude preparations up to 0.1 per cent from scheduling. The reasons for my decision are set out below.

2HEMA was first scheduled in 2015, based on evidence presented in the 2014 AICIS (formally NICNAS) IMAP report. The identified areas of toxicity were skin sensitisation (limited data), moderate eye irritancy and slight skin irritancy (limited data). In the current scheduling consideration, the applicant has not presented any new data to support a cut-off of 1 per cent and I am not persuaded by the statement made by the applicant that the skin sensitisation "studies referenced appear to be for concentrations of 25 per cent and over. The substance is classified as a category 1 skin sensitiser [GHS] so wouldn't be considered hazardous at a concentration less than 1 per cent."

I note that the proposed product consists of a gel containing 0.09 per cent 2HEMA, added as an active ingredient (crosslinking monomer) of the product and not present as a residual monomer in a polymer. For this reason, I do not agree with the applicants statement that the proposed cut-off is equivalent to the 1 per cent exemption in the methyl-methacrylate Schedule 6 entry and ethyl-methacrylate Schedule 5 entry. This cut-off applies only to these two substances when present "as a residual monomer in a polymer" i.e. as unavoidable impurities.

In making my decision to exempt 2HEMA at the lower limit of 0.1 per cent, I have taken into account two closely related substances, hydroxyethyl acrylate and hydroxypropyl acrylate. Both these substances have been assigned "Specific Concentration Limits" for sensitisation of 0.2% by EU harmonised classifications, indicating they are considered potent sensitisers. I am satisfied that a concentration of 0.1 per cent is protective based on the use pattern of products containing 2HEMA and the likely toxicity end point of concern being skin sensitisation.

I note that no public submissions were received in response to the pre-meeting consultation under regulation 42ZCZK.

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

Proposed implementation date

1 June 2021.

4.3 Interim decision in relation to magnesium hydroxide

Interim decision

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

Appendix B, Part 3 – New Entry

SUBSTANCE	REASON FOR LISTING	AREA OF USE
MAGNESIUM HYDROXIDE	A (Low toxicity)	7.1

INDEX – New Entry

MAGNESIUM HYDROXIDE

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 magnesium hydroxide;
- The 123 public submissions, including one written submission, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #26);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee recommended the down-scheduling of magnesium hydroxide to Appendix B in the current Poisons Standard.

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

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

The reasons for the advice included:

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

- Benefits

– Insecticide to control whiteflies, mites, thrips and aphids in vegetable crops.

– Is an active and excipient ingredient in biologicals, export only, listed medicines, over the counter, prescription medicines and as an excipient in devices.

– Magnesium hydroxide is also a constituent of fire retardants.

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

– Insecticide to control whiteflies, mites, thrips and aphids in vegetable crops.

– The intended use is up to 1200 L (1680 kg) of product per day, sufficient to treat 600 ha.

– The proponent states that the product is intended for 'professional use', however, as this will be an unscheduled item there is no regulatory framework to enforce this.

c) the toxicity of a substance:

– Not acutely toxic, is not an eye irritant, skin irritant or a skin sensitiser.

– Powder in the eye could be a moderate eye irritant.

– There is little evidence of carcinogenicity, genotoxicity, reproductive or developmental toxicity.

– There are a number of cases of magnesium-salt overdoses, some resulting in death. The main clinical symptoms related to hypermagnesaemia include muscle weakness, hypertonia and cardiovascular responses. The observed effects are mostly due to an electrolyte imbalance manifested by an increased Mg^{2+}/Ca^{2+} blood level ratio.

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

– Inclusion in Appendix B provides clarity for agvet chemical producers that the substance has been through the scheduling process.

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

I have made an interim decision to exclude magnesium hydroxide from scheduling via inclusion in Appendix B of the Poisons Standard. The reasons for my decision are set out below.

Magnesium hydroxide is present in a number of products, ranging from agricultural pesticides to medicines and cosmetics, and poses low risk in all product categories. Studies investigating chronic exposure to magnesium hydroxide do not identify any adverse effects or health problems. Products containing magnesium hydroxide for agricultural use are not acutely toxic, not eye or skin irritants or skin sensitisers. There is little evidence of carcinogenicity, genotoxicity, reproductive or developmental toxicity. I find this substance does not meet the factors for inclusion in the Schedules of the Poisons Standard.

I am making the new entry in Appendix B for magnesium hydroxide to provide clarity for AgVet chemical producers that the substance has been through the scheduling process.

I note the one written public submission which was in support of the proposal.

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

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

Proposed implementation date

1 June 2021

4.4 Interim decision in relation to tetrahydrofurfuryl alcohol

Interim decision

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

Schedule 6 – New Entry

TETRAHYDROFURFURYL ALCOHOL, excluding its derivatives.

Index

TETRAHYDROFURFURYL ALCOHOL, excluding its derivatives.

Schedule 6

Materials considered

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

- The application to amend the current Poisons Standard with respect to THFA;
- The 122 public submissions, which included no written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #26);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee recommended that THFA, excluding its derivatives, be entered in Schedule 6 of the Poisons Standard as follows:

Schedule 6 – New Entry

TETRAHYDROFURFURYL ALCOHOL, excluding its derivatives.

Index

TETRAHYDROFURFURYL ALCOHOL, excluding its derivatives.

Schedule 6

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

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included: (a) the risks and benefits of the use of a substance; (b) the 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; (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 toxicity of this substance

- Benefits

– Use in a wide variety of products

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

– THFA is intended for commercial/industrial use as a solvent in certain agricultural chemicals.

– In Australia, THFA is listed as a proprietary ingredient flavouring in two ARTG products, and as a component of fragrances (which is not exclusive to cosmetics). In these preparations it is expected to be in concentrations of <1%.

