



Australian Government

Department of Health

Therapeutic Goods Administration

Notice of final decision to not amend the current Poisons Standard - Psilocybin and MDMA

15 December 2021

TGA Health Safety
Regulation

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1 Notice of final decisions to not amend the current Poisons Standard

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

- the decisions made by a delegate of the Secretary pursuant to regulation 42ZCZR;
- the reasons for the final decisions; and
- the date of effect of the decisions.

2 Final decision on a proposed amendment referred to the Advisory Committee on Medicines Scheduling (ACMS #32, November 2020)

2.1 Final decision in relation to psilocybin

Proposal

The applicant proposed to down-schedule psilocybin from Schedule 9 (prohibited substance) to Schedule 8 (controlled substance) for use in a medically controlled environment. As a Schedule 9 substance, its use is limited to medical and scientific research, subject to regulatory controls. The request for down-scheduling to Schedule 8 was intended to increase patient access through additional pathways such as the Special Access Scheme (SAS).

The applicant specifically proposed the following amendment to the Schedule 9 entry and the creation of a new Schedule 8 entry with respect to psilocybin:

Schedule 9 – Amend entry

PSILOCYBINE **except** when included in Schedule 8.

Schedule 8 – New Entry

PSILOCYBINE for use in the treatment of medical conditions:

- a) in preparation for oral use as part of psychotherapy under the authorisation of a treating psychiatrist or specialist addiction physician in a medically controlled environment;
- b) manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or
- c) imported or manufactured in Australia as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or
- d) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989*.

Index – Amend Entry

PSILOCYBINE

Schedule 9

Schedule 8

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to confirm the interim decision and not amend the current Poisons Standard in relation to psilocybin.

Materials considered

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

- The [application](#) to amend the current Poisons Standard with respect to psilocybin;

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- The 575 [public submissions](#), 357 of which included a written component, 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);
 - The 728 [public submission](#), 271 of which included a written component, received in response to the [interim decision consultation](#) under regulation 42ZCZP of the Regulations;
 - 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 \(2020\)](#);
 - A clinical memorandum by *the Royal Australian and New Zealand College of Psychiatrists*, [Therapeutic use of psychedelic substances \(2020\)](#);
 - The [Independent expert panel report](#) on an evaluation of the therapeutic value, benefits and risks of methylenedioxymethamphetamine (MDMA) and psilocybin for the treatment of mental, behavioural or developmental disorders (the Expert Report) and the panel's analysis presented at ACMS meeting #36 regarding the quality of the studies that were evaluated;
 - Unsolicited submissions made to the Delegate and ACMS meeting #36 following publication of the Expert Report;
 - The advice received from the meeting #36 of the ACMS following the Expert Report;
 - The international regulatory status of psilocybin and access pathways;
 - Section 52E of the *Therapeutic Goods Act 1989* (the Act). In particular, subsection 52E(1) of the Act. Noting that the following matters must be taken into account (where relevant):
 - (a) the risks and benefits of the use of a substance;
 - (b) the purpose for which a substance is to be used and the extent of use of a substance;
 - (c) the toxicity of a substance;
 - (d) the dosage, formulation, labelling, packaging and presentation of a substance;
 - (e) the potential for abuse of a substance; and
 - (f) any other matters that the Secretary considers necessary to protect public health
 - The Australian Health Ministers' Advisory Council's [Scheduling Policy Framework for medicines and chemicals 2018](#) (the SPF);
 - The [Scheduling handbook: Guidance for amending the Poisons Standard](#).

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

I have made a final decision to confirm my [interim decision](#) to not amend the current Poisons Standard with respect to psilocybin. In making my final decision, I have considered:

- the material detailed in the interim decision published on the TGA website on 3 February 2021;
- the 728 public submissions received in response to the call for further submissions published on 20 July 2021 under regulation 42ZCZP of the Regulations;
- the Expert Report;
- further advice received at ACMS meeting #36 at which the Expert Report was considered;
- the SPF scheduling factors; and
- the criteria prescribed by s 52E of the Act.

