SHPA response to proposed quality standards for MDMA and psilocybin, January 2024

The Society of Hospital Pharmacists of Australia (SHPA) is the national, professional organisation for the 6,100+ Hospital Pharmacists, and their Hospital Pharmacist Intern and Hospital Pharmacy Technician colleagues working across Australia's health system, advocating for their pivotal role in improving the safety and quality of medicines use. Embedded in multidisciplinary medical teams and equipped with exceptional medicines management expertise, SHPA members are progressive advocates for clinical excellence, committed to evidence-based practice and passionate about patient care.

SHPA convenes numerous Specialty Practice groups, including Compounding Services, Clinical Trials, and Mental Health, comprising of a network of SHPA members who have pharmaceutical expertise and experience in the manufacturing and accessing of MDMA and psilocybin in Australia across various care settings.

SHPA also publishes the *SHPA Guidelines for Medicines Prepared in Australian Hospital Pharmacy Departments*[1] which is currently being reviewed and updated to form part of our *Standards of Practice Series.*

SHPA commends the Therapeutic Goods Administration (TGA) on its commitment to ensuring the safety and quality of MDMA and psilocybin supplied in Australia, and in principle supports the formation of quality standards for MDMA and psilocybin. SHPA members have however expressed concerns on how the proposed standards may further restrict access to MDMA and psilocybin, particularly for those who are established on these therapies for the treatment of post-traumatic stress disorder (PTSD). SHPA recommends the TGA to consider the proposed changes in this submission to ensure timely and equitable access to MDMA and psilocybin for those who most need it in Australia.

If you have any queries or would like to discuss our submission further, please do not hesitate to contact Jerry Yik, Head of Policy and Advocacy on jyik@shpa.org.au.

The Society of Hospital Pharmacists of Australia
PO Box 1774 Collingwood Victoria 3066 Australia
(03) 9486 0177 | shpa.org.au | shpa@shpa.org.au | ABN: 54 004 553 806

SHPA Response to consultation questions for MDMA

Question 1: Do you agree with the tests included in the draft standard for MDMA? If not, what changes do you propose and why?

Subsection b, under Part 2 Section 8 of *Attachment A – Draft standard for MDMA*, should be amended to state, "the amount or concentration of chloride present in MDMA hydrochloride must be not less than 15.3 per cent and not more than 15.9 per cent of the stated content of MDMA hydrochloride".

Question 2: Do you agree with the limits applied in the draft standard for MDMA? If not, what changes do you propose and why?

Proposed change 1: Implement content uniformity tests for MDMA

Part 3 Section 12 states, "The average content of MDMA hydrochloride in a pooled sample of not fewer than 20 capsules must be not less than 95.0 per cent and not more than 105.0 per cent of the stated content of MDMA hydrochloride". There is a concern for this statement as only testing for the average content of MDMA hydrochloride without regards for the content uniformity may show that the average content of 20 capsules may be within limits, but the individual doses may show great variability.

Content uniformity testing is an important quality measure of the final solid dosage product, as it ensures that a specified amount of active pharmaceutical ingredient (API) is consistently contained within a dosage unit, thereby ensuring patients consistently receive the correct dose. This may be particularly relevant for MDMA where smaller doses are used initially for PTSD treatment. Medicines that require smaller doses are at higher risk of potential API losses during the manufacturing process, thus would have greater consequences if greater variability is observed between each dosage unit.

Proposed change 2: Provide clarification for the testing of related substances for MDMA

Item 4 under Schedule 1 currently states, "not more than the limits specified in Ph Eur 2.2.46".
Ph Eur 2.2.46 is a general chapter in the European Pharmacopoeia (Ph.Eur.) that outlines chromatographic separation techniques. While it is acknowledged that APIs from different suppliers may have different impurity profiles not addressed by the pharmacopoeial test procedures, clarification of specific limits is still required to ensure manufacturers have a reference point to verify pharmacopoeial tests and limits for use with the proposed product.[2]

Question 3: Do you agree with the requirement for unlicensed compounding pharmacists to use an API that has been tested in an Australian GMP-licensed laboratory? If not, what changes do you propose and why?

Proposed change 3: Clarify and amend where appropriate the requirements for the API to be tested in an Australian GMP-licensed laboratory

SHPA members have raised concerns that the requirement for APIs to be tested in an Australian GMP-licensed laboratory introduces unnecessary restrictions for accessing MDMA and psilocybin for Australian patients, particularly in the setting of clinical trials.

