Australian Government
Department of Health
Therapeutic Goods Administration

Record of the 38th meeting of the Advisory Committee on Medicines Scheduling

22 June 2022

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TGA Health Safety Regulation

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1 Preliminary matters

1.1 Opening of the meeting

The 38th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**) was held at the Department of Health's Fairbairn (ACT) office and via video conference on 22 June 2022.

The meeting was chaired by s22 [redacted], who opened the meeting at 10:00 am (AEST) and welcomed attending members and observers.

Members were informed that the discussions and recommendations of the Committee are confidential until the interim decisions are published.

A quorum was present for all decisions. Those present at the meeting were:

Committee members

Name	Representation
s22 [redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
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[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Committee Secretariat (Commonwealth Department of Health)

Name
s22 [redacted]
[redacted]
[redacted]

s22

Observers

Name	Items
Commonwealth Department of Health (Therapeutic Goods Administration)	
s22 s22	All
s22	2.3 and 2.4 (MDMA and Psilocybine)
s22	All
s22	All
s22	All
s22	2.3 and 2.4 (MDMA and Psilocybine)
s22	s22
s22	2.3, 2.4 and 2.5 (MDMA, Psilocybine s22
s22	2.2 and 2.3 s22 and MDMA)
s22	2.1 and 2.2 s22
s22	2.3 and 2.4 (MDMA and Psilocybine)
NSW Ministry of Health	
s22	2.3 (MDMA) and 2.4 (Psilocybin)
s22	All

Apologies

Nil.

1.2 Conflict of interest

Conflicts of interest declared prior to the meeting by s22 were discussed.

s22 The Committee were of the view that the benefits of s22 input in relation to s22 outweighed any potential conflict, and no objections were raised to s22 participation in discussions during the meeting.

s22 No objections were raised to s22 full participation in discussions.

s22

s22 relating s22 . Similarly to s22 declared conflict and consistent with previous meetings, the Committee were of the opinion that s22 contributions to discussions outweighed any potential conflict.

s22 The Committee agreed that this indirect conflict should not preclude s22 from fully participating in discussions.

It was noted that none of the members with declared conflicts had been assigned to speak on items related to these conflicts.

1.3 Procedural matters

Members were informed of various housekeeping rules to ensure the smooth running of the meeting via videoconference.

All present were reminded of confidentiality in relation to all matters discussed by the Committee and that all decisions are to remain confidential until they are published along with the interim decision of the delegate[1] of the Secretary of the Department of Health and Aged Care responsible for chemicals scheduling (the **Delegate**).

Due to time requirements and outside commitments of some of the Committee members, items were not discussed in the order listed on the meeting agenda. The order of discussion is reflected in these minutes.

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

2 Proposed changes to the Poisons Standard

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[redacted]