I acknowledge that many written public submissions were in opposition to the interim decision and followed the same pattern as the pre-meeting submissions.

- The submissions against the interim decision not to make the proposed amendment (i.e. in support of the amendment), were predominantly from individuals who were consumers/patients with a personal interest in the scheduling decision, as well as experts who had previously provided input on the scheduling application and the initial public submissions. These submissions:
 - Cited a lack of evidence of abuse potential and contended that there are medicines that are more addictive and likely to be abused already included in Schedule 8 such as methadone, ketamine and cannabis.
 - Suggested that psychiatrists should not be the only health care provider group allowed to provide psychedelic-assisted psychotherapy and that consideration should be given to permitting health professionals such as psychologists, counsellors and other suitably qualified and trained mental health practitioners to provide this psychedelic-assisted psychotherapy.
- The Royal Australian and New Zealand College of Psychiatrists (RANZCP) supported the interim decision, i.e. did not support the proposed amendment. Similarly, the Australian Medical Association (AMA) did not support the down scheduling of psilocybin, indicating that more high-quality research using larger scale studies must be completed in order to determine the safety and efficacy of using psilocybin for mental illness.

In accordance with the reasons for my interim decision, I am not persuaded by the submissions against the interim decision. I remain of the view that psilocybin meets the scheduling factors for Schedule 9, and that retaining the current entry in Schedule 9 ensures appropriate control over access to this substance. I have reached this conclusion having weighed the risks to patients and public health from any increased access against the currently limited evidence of benefit. Specifically:

- The benefit is very limited because psilocybin studies indicate only potential therapeutic value in circumstances where the treatment was provided to subjects within the setting of a clinical trial;
 - the therapeutic value is not established, which corresponds to the scheduling factors for Schedule 9.

- In relation to the risks, I am satisfied that psilocybin poses a high danger for both acute and long-term effects if abused or misused by way of access outside of strictly controlled medical and scientific research settings. This could arise due to diversion for illicit purposes across the supply chain if there is down-scheduling from Schedule 9. Given this increased risk to individuals of acute and long-term effects, a high level of control across the supply chain commensurate with Schedule 9 is warranted.

The detailed reasons for my view are as follows.

In relation to paragraphs 52E(1)(a) and (b) of the Act, I have considered the conclusion of the Panel that psilocybin showed potential for the treatment of treatment-resistant depression (**TRD**) in highly selected populations when administered in closely supervised settings and with intensive support. I acknowledge the Panel's conclusion:

'We conclude that MDMA and psilocybin may show promise in highly selected populations but only where these medicines are administered in closely clinically supervised settings and with intensive professional support.'

The ACMS recommended at its 36th meeting that no change be made to the scheduling of psilocybin as the current scheduling remains appropriate and further data and evidence are required to justify down-scheduling at this time. I agree with the Committee that the preliminary findings from clinical trials (although still in early phases) evaluated by the Panel are promising for TRD using psilocybin-assisted psychotherapy. However, given the extent and issues with the quality of the completed studies detailed by the Panel, I reiterate my statement in my interim decision that I consider that evidence is still emerging, and the therapeutic value of psilocybin has not been established.

I agree that the safety profile of psilocybin under tightly supervised psychotherapy conditions used in clinical trials is quite reasonable (and differs from illicit use). I acknowledge in relation to paragraph 52E(1)(e) of the Act that the risk of addiction is low in a highly controlled environment for psilocybin-assisted psychotherapy. However, I am concerned about the increased likelihood of misuse and diversion (at any stage of the supply chain) for recreational use and the accompanying safety risk from acute and long-term effects that may follow, were there to be any down-scheduling.

In exercising the power under subsection 52D(2), I must comply with the SPF.

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

1. The substance is included in Schedule I or II of the *United Nations Single Convention on Narcotic Drugs 1961* or in Schedule II or III of the *United Nations Convention on Psychotropic Substances 1971*.
2. The substance has an established therapeutic value but its use, at established therapeutic dosage levels, is recognised to produce dependency and has a high propensity for misuse, abuse or illicit use. The substance has an established therapeutic value but by reason of its novelty or properties carries a substantially increased risk of producing dependence.

