



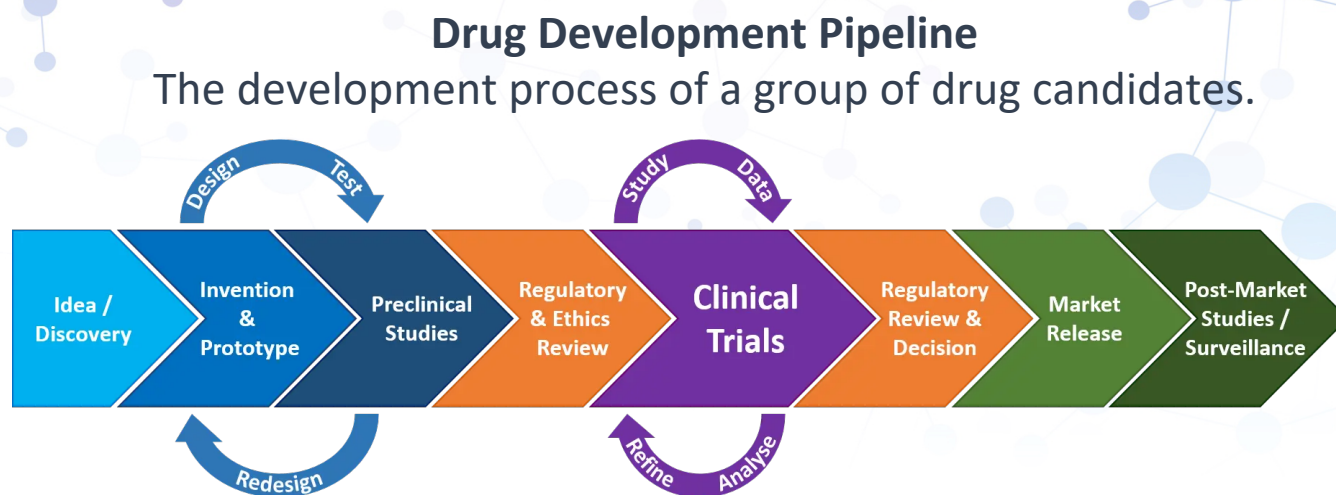
MIND MEDICINE

A U S T R A L I A

Student Induction: Research Methodology

Student Induction

What are clinical trials?



The Therapeutic Goods Administration (TGA) is the relevant Australian Government regulatory body. It serves as a safety mechanism to ensure drugs on the Australian market are safe.



Australian Government

Department of Health
Therapeutic Goods Administration

Clinical Trials

Phase 1

After *in vitro* trials are complete, the first phase is often held with small groups of healthy volunteers. Regarding psychedelic-assisted therapy, the volunteers in phase 1 trials have had diagnoses & trauma, although some diagnoses are excluded. The focus is safety.

Phase 2

If phase 1 proves to demonstrate an acceptable safety profile, the research will begin to enroll larger number of individuals with characteristics/ severity of illness or trauma. These trials may utilise placebo and other controls. The focus is efficacy.

Phase 3

The extent to which drugs are tested to be safe and effective is increased, with a higher enrolment of individuals to test any side effects and the true effectiveness. The focus is balance of safety and effectiveness..

Phase 4

After the drug is approved by the TGA, the drug is continued to be monitored for effectiveness and safety.

*Psilocybin trials in Australia are Phase 1, however psychedelic clinical trials across the world are in various phases. Psilocybin in Oregon, US, has been legalised for medicinal use.



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Student Induction Research Methodology

Research in the field of psychedelic-assisted therapies is often a mix of observational research and survey research.

Qualitative Research

- Descriptive studies
- Surveys
- Needs Assessments
- Randomised controlled (RCT)
- Program evaluations
- Cost-procedure-process-outcome analysis

Quantitative Research

- Narrative Case studies
- Ethnographic research
- Participant observation
- Inductive research methods

Co-design & Co-production

- Participant collaboration
- Prioritises lived experience
- Focus on relationships, sharing power and building capacity
- Co-planning of decision making in resource allocation, service delivery and evaluation.
- Often utilises volunteers.

Meta Analysis

- Focus on the combined results of multiple studies synthesizing the quantitative data on treatment effects.
- This methodology often informs clinical practice and social policy.

Randomised Control

- Randomisation of subject allocation between two or more groups
- Aims to reduce bias when testing the efficacy of treatments
- Often uses placebo, no intervention or may be a 'blinded' trial

Mixed Method

- Systematic integration of qualitative and quantitative data in a single study
- Integrates both methods of data collection and analysis giving a more comprehensive understanding of the data
- Can be an ideal technique to assess complex interventions

Longitudinal

- Descriptive studies
- Surveys
- Needs Assessments
- Randomised controlled (RCT)
- Program evaluations
- Cost-procedure-process-outcome analysis



Student Induction Psychedelic Research



[An example of a MDMA phase 3 study utilizing randomized, double-blind and placebo controls.](#)