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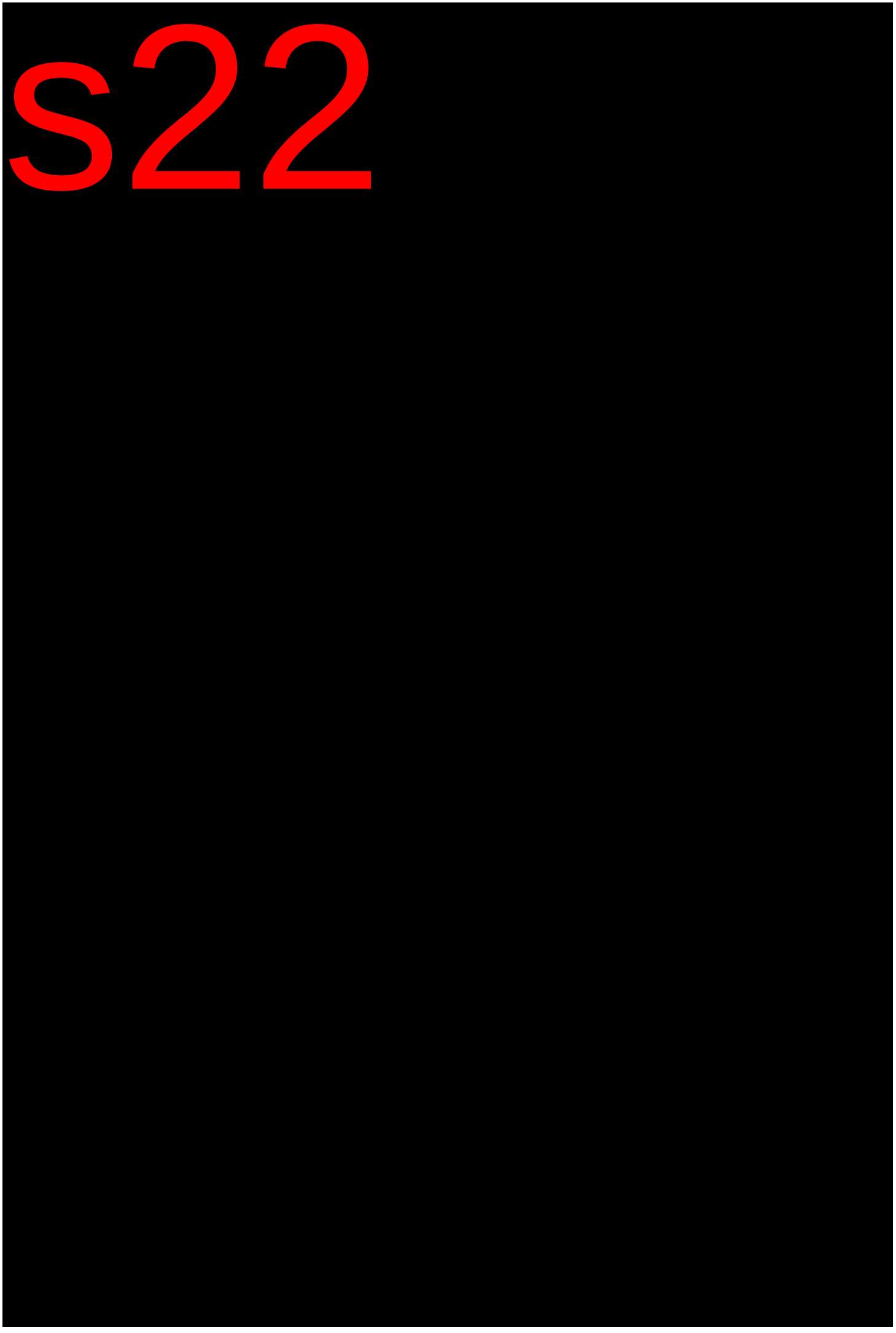
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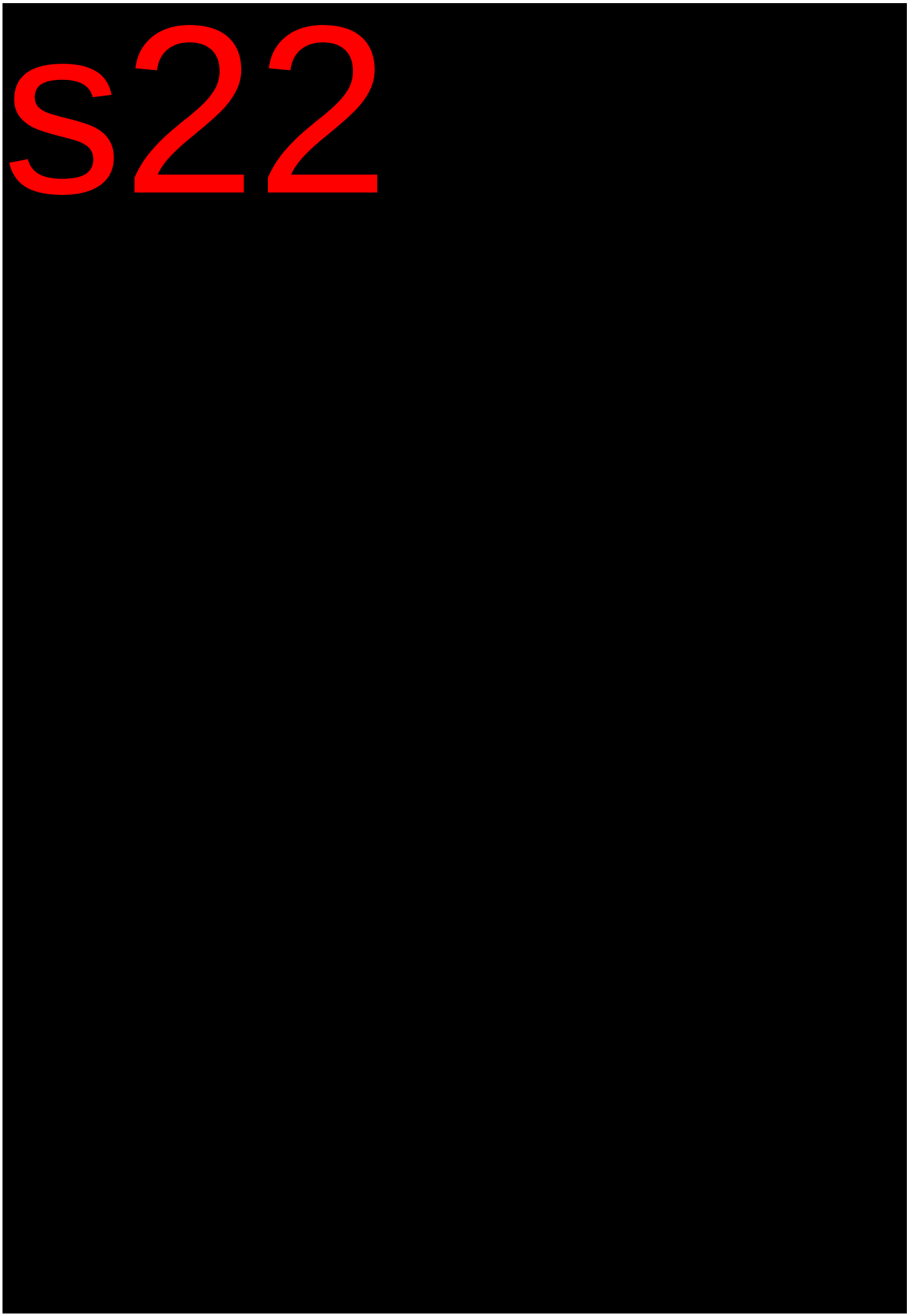
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2.4 Psilocybine