The factors to consider for Schedule 9 are:

1. The substance is included in either Schedule IV to the *United Nations Single Convention on Narcotic Drugs 1961* or in Schedule I of the *United Nations Convention on Psychotropic Substances 1971*.
2. The substance has no currently established therapeutic value and is likely to present a high risk of dependency, abuse, misuse or illicit use.

Considering paragraphs 52E(1)(a) and (c) of the Act, psilocybin can cause tachycardia and transient increases in blood pressure, and the risk of developing psychosis when misused may be high. The medium to long-term effects of psilocybin-assisted psychotherapy are unknown, particularly in vulnerable populations, and these must be established in a clinical setting. The lethal dose is thought to be 6 g although evidence around toxicity requires further investigating as does potential adverse effects relating to multi-drug toxicity.

Outside a highly controlled environment, these potential effects do pose a risk to the community, were there to be increased access by way of down-scheduling from Schedule 9. At this time it is appropriate for psilocybin to remain in Schedule 9 where a high level of control can be maintained through prohibition of access and supply to minimise risk of misuse or diversion into illicit activities.

Moreover, I am of the view that ensuring administration of psilocybin according to the strict protocols used in clinical trials that have showed promise of efficacy to date would be hard to achieve outside a clinical trial framework. A key qualification of the Expert Report's conclusion that psilocybin may show promise in highly selected populations would not exist. Appropriate controls are best supported by psilocybin remaining a Schedule 9 substance. In addition, considering paragraph 52E(1)(d) of the Act, it is unclear to me how psilocybin would be dispensed/supplied to a practitioner were it to be down-scheduled, and an optimal therapeutic dose has not yet been established.

I agree with the findings from a paper published with the Australian clinical context in mind (referenced in a public submission in response to the Expert Report and interim decision) that translation from a clinical trial setting to the community will depend on adequate expertise, procedures and ethical standards.¹ The potential for poor clinical practice is significant and could prove to be a hurdle affecting public health. Given evidence of the risks of psilocybin, and that its benefits are still emerging, I am of the view that limiting access to psilocybin as a Schedule 9 substance is most appropriate to ensure more information is obtained through rigorous clinical trials. There have to date only been a small number of studies which have been of low quality and the potential risks to patients remains.

These observations taken together lead me to the view that psilocybin best fits the SPF scheduling factors for Schedule 9 for the purpose of paragraph 52E(2)(a) of the Act. In relation to the matters specified under subsection 52E(1) of the Act, maintaining the current entry for psilocybin in Schedule 9 provides the appropriate controls over access to address the risks of the substance when weighed against the emerging evidence of benefit.

Consistent with the advice provided to me by the ACMS, I am not satisfied that psilocybin fits the Schedule 8 scheduling factors set out in the SPF as (i) the therapeutic value has, without the completion of further high-quality clinical trials, not been established; and (ii) psilocybin is in Schedule 1 to the United Nations Convention on Psychotropic Substances 1971. Psilocybin best fits the factors for Schedule 9 also in relation to the high propensity for misuse outside of a strict clinical trial setting due to an increased likelihood of diversion under any down-scheduling; a high level of control is required through prohibition of possession, sale, or use commensurate with the factors for Schedule 9.

Considering paragraph 52E(1)(f) of the Act, regarding any other matters considered relevant to protect public health, I note that in Australia all States and Territories permit clinical trials for

¹ Williams ML, Korevaar D, Harvey R, Fitzgerald PB, Likhaitzky P, O'Carroll S, Puspanathan P, Ross M, Strauss N and Bennett-Levy J (2021) Translating Psychedelic Therapies From Clinical Trials to Community Clinics: Building Bridges and Addressing Potential Challenges Ahead. *Front. Psychiatry* 12:737738. doi: 10.3389/fpsy.2021.737738 referred to as part of a submission to the Delegate and ACMS following publication of the Expert Report.