Mitchell, J.M., Bogenschutz, M., Lilienstein, A. *et al.* MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. *Nat Med* **27**, 1025–1033 (2021). doi.org/10.1038/s41591-021-01336-3

[An example of a Psilocybin phase 2, double-blind, randomised controlled trial.](#)

Carhart-Harris, R., Giribaldi, N., Watts, R., Baker-Jones, M., Murphy-Beiner, A., Murphy, R., Martell, J., Blemings, A., Erritzoe, D., Nutt, D.J. Trial of Psilocybin versus Escitalopram for Depression. *N Engl J Med* **384**, 1402-1411 (2021) [DOI: 10.1056/NEJMoa2032994](https://doi.org/10.1056/NEJMoa2032994)

[An example of a Psilocybin-Assisted therapy phase 3 randomised controlled trial.](#)

Davis A.K., Barrett F.S., May D.G., et al. Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder: A Randomized Clinical Trial. *JAMA Psychiatry* **78**(5), 481–489 (2021) [doi:10.1001/jamapsychiatry.2020.3285](https://doi.org/10.1001/jamapsychiatry.2020.3285)

[An example of an LSD randomised, double-blind, placebo-controlled study.](#)

Yanakieva, S., Polychroni, N., Family, N. *et al.* The effects of microdose LSD on time perception: a randomised, double-blind, placebo-controlled trial. *Psychopharmacology* **236**, 1159–1170 (2019). <https://doi.org/10.1007/s00213-018-5119-x>

[An example of a Psilocybin study for treatment-resistant depression.](#)

Carhart-Harris, R.L., Roseman, L., Bolstridge, M. *et al.* Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms. *Sci Rep* **7**, 13187 (2017). <https://doi.org/10.1038/s41598-017-13282-7>



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Student Induction Glossary (1/2)

An Introduction [Psychedelic] Research Glossary

- **Efficacy** (efficacious): 'the ability, especially of a medicine or a method of achieving something, to produce the intended result'
- **Agonist**: 'a compound that can bind to and cause activation of a receptor, thus mimicking an endogenous ligand or neurotransmitter'
- **Antagonist**: 'biological structure or chemical agent that interferes with the physiological action of another. Supplement'
- **Endogenous**: 'found or coming from within something, for example a system or a person's body or mind'
- **Serotonin** (serotonergic): 'is the key hormone that stabilises our mood, feelings of well-being, and happiness'.
- **Dopamine**: 'dopamine is a chemical released in the brain that makes you feel good. Having the right amount of dopamine is important for your body and brain'
- **Pharmacotherapy**: 'the treatment of disease and especially mental illness with drugs'.
- **Placebo**: 'a placebo is an inert treatment or substance that has no known side effects. Researchers may utilise a placebo control group, which is a group of participants who are exposed to the placebo or fake independent variable'
- **Active Placebo**: 'a substance used in controlled experiments (such as a double-blind study of a drug) that has no therapeutic effect on the condition being treated but may produce effects (such as drowsiness or nausea) similar to those of the substance whose effectiveness is being tested'
- **Default Mode Network (DMN)**: 'the default mode network (sometimes called the default network) refers to a group of interconnected brain structures that are hypothesised to be part of a functional system activated when one is awake but not involved in any specific mental exercise'.
- **Chief Principal Investigator (CPI)**: 'responsible for the direction and oversight of compliance, financial, personnel, and other related aspects of a research project'



Student Induction Glossary (2/2)

An Introduction [Psychedelic] Research Glossary

- **Neurotransmitter:** 'a chemical that carries messages from nerve cells to other nerve cells or muscles'
- **Chemical compound:** 'refers to a substance made up of two or more elements that are chemically bonded together'
- **Neurological:** 'of, or relating to, or affecting the nervous system: of or relating to neurology'
- **Novel Drugs:** 'Novel drugs are often innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient care and public health'
- **Hallucinogens:** 'a group of drugs that work on the brain to affect the senses and cause hallucinations – seeing, hearing, smelling, testing, tasting or touching things that do not exist'
- **Phenethylamine:** 'refers to a class of substances with documented psychoactive and stimulant effects and include amphetamine, methamphetamine and MDMA'
- **5-HT_{2A} receptor:** 'serotonin 5-HT_{2A} receptors (5-HT_{2ARs}) are widely considered distributed in the central nervous system, especially in the brain regions essential for learning and cognition. In addition to endogenous 5-HT, several hallucinations, antipsychotics, and antidepressants function by targeting 5-HT_{2ARs}'.
- **Set & Setting:** 'describes the physical, mental, social and environmental context rather than what an individual brings into a psychedelic experience. The phrase is credited to Timothy Leary, who popularized psychedelic use in the 1960's'
- **Tryptamine:** 'a diverse group of 5HT_{2A} agonist compounds. The predominant clinical effect produced by tryptamine exposure is hallucinations, mediated by agonism at 5HT_{2A} and 5HT_{1A} receptors.'
- **Neural Plasticity:** 'refers to the capacity of the nervous system to modify itself, functionally and structurally, in response to experience and or injury'.