Advice for the Delegate's consideration

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

Committee discussion

- The Committee considered a proposal to create a new Schedule 8 entry for the use of psilocybine in combination with psychotherapy for treatment-resistant mental illness in medically controlled environments under certain circumstances. This application followed a similar one from the same applicant that was considered by the Committee in November 2020 and November 2021, in relation to which a final decision was made in December 2021.
- Members noted that the applicant had proposed a number of additional controls in this application compared to their previous proposal, in an attempt to address the concerns of the Committee, the Delegate and the expert panel that produced an independent report completed in September 2021, regarding the proposed down-scheduling of psilocybine.
- Members agreed that there was little additional evidence presented in this application compared to that considered by the Committee and the Delegate in connection with the previous application. As such, the main barrier to down-scheduling psilocybine was therefore still a lack of established therapeutic value, as required by the Schedule 8 factors in the Scheduling Policy Framework (SPF).[2]
- Members noted the completion of one phase II trial since the previous application and the independent expert panel review, however this is yet to be published and has not been peer

[2] AHMAC – Scheduling policy framework for medicines and chemicals https://www.tga.gov.au/sites/default/files/ahmac-scheduling-policy-framework-medicines-and-chemicals.pdf

reviewed. It was noted from this study that there was significant improvement in patient outcomes for 25 mg dosages, but not for 1 mg or 10 mg.

- An additional published study was discussed, which was a 12-month follow up of 24 patients who were given two doses at 25 mg or 30 mg two weeks apart with assisted psychotherapy. The results showed a persistence of effect at 12 months and it was agreed that there seems to be increasing evidence that even a relatively small dose of psilocybine, given as a one-off in conjunction with psychotherapy, produces long term benefits.

- Members agreed that early trials do show promising results for TRD, with a therapeutic dose of 25 mg reaching some reproducibility of results and it has a large therapeutic window (240 times the typical dose). However, members expressed several concerns, including the broadness of the indication included in the proposal (treatment-resistant mental illness), the lack of phase III trials, and the problems associated with the translation from a clinical trial setting to clinical practice.

- The Committee agreed that the risk of diversion is low in a controlled medical environment, but noted that, contrary to the assertions of the applicant, there are significant risks of diversion at other points in the supply chain. In addition, not dispensing from a pharmacy would bypass the real-time prescription monitoring system, hence limiting oversight and governance. These issues argue for retaining psilocybine in Schedule 9, consistent with the relevant scheduling factors.

- The Committee agreed that, internationally, the regulation of access to psilocybine for therapeutic use is consistent with the controls associated with Schedule 9 (prohibited) of the Poisons Standard. It was mentioned that the "Breakthrough Therapy" status of psilocybine in the USA, designated by the Food and Drug Administration (FDA), was for treatment-resistant depression (TRD) and not the broader indication proposed by the applicant. It was also noted that this status is not connected to controls over access, but rather pathways to promote research and to market products. There remains no approved therapeutic product containing psilocybine anywhere in the world.