Schedule 9 substances, subject to individual regulatory controls. To date the TGA has been notified of seven clinical trials, and the Australian New Zealand Clinical Trials Registry lists two clinical trials (not yet recruiting), investigating the use of psilocybin in mental illness. Considering the applicant's proposal and public submissions received, I note that access to psilocybin internationally in comparable jurisdictions, including Canada, the United States, and the United Kingdom, is generally limited to clinical trials. In the US psilocybin has been designated by the United States Food and Drug Administration (FDA) as a 'breakthrough therapy' for [TRD](#).²

In summary, I am of the view that although findings from clinical trials are promising for TRD further evidence is required to establish therapeutic value and outweigh the risks from misuse or diversion for illicit use across the supply chain that may arise from any down-scheduling. I note that my decision does not affect current access to psilocybin for use in a clinical trial setting under Schedule 9. The outcomes of further clinical trials could result in there being more supportive evidence in the future. Down-scheduling could be further considered if there were more evidence of therapeutic value from such clinical trials. There are still provisions for clinical trials by approval of Commonwealth and/or State or Territory health authorities, with the potential to obtain further evidence which could inform future application for the down-scheduling of psilocybin.

² Psychedelics and Psychedelic-Assisted Psychotherapy – <https://doi.org/10.1176/appi.ajp.2019.19010035>

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

Proposal

The applicant proposed to down-schedule MDMA from Schedule 9 (prohibited substance) to Schedule 8 (controlled substance) for use in a medically controlled environment. As a Schedule 9 substance, its use is limited to medical and scientific research, subject to regulatory controls. The request for down-scheduling to Schedule 8 was intended to increase patient access through additional pathways such as the Special Access Scheme (SAS).

The applicant specifically proposed the following amendment to the Schedule 9 entry and the creation of a new Schedule 8 entry with respect to N, α -Dimethyl-3,4-(methylenedioxy)phenylethylamine (MDMA) as follows:

Schedule 9 – Amend entry

N, α -Dimethyl-3,4-(methylenedioxy)phenylethylamine *(MDMA) **except when in Schedule 8.**

Schedule 8 – New Entry

N, α -Dimethyl-3,4-(methylenedioxy)phenylethylamine *(MDMA) for use in the treatment of medical conditions:

- a) in preparation for oral use under the authorisation of a treating psychiatrist or addiction specialist physician in a medically controlled environment;
- b) manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or
- c) imported or manufactured in Australia as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or
- d) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989*.

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N, α -Dimethyl-3,4-(methylenedioxy)phenylethylamine

cross reference: 3,4-METHYLENEDIOXY-N- α -DIMETHYLPHENYLETHYLAMINE, mdma

Schedule 9

Schedule 8

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to confirm the interim decision and not amend the current Poisons Standard in relation to MDMA.

Materials considered

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

- The [application](#) to amend the current Poisons Standard with respect to MDMA;
- The 478 [public submissions](#), 254 of which included a written component, received in response to the [pre-meeting consultation](#) under regulation 42ZCZK of the Regulations;

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- The advice received from the meeting of the Advisory Committee on Medicines Scheduling (ACMS #32);
 - The 605 [public submissions](#), 234 of which included a written component, received in response to the [interim decision consultation](#) under regulation 42ZCZP of the Regulations;
 - The [ClinicalTrials.gov](#) database, provided by the US 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](#);
 - A clinical memorandum by *the Royal Australian and New Zealand College of Psychiatrists*, [Therapeutic use of psychedelic substances \(2020\)](#);
 - The [Independent expert panel report](#) on an *evaluation of the therapeutic value, benefits and risks of methylenedioxymethamphetamine (MDMA) and psilocybin for the treatment of mental, behavioural or developmental disorders* (the **Expert Report**) and the panel's analysis presented at ACMS #36 regarding the quality of the studies that were evaluated;
 - Unsolicited submissions made to the Delegate and ACMS meeting #36 following publication of the Expert Report;
 - The advice received from the 36th meeting of the Advisory Committee on Medicines Scheduling following the Expert Report;
 - Section 52E of the Therapeutic Goods Act 1989 (the **Act**). In particular, subsection 52E(1) of the Act. Noting that the following matters must be taken into account (where relevant):
 - (a) the risks and benefits of the use of a substance;
 - (b) the purpose for which a substance is to be used and the extent of use of a substance;
 - (c) the toxicity of a substance;
 - (d) the dosage, formulation, labelling, packaging and presentation of a substance;
 - (e) the potential for abuse of a substance; and
 - (f) any other matters that the Secretary considers necessary to protect public health;
 - The Australian Health Ministers' Advisory Council's [Scheduling Policy Framework](#) for medicines and chemicals 2018 (the **SPF**);
 - The [Scheduling handbook: Guidance for amending the Poisons Standard](#).