Access and supply of MDMA and psilocybin products for a registered clinical trial are regulated under ethical and other clinical trials governance frameworks in addition to the therapeutic goods legislation in Australia.[3] This includes the requirement for manufactured investigational medicinal products (IMPs) to comply with the

Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) guide to Good Manufacturing Practice (GMP).[4]

Recognised as the international standards adopted by countries and pharmaceutical inspection authorities, the *PIC/S guide to GMP* provides a harmonised and constructive co-operation in the field of GMP. Within Australia, the *PIC/S guide to GMP* has legislative power through the operation of section 36 of the *Therapeutic Goods Act 1989*.[5]

MDMA and psilocybin accessed through clinical trials are commonly supplied to site from an overseas GMP facility in a ready to use form. The additional requirement for an API manufactured in an overseas facility regulated by a PIC/S participating authority, to then be further tested in an Australian GMP-licensed facility upon import to Australia, adds unnecessary steps and creates significant access barriers for current and future clinical trials involving MDMA and psilocybin. As they are now classified as Schedule 8 medicines, access to MDMA and psilocybin must not be burdened with unnecessary restrictions, which are not otherwise imposed on other registered medicines listed under Schedule 8.

SHPA recommends that for cases where an API has been manufactured under the operation of *PIC/S guide to GMP*, it is made exempt from further testing at an Australian GMP-licensed facility. This will help to minimise the anticipated harm if timely access to MDMA and psilocybin is compromised for patients established on MDMA and/or psilocybin, and ensure clinicians can freely consider the benefits of these therapies for their patients with PTSD without being concerned for potential delays and inconsistencies in accessing these therapies.

PTSD is a particularly persistent and incapacitating condition which severely impedes on quality of life. It is estimated that 75% of Australian adults have experienced a traumatic event at some point in their lives.[6] Furthermore, stress and trauma impose considerable costs and burden on society. According to *The economic cost of the social impact of natural disaster* report[7], Queensland residents affected by floods were 2.3 times more likely to develop PTSD, and mental health issues represented the largest financial impact of the floods, with a lifetime cost estimated at $5.9 billion. Minimising unnecessary restrictions imposed on accessing MDMA and psilocybin in Australia should therefore be a key consideration in forming these quality standards.

In the case that the TGA must implement a requirement for all MDMA and psilocybin API to be tested in an Australian GMP-licensed facility, the TGA must provide explicit guidance on API testing in Australia in consultation with key stakeholders in the Pharmacy sector across all states, including, but not limited to, identifying acceptable GMP laboratories in each state and detailing the logistics of moving API from pharmacies to GMP laboratories for testing. SHPA notes that in scenarios where the API was manufactured in Australia, testing these at an Australian GMP-licensed laboratory would be considered appropriate and in compliance with PIC/S requirements.

Proposed change 4: Remove ‘unlicensed compounding pharmacists’ and replace with ‘registered pharmacists who compound’

In Australia, all pharmacists entering the profession are expected to have had the appropriate education and training to undertake simple compounding, which involve compounding of medicines from published formulations utilising current clinical and pharmaceutical knowledge and appropriate compounding techniques.[8]

While complex compounding requires pharmacists to upskill and update their practice profile in line with the *Professional practice profile for pharmacists undertaking complex compounding*[8], a compounding pharmacist

is not a recognised specialty in Australia. Hence all registered pharmacists may legally compound therapeutic goods if they meet the legislative requirements.

To remove confusion and misinterpretation, SHPA recommends removing the phrase, “unlicensed compounding pharmacists” and replacing it with “registered pharmacists who compound”.

Question 4. Do you agree with implementation of the new TGO to commence with its registration on the Federal Register of Legislation in March 2024. If not, what changes do you propose and why?

SHPA agrees with implementation of the new TGO to commence with its registration on the Federal Register of Legislation in March 2024, provided that this consultation has adequately addressed the issues and concerns identified in this submission.

Question 5. Do you have any other comments in relation to the new draft standard for MDMA?

Proposed change 5: Develop and publish a standardised formulation and procedure for compounding MDMA and psilocybin capsules

SHPA recommends the development and publication of standardised formulations and procedures for compounding MDMA and psilocybin capsules. The current consultation seeks to focus on the quality of the API. However, ensuring the quality of the API alone is insufficient to ensure the quality of the finished dosage form, particularly when there are insufficient number of capsules made to allow for destructive testing. In general, compounding of low-dose capsules is often problematic due to:

1. API losses in compounding, especially within powder containment cabinets; and
2. Inadequate mixing of powders resulting in non-homogenous mixture and unacceptable dose variability.