- The Committee acknowledged a very large number of public submissions were received and noted that those in favour of down-scheduling cited a perceived clinical need and low risk of diversion for misuse. Of particular note, both the Australian Psychological Society (APS) and Royal Australian and New Zealand College of Psychiatry (RANZCP) were against the proposal to down-schedule psilocybine.

- The APS was of the opinion that until additional evidence is available from phase III clinical randomised controlled trials, there is insufficient evidence to endorse widespread adoption of psychedelic-assisted therapy. In the view of the APS there was insufficient data regarding the efficacy, safety, potential for abuse and tolerability of psilocybine in vulnerable patient populations. The RANZCP stated that until further research to clearly determine the therapeutic value, benefits and risks, and the development of best practice frameworks for clinical use have been subsequently developed, down-scheduling psilocybine should not occur. The Committee identified further questions raised by the submissions regarding what clinical governance and regulatory controls would need be in place should a Schedule 8 entry be considered.

- The Committee agreed that the additional requirements proposed in the application would be exceedingly difficult, if not impossible to regulate and enforce at State and Territory level in relation to preparations that are not products included in the Australian Register of Therapeutic Goods (ARTG). In particular, the Committee recognised that States and Territories are unable to regulate training as suggested by the proposal (including accreditation by an appropriate body) or oversee the requirement for review by two

additional psychiatrists. In addition, Appendix D of the Poisons Standard is not adopted by all States and Territories, hence they would not be able to enforce the proposed requirement for prescribing by a psychiatrist only. This would create a significant impediment to patient access due to the cost involved and the shortage of available psychiatrists, particularly if specific training is required as proposed.

- The Committee observed that the controls for Schedule 8 substances implemented under State and Territory legislation align with the corresponding scheduling factors. Schedule 8 controls are not established to give effect to highly specialised restrictions on clinical practice in situations where therapeutic value of the substance has not been established.
- In summary, as the Committee had identified insufficient new evidence in this application to support down-scheduling, principally relating to therapeutic value, it was agreed that the advice not to amend the existing scheduling for psilocybine be given to the Delegate.

The reasons for the advice

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the 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.

As the Committee identified that there was insufficient additional evidence of therapeutic value provided in this application, it was agreed that the reasons pertinent to these matters that were provided in relation to the previous application are equally applicable to this application.

The Committee's reasons were:

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

Risks:

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

Benefits:

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

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

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

c) the toxicity of a substance

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

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

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

e) the potential for abuse of a substance

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

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

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

2.3 MDMA

Advice for the Delegate's consideration

The Committee recommended 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.

Committee discussion

- The Committee considered a proposal to create a new Schedule 8 entry for the use of N,α-DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE (MDMA) in the treatment of treatment resistant mental illness when used as part of psychotherapy in a medically controlled environment. Members noted that the proposed Schedule 8 entry was similar to that from the same applicant previously considered by the Committee in November 2020 and November 2021, in relation to which a final decision was made in December 2021.
- The applicant had proposed a number of additional controls in this application, in an attempt to address the concerns of the Committee, the Delegate and the expert panel that produced an independent report completed in September 2021, regarding the proposed down-scheduling of MDMA. Most notably, it proposes a specific requirement for authorisation of the treatment by a psychiatrist (i.e. removal of "specialist addiction physician") and the requirement for the patient's diagnosis and proposed treatment plan to be confirmed by at least two independent reviewing psychiatrists.

- The Committee agreed that there was no new evidence establishing the therapeutic value of MDMA presented in this application compared to that considered by the Committee and the Delegate in connection with the previous application. As such, the main barrier to down-scheduling of MDMA to Schedule 8 was still a lack of established therapeutic value, as required by the Schedule 8 factors in the Scheduling Policy Framework (SPF).[3]

- Members noted the Phase III trial (MAPP1) referenced by the applicant in the most recent application had previously been considered in the independent review. A second phase III study, MAPP2, is currently listed as active (not recruiting) with results anticipated in March 2023. It was noted that the MAPP2 study protocol is not yet publicly available.