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

I have made a final decision to confirm my [interim decision](#) to not amend the current Poisons Standard with respect to MDMA. In making my final decision, I have considered:

- the material detailed in the interim decision published on the TGA website on 3 February 2021;
- the 478 public submissions received in response to the call for further submissions published on 20 July 2021 under regulation 42ZCZP of the Regulations;

- the Expert Report;
- further advice received at ACMS meeting #36 at which the Expert Report was considered;
- the SPF scheduling factors; and
- the criteria prescribed by section 52E of the Act.

I note that submissions in response to the interim decision broadly followed the same pattern as the pre-meeting submissions.

- The submissions against the interim decision not to make the proposed amendment (i.e. in support of the amendment), were predominantly from individuals who were consumers/patients with a personal interest in the scheduling decision, as well as experts who had previously provided input on the scheduling application and the initial public submissions. These submissions:
 - Cited a lack of evidence of abuse potential and contended that there are medicines that are more addictive and likely to be abused that are already included in Schedule 8 such as methadone, ketamine and cannabis.
 - Suggested that psychiatrists should not be the only health care provider group allowed to provide psychedelic-assisted psychotherapy and that consideration should be given to permitting health professionals such as psychologists, counsellors and other suitably qualified and trained mental health practitioners to provide this psychedelic assisted psychotherapy.
- The Royal Australian and New Zealand College of Psychiatrists (RANZCP) supported the interim decision, i.e. did not support the proposed amendment. Similarly, the Australian Medical Association (AMA) did not support the down scheduling of MDMA, indicating that more high-quality research using larger scale studies must be completed in order to determine the safety and efficacy of using MDMA for mental illness.

In accordance with the reasons for my interim decision, I am not persuaded by the submissions against the interim decision. Consistent with the reasons for my interim decision, I remain of the view that MDMA meets the scheduling factors³ for Schedule 9, and that the controls surrounding access under Schedule 9 remain appropriate.

In reaching this view, I have weighed the risks to patients and public health from any increased access, against the currently limited evidence of benefit in accordance with paragraph 52E(1)(a) of the Act. Specifically:

- The benefit is very limited because MDMA studies indicate only potential therapeutic value in circumstances where the treatment was provided to subjects within the setting of a clinical trial;
 - the therapeutic value is not established, which corresponds to the scheduling factors for Schedule 9.
- In relation to the risks, I am satisfied that MDMA poses a high danger for both acute and long-term effects if abused or misused by way of access outside of strictly controlled medical and scientific research settings. This could arise due to diversion for illicit purposes across the supply chain if there is down-scheduling from Schedule 9. Given this increased risk to

³ AHMAC – Scheduling policy framework for medicines and chemicals

<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>

individuals of acute and long-term effects, a high level of control across the supply chain commensurate with Schedule 9 is warranted.

The details of my reasons for this view are as follows.

In relation to paragraphs 52E(1)(a) and (b) of the Act, I have considered the findings of the Panel that there is evidence of statistically significant differences in symptom scores when trial participants were administered MDMA doses of greater than 100 mg in comparison with inactive or active controls – when combined with psychotherapy. Furthermore, that MDMA also resulted in statistically significant improvements in social anxiety in adults with autism when compared to placebo.

However, I am of the view that there were several limitations to these findings including the small number of studies (eight in total and only six looked at Post Traumatic Stress Disorder (PTSD)). Moreover, the Panel assessed the study quality as being poor (low credibility – namely, despite studies being described as double-blinded, patients may still have been aware of their treatment allocation) and the overall certainty of the conclusions from the evidence is low. I acknowledge the Panel's conclusion:

'We conclude that MDMA and psilocybin may show promise in highly selected populations but only where these medicines are administered in closely clinically supervised settings and with intensive professional support.'