Establishing a standardised formulation will allow manufacturers of MDMA and psilocybin to adhere to the same standardised manufacturing process, ensuring consistency in the finished product of MDMA and psilocybin within Australia. This also aligns with the recommendations in *PIC/S guide to GMP* Chapter 4[4], where it is recommended that an approved, written manufacturing formula and processing instructions should exist for each product and batch size to be manufactured.

Proposed change 6: Change the term “compounders” to “pharmacists/pharmacies that compound”

Currently within the Scope section of the consultation document, there is reference to the term, “compounders”. This terminology is confusing and may be misinterpreted. SHPA recommends changing this to refer to pharmacists and/or pharmacies that compound MDMA or psilocybin containing medicine.

SHPA response to consultation questions for psilocybin

Question 1: Do you agree with the tests included in the draft standard for psilocybin? If not, what changes do you propose and why?

SHPA agrees with the tests included in the draft standard for psilocybin.

Question 2. Do you agree with the limits applied in the draft standard for psilocybin? If not, what changes do you propose and why?

Similar to the concerns raised for MDMA, SHPA recommends that content uniformity testing is implemented for psilocybin.

Question 3: Do you agree with the requirement for unlicensed compounding pharmacists to use an API that has been tested in an Australian GMP-licensed laboratory? If not, what changes do you propose and why?

As mentioned in the consultation question 3 for MDMA, there are concerns for introducing unnecessary barriers to accessing psilocybin if all batches of API are required to be tested in an Australian GMP-licensed laboratory. SHPA recommends that the TGA acknowledges the quality of API tested in an overseas GMP-licensed laboratory that implements the *PIC/S guide to GMP* under legislation, so that further unnecessary testing of API is not required upon import into Australia, which may impact timely access of psilocybin for patients requiring treatment.

Question 4. Do you agree with implementation of the new TGO to commence with its registration on the Federal Register of Legislation in March 2024. If not, what changes do you propose and why?

SHPA agrees with implementation of the new TGO to commence with its registration on the Federal Register of Legislation in March 2024, provided that this consultation has adequately addressed the issues and concerns identified in this submission.

Question 5. Do you have any other comments in relation to the new draft standard for psilocybin?

As previously mentioned for MDMA, SHPA recommends developing and publishing a standardised formulation and procedure for compounding psilocybin capsules.

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(03) 9486 0177 | shpa.org.au | shpa@shpa.org.au | ABN: 54 004 553 806

References

[1] SHPA Manufacturing Working Party. (2010). SHPA Guidelines for Medicines Prepared in Australian Hospital Pharmacy Departments. Journal of Pharmacy Practice and Research. 40. 133-143. 10.1002/j.2055-2335.2010.tb00521.x.

[2] Therapeutic Goods Administration. (2021). Control of finished product. Available at: https://www.tga.gov.au/resources/resource/guidance/argom-appendix-2-guidelines-quality-aspects-otc-applications/7-control-finished-product#s79

[3] Therapeutic Goods Administration. (2023). Legislation and legislative instruments. Available at: https://www.tga.gov.au/about-tga/legislation/legislation-and-legislative-instruments

[4] PIC/S. (2023). Publications. Available at: https://picscheme.org/en/publications?tri=gmp#zone

[5] Therapeutic Goods Administration. (2022). PIC/S Guide to GMP: Manufacturing principles for medicinal products. Available at: https://www.tga.gov.au/resources/publication/publications/pics-guide-gmp-manufacturing-principles-medicinal-products#:~:text=PIC%2FS%20Guide%20to%20GMP%3A%20Manufacturing%20principles%20for%20medicinal%20products,-PIC%2FS%20Guide&text=Section%2036%20of%20the%20Therapeutic,the%20manufacture%20of%20therapeutic%20goods.

[6] Australian Institute of Health and Welfare. (2022). Stress and trauma. Available at: https://www.aihw.gov.au/reports/mental-health/stress-and-trauma

[7] Australian Business Roundtable for Disaster Resilience & Safer Communities. (2016). The economic cost of the social impact of natural disasters. Available at: https://australianbusinessroundtable.com.au/assets/documents/Report%20-%20Social%20costs/Report%20-%20The%20economic%20cost%20of%20the%20social%20impact%20of%20natural%20disasters.pdf

[8] Pharmacy Board of Australia. (2015). Guidelines on compounding of medicines. Available at: https://www.pharmacyboard.gov.au/documents/default.aspx?record=WD15%2F16205&dbid=AP&chksum=3QlnioMt0DhI0PsjaoB83A%3D%3D