

FDA Request for Comments; Considerations for Potential Future Therapeutic Use of Psychedelic Drugs

Response from the Hub at Oxford for Psychedelic Ethics

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Summary of recommendations:

For the delivery of psychedelic treatments after potential approval, we recommend that FDA and its federal partners:

1. Establish an initial safety floor for routine care that preserves what trial safeguards were for (e.g., emergency medical response, psychological containment, protection against misconduct), while allowing flexibility in how each is provided. Set minimum standards where necessary.
2. Require follow-up across the days and weeks after dosing, including assessment of adverse events, escalation to a licensed clinician where necessary, and referral plans for emergency services.
3. Ensure recording of delivery of care alongside outcomes. Mandate an explicit process within post-approval requirements for learning from safety data over time, allowing for adjustments in potentially costly requirements where appropriate.

The need for a learning system in routine psychedelic care

The safety and benefit estimates that support psychedelic treatments in psychiatry are drawn almost entirely from clinical trials. They may also be somewhat informed by Oregon's "supported adult use" program for psilocybin. Such estimates are informative, but they cannot be treated as reliable guides to the risk profile of clinical care.

Research trials screen for lower medical and psychiatric risk, frequently excluding those with significant comorbidity, active suicidality, or the most serious mental illness. Participants are treated in settings with extensive clinical and medical safeguards. State programs like that in Oregon operate under comparatively limited reporting requirements, and data is drawn from a self-selected population, often without clinical indications, likely making it a less risky population than clinical services will see.

The further routine practice diverges from the contexts that generated risk data, the less generalizable the trial data will be to clinical contexts. Real-world risk is likely to be underestimated—caution is therefore warranted. But we are mindful that every safeguard carries costs that will impact the accessibility of care. Efforts to minimize harms from treatment may lead to unduly burdensome requirements. This would carry costs in terms of patients who might have benefited but were priced out of care. It could also lead some to turn to unregulated settings with fewer safeguards and much less oversight.

We do not yet know how much each trial safeguard contributes to safety. Knowing this would allow more informed choices about how much safety each safeguard buys, and at what cost to access. After approval, clinics will vary in how they deliver care. That variation, if recorded alongside patient characteristics, adverse events, benefits, and durability, can provide evidence about which practices

are most important for safety, which are unnecessarily burdensome and expensive, and which patients require additional safeguards.

One route to common data elements for delivery configuration is the ReSPCT guidelines for reporting psychedelic trials¹. Its items on staffing, personnel qualifications, in-session interventions, discharge conditions, preparation and follow-up, and patients' sense of safety cover much of what routine care would need to record, and would allow some comparability with trial reporting. Adverse events should be recorded using standardized definitions and instruments across clinics, reported whether or not they are judged drug-related, and followed through the weeks after dosing. This collated data should inform scheduled reviews of the initial requirements, judged against criteria set in advance, such that requirements can be relaxed if warranted by the safety data.

Working from limited data

Until outcome data accrues, optimizing the risk-benefit profile of safeguards for routine psychedelic care rests on judgment. We ground our recommendations for initial safety requirements in three principles:

1. **Reasoning from analogous cases in medicine.** Where features of psychedelic treatments are shared by or analogous to established interventions, the standards of care that already govern those interventions should inform practice. For example, any drug that induces an hours-long perceptual/cognitive incapacitation is not suitable as a take-home pharmacotherapy. In other areas of medicine that involve similar degrees of incapacity (such as procedural sedation and electroconvulsive therapy recovery), continuous trained observation, with discharge governed by defined recovery criteria, is the norm.
2. **Reasoning from function to requirement.** In the absence of evidence of which trial features carry the safety signal, we can still ask what each feature is for. The risk of medical emergencies warrants both preventative and responsive defenses, requiring medical evaluation before administration sessions and rapid medical availability during. Psychological destabilization requires a trained monitor to be continuously present, and the risk of misconduct requires independent oversight, ideally taking the form of a second person in the treatment room. Requirements that discharge key functions are part of the floor for safety, whereas those with weaker ties to safety functions (e.g., the aesthetics of the setting, the therapeutic modality, the credentials attached to auxiliary roles) are where flexibility can most defensibly be sought.
3. **Population-conditional safety.** Serious adverse event (SAE) rates in modern psychedelic trials are encouraging, but highly population-conditional. A recent meta-analysis from our group found no SAEs reported among healthy participants, but a rate of some 4% among those with pre-existing neuropsychiatric disorders (though note some of these may not have been related to the study drug; Hinkle et al., 2024), a figure itself conditioned on trial-grade screening and the near-exclusion of serious mental illness. Careful screening has been endorsed as among the most important mitigations against inducing psychological destabilization (King et al., 2026). Risk is likely to be greater in less stringently screened patients.

¹ Pronovost-Morgan et al. (2025). Relevant items: 8, 12, 15, 16, 20-24, 29-30.