– Internationally, THFA is reported to be used as a solvent in a wide range of products, including adhesives, cosmetics, fertilisers and washing & cleaning products.

c) the toxicity of a substance:

– Acute oral and inhalational toxicity.

– Eye irritation (not reversible within 7 days).

– Slight skin irritant.

– Moderate reproductive toxicity (with effects on the male reproductive tract).

– Developmental toxicity.

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

Labelling:

Appendix E, Part 1
Standard Statement

- E1 If in eyes wash out immediately with water

Appendix F, Part 1
Warning Statement

- 67 Do not use if pregnant or likely to become pregnant

Appendix F, Part 2
Safety Direction

- 1 Avoid contact with eyes
- 31 Do not use on broken skin

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

– There are currently no products containing THFA listed on the Public Chemical Registration Information System Search (PubCRIS). Its inclusion in formulations is currently protected information as it is not a scheduled solvent.

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

I have made an interim decision to amend the current Poisons Standard and create a new Schedule 6 entry for THFA, excluding its derivatives. The reasons for my decision are set out below.

I have determined that THFA meets the Schedule 6 Scheduling Factors as outlined in the Scheduling Policy Framework (SPF) 2018. Concordant with the Scheduling Factors for inclusion in Schedule 6, THFA is of low acute oral (LC_{50} >2000 mg/kg bw), dermal (LD_{50} > 5000 mg/kg bw) and inhalation toxicity (LC_{50} > 3100 mg/m^3) and is not a skin sensitiser and is a slight skin irritant. However, THFA is a severe eye irritant and shows evidence of reproductive and developmental toxicity that are consistent with inclusion in Schedule 6. I am of the view that THFA poses a moderate health hazard and a moderate risk of producing irreversible toxicity.

The new entry in the Poisons Standard is required to mitigate the risk of the substance by including the corresponding "POISON" warning and the requirement of personal protective equipment on product label. This inclusion is important in providing suitable product-based safety directions to reduce reasonably foreseeable harm to users. The APVMA has confirmed that the management of health risks associated with AgVet use of THFA is achieved primarily via label directions, established from a consideration of the acute hazards of the product in conjunction with possible adverse health effects from repeated exposure to both workers and the general-public.

I have excluded THFA derivatives from the Schedule 6 entry, as there is evidence that they may have a different hazard profile to THFA. As of December 2020, THFA was listed as a proprietary ingredient in two ARTG products, and as a component of fragrances (which is not exclusive to cosmetics). In these preparations it is expected to be in concentrations of <1%. At present I am unable to implement a concentration cut-off or exemption for THFA in Schedule 6, as there is insufficient evidence to support reduced toxicity of THFA at lower concentrations.

Due to the widespread presence of the substance in many different products, I have decided on a later implementation date of 1 June 2021, to allow time for industry to implement appropriate labelling.

I note that no public submissions were received in response to the pre-meeting consultation under regulation 42ZCZK.

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

Proposed implementation date

1 June 2021

4.5 Interim decision in relation to cannabidiol (private application)

Interim decision

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

Materials considered

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

- The application to amend the current Poisons Standard with respect to cannabidol;
- The 228 public submissions, including 20 written submissions, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #26);
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of the substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of Joint ACMS-ACCS advice to the Delegate

The Committee advised against amending the current Schedule 4 entry for cannabidiol to explicitly capture synthetic and semi-synthetic cannabidiol.

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

The reasons for the advice included:

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

- Benefits:

– Synthetic (-)-CBD has a similar safety profile when compared with naturally derived CBD, provided related substances and impurities are the same or excluded.

- Risks:

– (+)-CBD has been shown to have modest affinity at CB1 and CB2 receptors and therefore could potentially have psychoactive effects, however this is currently no substantive evidence that (+)-CBD causes THC-like psychoactive effects.

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

– A number of emerging therapeutic indications for CBD including epilepsy.

c) the toxicity of a substance

- Safety and tolerability of (-)-CBD is well established.
- Pharmacological effects of (+)-CBD are uncertain. Potential for psychoactive effects but not demonstrated. Limited available clinical evidence for (+)-CBD products does not suggest significant psychoactive effects.

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

Nil

e) the potential for abuse of a substance

- Limited potential for abuse of (-)-CBD containing products.
- (+)-CBD may be psychoactive; whether there is a potential for abuse is unknown.

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

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

I have made an interim decision not to amend the Schedule 4 entry for cannabidiol (CBD) to explicitly capture synthetic and semi-synthetic cannabidiol. The reasons for my decision are set out below.

I am of the view, that whilst not explicitly stated in the current Schedule 4 entry, both synthetic and non-synthetic forms of CBD are already captured under this entry. This is in line with *Part 1 Interpretation section 1 (2) (a)* of the Poisons Standard, which states "Unless the contrary intention appears a reference to a substance in a Schedule or an Appendix to this Standard includes that substance prepared from natural sources or artificially."

I note that CBD is normally taken to refer to the naturally occurring (-)-enantiomer extracted from cannabis, however the current Schedule 4 entry for CBD does not specify an enantiomer. I have considered currently available data on (-)-CBD and (+)-CBD and find, there is limited evidence of significant differences in pharmacological activity. For this reason, I have decided not to individually schedule the two CBD enantiomers.

I have considered the need to limit synthetic cannabinoid impurities in the Schedule 4 entry and find there is no justification for the inclusion of impurities in a synthetically derived CBD product. It is important to prevent presence of synthetic cannabinoids in CBD products as they are potentially of greater potency than those that are naturally occurring and at the 2% limit proposed in the application, could exert a psychoactive effect.

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