## Purpose

This document provides guidance for the considerations in the review of studies involving the use of psychedelic drugs.

## Background

The therapeutic potential of psychedelic drugs is growing in interest. This includes the use of MDMA and psilocybin.

In Australia, from 1 July 2023, the TGA amended the Poisons Standards to add MDMA to assist in the treatment of PTSD, and to add psilocybin in the treatment of treatment resistant depression (TRD). Prescription is only permitted by registered psychiatrists following approval through the Authorised Prescriber Scheme. Bellberry does not provide reviews under the Authorised Prescriber Scheme. Psychiatrists will need to work with their affiliated medical/hospital HREC for Authorised Prescriber approvals, and are also required to comply with all legislation of the State or Territory in which they practice.

Clinical trials involving psychedelic drugs are subject to the same regulations and same evidentiary standards as other drug studies for HREC approval. However these drugs are also considered to provide a number of unique challenges in the evaluation of their safety and efficacy.

In June 2023, The FDA released Guidance for Industry on Psychedelic Drugs: Considerations for Clinical Investigations.

## Guidance

The FDA guidance will be considered in the reviews by the HREC. An overview of considerations is provided in the following table.

**Reference documents for guidance:**

FDA Guidance for Industry: Psychedelic Drugs: Considerations for Clinical Investigations June 2023

| | As for other trials | | Additional considerations |
|---|---|---|---|
| Chemistry, Manufacturing and Controls (CMC) | √ | • Must be sufficient information to ensure the proper identification, quality, purity, and strength of the product.<br>• The drug must be manufactured in accordance with cGMP. Phase I products should follow the recommendations in the industry guidance for cGMP for Phase I Investigational Drugs (July 2008). | |
| Non-clinical studies | √ | • ICH Guidance for Industry M3(R2) Non clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorisation for Pharmaceuticals (Jan 2010) | • Must have adequate pharmacological and toxicology information<br>• Could consider absence of typical animal tox studies if there is extensive human information available from previous studies and no safety concerns (literature review). Supporting non clinical studies may still be required<br>• Non clinical studies to support chronic or chronic-intermittent dosing required<br>• Appropriate dosing paradigm<br>• Assessment of functional activity at the 5-HT2B receptor subtype due to drug serotonin activity<br>• Cardiac considerations |
| Clinical Pharmacology | √ | | • Food effects<br>• Drug-drug and drug-disease interactions<br>• Long term exposure to 5-HT2B agonists – cardiac considerations<br>• PD - use of serotonin reuptake inhibitors or monoamine oxidase inhibitors, use of tricyclic antidepressants<br>  • May increase or reduce effect of psychedelic drug<br>• Characterise dose- response relationship |
| Abuse Potential Assessment | √ | • Generally conducted as a component of the safety evaluation for relevant drugs | • Need to evaluate abuse potential<br>• Need to comply with state/national controlled substances handling requirements<br>• Human abuse potential study<br>• Adverse event reporting related to the use of the drug whether or not drug related<br>• Assessment of potential for physical dependence<br>  - possibly after dose range determined ie when Ph II completed |
| Clinical | √ | | • Traditional placebo control may be an issue due to perceptual disturbances<br>• Consider blinding to minimise bias<br>• Consider complementary trial designs across phases. Assessment of effectiveness complications due to acute drug effects<br>• Observational monitors for the duration of treatment session with appropriate clinical expertise eg psychology<br>• Site considerations for who is in the room, who is on site, who is available at any given point of the study for each participant<br>• Additional training for study site staff<br>• Robust study recruitment screening, with particular consideration for 'healthy volunteer' studies<br>• PICF clearly describe possible potential experiential effects<br>• Characterise dose-response relationship early<br>• Relevant cardiac tests<br>• Mitigation plan for adverse effects<br>• Public health effects |