The Expert Report stated that there was evidence showing potential for efficacy of MDMA-assisted psychotherapy for PTSD, with weaker evidence of an effect for the treatment of social anxiety in adults with autism. The emerging evidence of efficacy has only been demonstrated in highly selected populations and where MDMA was administered in closely clinically supervised settings with intensive professional support.

The ACMS recommended at its 36th meeting that no change be made to the scheduling of MDMA as the current scheduling remains appropriate. The Committee's view was that further data and evidence are required in order to justify down-scheduling MDMA at this time.

In exercising the power under subsection 52D(2), I must comply with the SPF.

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

1. The substance is included in Schedule I or II of the *United Nations Single Convention on Narcotic Drugs 1961* or in Schedule II or III of the *United Nations Convention on Psychotropic Substances 1971*.
2. The substance has an established therapeutic value but its use, at established therapeutic dosage levels, is recognised to produce dependency and has a high propensity for misuse, abuse or illicit use. The substance has an established therapeutic value but by reason of its novelty or properties carries a substantially increased risk of producing dependence.

The factors to consider for Schedule 9 are:

1. The substance is included in either Schedule IV to the *United Nations Single Convention on Narcotic Drugs 1961* or in Schedule I of the *United Nations Convention on Psychotropic Substances 1971*.
2. The substance has no currently established therapeutic value and is likely to present a high risk of dependency, abuse, misuse or illicit use.

I am of the view, consistent with the advice provided to me by the ACMS and for the purposes of paragraph 52E(2)(a) of the Act, that MDMA does not fit the Schedule 8 scheduling factors set out in the SPF because:

- MDMA is in Schedule 1 to the *United Nations Convention on Psychotropic Substances 1971*; and
- there is only emerging evidence of potential benefits of MDMA in treatment of PTSD, noting that research is promising but the therapeutic value has not been established.

MDMA more appropriately fits the Schedule 9 scheduling factors.

In accordance with paragraph 52E(1)(a) of the Act, I consider that the benefits of MDMA have not been fully established, although there is emerging evidence in treating PTSD, with demonstrated low risk of adverse events in controlled settings. Furthermore, I am concerned with how, in accordance with the qualification included in the Expert Report's conclusion about the promise of MDMA in highly selected populations, namely the controlled clinical trial environment, can be replicated in real-world settings. In relation to paragraph 52E(1)(d) of the Act, it is unclear to me how MDMA would be dispensed/supplied to a practitioner were it to be down-scheduled, and an optimal therapeutic dose has not yet been established.

I agree with the ACMS that MDMA appeared to be well tolerated in all the studies evaluated for the Expert Report and that MDMA appears to have an acceptable adverse effect profile. However, this was in a highly controlled environment with short-term dosing only and cannot be extrapolated to use in environments with less control.

I have considered the impacts on public health, were access to MDMA to be increased through an entry in Schedule 8 of the Poisons Standard, in relation to paragraphs 52E(1)(a), (e) and (f) of the Act. I am of the view that there would be an increased risk of misuse by individuals outside of a highly controlled environment or diversion for illicit purposes, including due to how Schedule 8 substances are controlled through State and Territory implementation of the Poisons Standard.

Further, in relation to paragraph 52E(1)(e) of the Act and the potential for abuse of the substance, I have considered the risks of MDMA use outside of the highly controlled environment, in the situation of diversion. 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 shows some evidence of causing dependence and may additionally lead to cognitive dysfunction in the medium or long term. These effects, including dependence, are also relevant to paragraph 52E(1)(c) of the Act and the toxicity of the substance, and 52E(1)(d) and the potential for abuse of the substance.