Recommendations for practice

In Table 1 below, we propose a minimum set, or safety floor, of functions that must be reliably performed in every setting, developed primarily for psilocybin but likely relevant to other substances considered under the broad sense of the term “psychedelics”. However, not all psychedelic compounds are alike, and requirements will need to be set for each according to the medical risk and degree of impairment associated with the treatment. Ibogaine's cardiac risk, for example, would require additional safeguards that the provisions below, indexed to psilocybin, were not designed to provide. For each requirement that we propose, we flag potential areas of flexibility that might ease costs and burden and therefore improve access to care.

Above this minimum set of requirements, safety is jointly produced by several levers: screening stringency, the number and experience of in-room providers, patient complexity, and intensity of follow-up. Together, they determine whether the clinical capacity available to each patient is adequate to the risk that patient brings. These plausibly compensate for each other in part, with flexibility in one best purchased by conservatism in the others, but they do not substitute for the floor itself: stringent screening, for example, does not buy out the need for an accountable licensed clinician. We would advise against relaxing several at once, since each relaxation draws on the same margin of safety.

Table 1. Proposed initial requirements for psilocybin and psilocybin-like treatments in routine care.

The safety floor: functions to be met	Options for flexibility in delivery
Screening. Screening is tiered: defined risk signals trigger triage to an appropriately qualified clinician for clearance or consultation. Screening should not be conducted on the same day as drug administration, to allow consultation and medical review to proceed unhurried and with all due diligence, and to provide lead time for any medication tapering if needed. Final eligibility sign-off is provided by a licensed prescriber acting within their scope of practice; where risk signals are medical (e.g., drug interactions, medication tapering, cardiovascular contraindications), sign-off is by, or on the documented advice of, a physician. Eligibility decisions that turn on medical risk signals or diagnostic ambiguities (e.g., bipolar vs unipolar depression) require clinical judgment and cannot be delegated or automated. Initial eligibility criteria should hew closely to those of the trials that generated the current evidence.	Who performs the initial screen, including trained non-licensed providers. Screening and sign-off may be conducted remotely.
Consent, preparation and boundaries. Consent is obtained through conversation and documentation before the day of administration. Patient understanding is checked, and consent is reconfirmed before dosing. Consent covers alternative treatments; a realistic characterization of outcomes; the acute experience; possible lasting changes; and what happens if the patient wants to leave during the session. Boundaries, including physical touch, are agreed during preparation given the difficulty of reliably renegotiating consent under acute drug effects.	Number and format of preparation sessions, including modality of delivery, provided understanding is confirmed.
Presence. Each patient is continuously attended throughout acute drug effects by at least one session monitor in the drug administration room, with a responsible licensed clinician present in the room or with immediate access from an adjoining shared space.	The setting itself (including its aesthetics) should not be prescribed, so long as the space remains monitoring-capable. Therapeutic orientation or modality need not be prescribed but should be empirically supported.

The safety floor: functions to be met	Options for flexibility in delivery
Providers in training may form part of the in-room team under that clinician's supervision, but must not constitute the only clinical presence.	Group dosing models, including adjacent rooms opening onto a shared space, could potentially alleviate some staffing pressure, although these have rarely been tested.
Personnel and training. The responsible clinician holds state licensure, has training and experience in managing psychiatric emergencies, and has completed psychedelic-specific training (e.g., accredited continuing education). Session monitors hold graduate-level training in a mental health discipline, or a nursing qualification, with psychedelic-specific training.	Trained providers without independent licensure can undertake initial screening, preparation and follow-up, provided that escalation to senior clinicians is available. Session monitors may be pre-licensure. The responsible clinician's discipline (e.g., psychiatry, psychology, social work, counseling or psychiatric nursing), provided the licensure and training requirements are met. Psychedelic-specific training credentials that are competency-based, portable across employers and states, and set through existing professional bodies independent of product sponsors.
Medical. Medical evaluation as part of screening. On the day of administration, confirmation that nothing relevant has changed since screening (e.g., new medications, supplements, or other substance use), with any change referred to the prescriber before dosing. An on-call physician able to reach the site within a defined response time throughout administration sessions.	The continuously present monitor need not hold a medical degree, because medical capability is separately guaranteed on call. Non-physician prescribers may provide sign-off where no medical risk signals were raised.
Accountability. An independent check on misconduct throughout administration.	In descending order of protection: a second person in the room; live remote observation (never in place of on-site presence); audiovisual recording and review. In group dosing models, an overseeing licensed clinician may discharge this function at the group level.
Discharge. Readiness for discharge is determined in person by the responsible clinician and documented against stated criteria, including confirmation of safe passage home, with an escort as default.	Specific criteria for discharge can be set clinically and locally, rather than centrally prescribed. Where no escort is available, alternatives that discharge the same function (e.g., extended observation, clinic-arranged transport) can be used to prevent the requirement from excluding socially isolated patients.
Follow-up. Structured follow-up through the post-administration period is likely beneficial for enduring symptom relief, and at a minimum must check for adverse events, including psychological destabilization (e.g., mania, delusions, psychosis) and suicidality, that can arise in the days and weeks following treatment, with a defined route of escalation to licensed clinicians or emergency services. Patients leave the clinic knowing how to reach help, including crisis and emergency services.	Intensity, therapeutic intent, and the mix of providers undertaking follow-up may vary, and follow-up may be conducted by telehealth. Lower-intensity contact may be provided by trained providers under supervision.

References

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