- Members agreed that, for the evidence that was provided with the application, early trials do show promising results for post-traumatic stress disorder, as was concluded in the independent review. There were statistically significant differences in endpoint scores for MDMA doses of greater than 100 mg in comparison with inactive controls, relative to change scores in comparison with active controls. The Committee observed that the typical dose in the context of psychotherapy ranges from 30-125 mg, often followed by an optional half-dose 1.5 to 2.5 hours into the session. However, the independent review concluded that overall study quality was not optimal and the Committee members expressed concern that optimal dosages have not been established, especially outside of clinical trials for the treatment of post-traumatic stress disorder (PTSD).

- The Committee noted international settings for MDMA access and how these were different to psilocybin, e.g, expanded access in other countries, including the United States, Israel and Switzerland for patient access under compassionate grounds for PTSD. It was mentioned that the "Breakthrough Therapy" status of MDMA in the USA, as designated by the FDA and the UK ILAP (innovation passport) scheme, was aimed at accelerating product approval. This is analogous to TGA priority evaluation pathways for registration of medicines on the Australian Register of Therapeutic Goods (ARTG) and does not represent a change to controls over access comparable to a scheduling change. The Committee noted that there remain no products containing MDMA approved for therapeutic use anywhere in the world.

- The Committee discussed the current use of the Special Access Scheme (SAS) for medical access to MDMA, and international equivalents of this scheme. Health Canada has also recently expanded its Special Access Program (SAP) to provide medical access to both psilocybin and MDMA (and potentially other psychedelic medicines). This a similar scheme to Australia's Special Access Scheme-B; however, unlike Australia, Canada does not have additional jurisdictional approval requirements for access.

- The Committee suggested that the applicant appeared to have undertaken extensive political and consumer lobbying, evidenced by the volume of public submissions received, which were largely in support of down-scheduling MDMA. It was noted that those in favour of down-scheduling cited a perceived clinical need for patients with treatment resistant PTSD, social anxiety disorder (SAD) and emotional processing in adults with autism, general anxiety disorder (GAD), and addictions. Feedback within the submissions indicated the belief that MDMA has a high potential to treat these conditions, and cited first responders, defence force personnel and sufferers of treatment resistant depression and anxiety as the populations to benefit from increased access to psychedelic-assisted therapy.

[3] AHMAC – Scheduling policy framework for medicines and chemicals https://www.tga.gov.au/sites/default/files/ahmac-scheduling-policy-framework-medicines-and-chemicals.pdf

- However, the Committee's view was that the submissions in support did not identify any new or compelling evidence, and instead focused on emphasising human interest or philosophical points of view. This was contrasted with the submissions in opposition that generally presented an assessment of the evidence base and pathways for eventual broader access to this substance when evidentiary thresholds are met.
- The Committee identified further questions raised by the public submissions regarding clinical governance, regulatory controls and training that would need to be in place should a Schedule 8 entry be implemented as proposed.
- The Committee specifically noted the submission from the Royal Australian and New Zealand College of Psychiatrists (RANZCP), which maintained their stance regarding the scheduling of MDMA. The RANZCP supported the decision to not amend the Poisons Standard until further research has more clearly determined the therapeutic benefits and risks, and a best practice framework for clinical use has been subsequently developed. The RANZCP submission acknowledged the proposed restrictions related to training and the requirement for independent psychiatrists' review of the treatment plan, but expressed concerns that adequate protocols do not exist to support translation from a clinical trial setting to a community setting. A Committee member highlighted that the training proposed by the applicant was not accredited by a board or organisation recognised by the Australian Health Practitioner Regulation Authority (AHPRA) or the RANZCP.
- The submission from the Australian Psychological Society (APS) was also highlighted by the Committee. The APS considers that it would be premature to support the therapeutic use of psychedelic substances as proposed without sufficient data regarding the efficacy, safety, potential for abuse, and tolerability of these substances in vulnerable patient populations. The Committee noted that the APS anticipates that it may reconsider the position as additional evidence becomes available.
- The Committee noted the submission from the Australian Medical Association (AMA), which maintained the same fundamental position as in November 2020. More high-quality research using larger scale studies is needed before MDMA can be used more widely by medical practitioners. The Committee agreed with the AMA stance that any barriers to research under the existing scheduling should be addressed outside of the Poisons Standard, and that the need to reduce research barriers does not warrant making MDMA more readily available to practising medical practitioners through down-scheduling.
- On advice from representatives from the States and Territories, the Committee agreed that the additional requirements proposed in the application would be exceedingly difficult, if not impossible to regulate and enforce at State and Territory level in relation to preparations that are not products included in the Australian Register of Therapeutic Goods (ARTG):
  - The Committee recognised that States and Territories are unable to regulate training as suggested by the proposal (including accreditation by an appropriate body) or oversee the requirement for review by two additional psychiatrists.
  - There is no definition of "medically controlled environments" and there is ambiguity in relation to the regulatory threshold for determining the suitability of the specific training required.
  - There were concerns regarding the potential conflict of interest arising from the requirement for specialist training, which currently appears to be provided solely by the applicant and no other independent accredited providers. The Committee observed that this diminishes the weight of the evidence that suitable clinical protocols have been established commensurate with inclusion in Schedule 8.