The risks for individuals undergoing MDMA-assisted psychotherapy in a highly controlled environment are not high. However, outside a highly controlled environment, the above acute and long-term effects do pose a risk to the community, were access provided under Schedule 8. At this time, I am of the view that it is not appropriate for MDMA to be accessed under Schedule 8 and it is appropriate for MDMA to remain in Schedule 9 where a high level of control can be maintained through prohibition of access and supply to minimise risk of misuse or diversion into illicit activities.

In alignment with the scheduling factors for Schedule 9 substances in the SPF and pursuant to paragraph 52E(2)(a) of the Act, I consider that a rigorous clinical trial process is important at a

stage when evidence is only emerging and there are potential risks to individual patients such as to warrant limiting use to strictly controlled medical and scientific research. Scheduling exclusively in Schedule 9 is best suited to this requirement. There is currently only a small number of completed studies and I agree with the Panel's view that these studies are of low quality. Consequently, I am of the view that clinical trial controls provided under Schedule 9 should remain to ensure that further information of the appropriate quality is obtained.

I agree with the findings from a paper published with the Australian clinical context in mind (referenced in a public submission in response to the Expert Report and interim decision) that translation from a clinical trial setting to the community will depend on adequate expertise, procedures and ethical standards.⁴ The potential for poor clinical practice is significant and could prove to be a hurdle affecting public health.

In relation to paragraph 52E(1)(e) of the Act, I acknowledge that although the risk of addiction is low in a highly controlled environment for MDMA-assisted psychotherapy, there is a risk of diversion at any stage of the supply chain for recreational use that would be greater were MDMA down-scheduled to Schedule 8, even with Appendix D controls.

Considering paragraph 52E(1)(f) of the Act, regarding any other matters considered relevant to protect public health, I note that in Australia all States and Territories permit clinical trials for Schedule 9 substances, subject to individual regulatory controls. To date the TGA has been notified of one clinical trial, and the Australian New Zealand Clinical Trials Registry lists two clinical trials (one recruiting and one not yet recruiting), investigating the use of MDMA in mental illness.

I acknowledge the information provided by the applicant and respondents to the calls for public submissions about access to MDMA internationally and note that access in comparable jurisdictions is generally limited to clinical trials. I note that there have been clinical trials of MDMA for its potential to treat conditions such as anxiety and PTSD in countries including Canada, Israel and the United States. In the United States, the Food and Drug Administration (FDA) has approved an expanded access program of trials for a small number of people with treatment-resistant PTSD. These trials are for individuals who do not meet the criteria to participate in standard Phase 3 trials, have access to the treatment for a serious or life-threatening condition, and for whom conventional treatments have failed.⁵ The FDA has granted 'breakthrough therapy' designation for the use of MDMA in PTSD.⁶

In summary, I agree that there is potential benefit of MDMA in treatment of PTSD, however MDMA should remain in Schedule 9 at this time. I note that my decision does not affect current access to MDMA for use in a clinical trial setting. Pending the outcome of current clinical research, the scheduling of MDMA could be reconsidered in future applications. There are still provisions for clinical trials by approval of Commonwealth and/or State or Territory health authorities, with the potential to obtain further evidence which could inform future application for the down-scheduling of MDMA.

⁴ Williams ML, Korevaar D, Harvey R, Fitzgerald PB, Liknaitzky P, O'Carroll S, Puspanathan P, Ross M, Strauss N and Bennett-Levy J (2021) Translating Psychedelic Therapies From Clinical Trials to Community Clinics: Building Bridges and Addressing Potential Challenges Ahead. *Front. Psychiatry* 12:737738. doi: 10.3389/fpsy.2021.737738 referred to as part of a submission to the Delegate and ACMS following publication of the Expert Report.

⁵ Multidisciplinary Association for Psychedelic Studies (MAPS) – <https://maps.org/news/media/press-release-fda-agrees-to-expanded-access-program-for-mdma-assisted-psychotherapy-for-ptsd/>

⁶ Multidisciplinary Association for Psychedelic Studies (MAPS) – <https://maps.org/news/media/press-release-fda-grants-breakthrough-therapy-designation-for-mdma-assisted-psychotherapy-for-ptsd-agrees-on-special-protocol-assessment-for-phase-3-trials/>