  - It was noted that Appendix D of the Poisons Standard is not adopted by all States and Territories, hence they would not be able to enforce the proposed requirement for prescribing by a psychiatrist only.

- Regarding MDMA, the Committee observed that there is a high risk of diversion for misuse, even with Schedule 8 controls. The Committee agreed that the risk of diversion is low in the controlled environment, however noted there are risks associated with other aspects of the supply chain. In addition, not dispensing from a pharmacy would bypass the real-time prescription monitoring system, hence limiting oversight and governance.

- A Committee member stated that scheduling is not an appropriate mechanism for establishing clinical governance of the therapeutic use of MDMA by inclusion of caveats and conditions within the Poisons Standard. Furthermore, these additional controls would create a significant impediment to patient access due to the cost involved and the shortage of available psychiatrists, particularly if specific training is required as proposed by the applicant. The Committee was unanimous in agreeing that time was required to develop a curriculum and accredited training process for psychiatrists that is supported by an evidence base.

- The Committee agreed that the Schedule 9 scheduling factors were met in relation to MDMA, being that:

  - Therapeutic value is not established, as evidenced by there being no approved indications for a product registered by a medicines regulator in any jurisdiction. There is evidence only of potential benefits of MDMA in treatment of PTSD, noting that research is promising but not fully established and requires further study.

  - There are significant risks to individuals and the community of MDMA-containing medicines that have not been approved by the TGA or other comparable regulators being available on prescription.

- In summary, principally as the Committee identified no additional or compelling new evidence of therapeutic value in this application to support down-scheduling, but observed that the risks remained consistent, it was recommended to not amend the existing scheduling for MDMA.

The reasons for the advice

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the 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.

As the Committee identified that there was insufficient additional evidence of therapeutic value provided in this application, it was agreed that reasons pertinent to these matters that were provided in relation to the previous application are equally applicable to this application.

The Committee's reasons were:

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

Risks:

  - Acute effects include high blood pressure and pulse rate, faintness and panic attacks. In severe cases, MDMA can cause loss of consciousness and seizures.

- Secondary effects include involuntary jaw clenching, lack of appetite, depersonalisation, illogical or disorganised thoughts, restless legs, nausea, hot flashes or chills, headache, sweating and muscle/joint stiffness.
- Long-term use can result in sleep disturbances, difficulties with concentration, depression, heart disease, impulsivity and decreased cognitive function.

Benefits:

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

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

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

c) the toxicity of a substance

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

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

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

e) the potential for abuse of a substance

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

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

- There remains significant doubt regarding the degree to which the psychedelic/psychotherapy interaction is dependent on the specific type of psychotherapy administered. This raises the question as to the stringency with which protocols need to be followed and the practicality for implementing these in clinical practice outside of the highly controlled clinical trial environment.
- There are currently no medicines containing MDMA proposed for inclusion or already included in the ARTG.
- There are significant benefits to waiting for the results of clinical trials. MDMA-assisted psychotherapy may prove to be safe and efficacious, but the evidence does not yet suggest this - especially for conditions outside of PTSD.

- It will take time to develop a curriculum and accredited training process for psychiatrists. To protect public health and prevent inappropriate use, MDMA should not be down-scheduled until all necessary safeguards have been established and implemented.
- A substantial evidence base will be required to inform a curriculum and accredited training process for psychiatrists. To protect public health and prevent inappropriate use, MDMA should not be down-scheduled until all necessary safeguards have been established and implemented.
- There is a high risk of diversion for misuse, even in conjunction with Schedule 8 controls.
- Scheduling is not an appropriate mechanism for establishing clinical governance of the therapeutic use of MDMA.

3 Other matters for consideration

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4 Next meeting

The members noted that the next meeting of the Committee is scheduled for 8-10 November 2022.

5 Closure

The Chair closed the meeting at 3:20 pm, 22 June 2022.

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Date 8th August 2022

Chair

38th Meeting of the Advisory Committee on Medicines Scheduling