CLINICAL TRIALS

Clinical Research Trials in Australia

Before a new medical treatment can be approved for general use, its safety and effectiveness must be tested in a *clinical trial*. Clinical trials involve human volunteers who may benefit from the new treatment. There are many restrictions to determine who can participate in clinical trials, and participants are protected by rigorous safety and ethical standards.

Before a new treatment can be approved many research studies must be conducted. Scientists first test the treatment in cell models and then in animal studies. Even if the treatment shows promise in early stages, significant amounts of time will pass between when it is discovered and when it is approved. This is to ensure that the treatment is effective and does not have dangerous side effects. The clinical trial process ensures a balance between bringing new treatments to the market quickly, and ensuring that they are safe and effective.

Key Concepts of Clinical Trials

Clinical trials are conducted using **randomised double-blind placebo controlled** (RDBPC) studies. RDBPC studies are considered the 'gold standard' in science because they establish cause and effect; RDBPC studies allow scientists to prove that treatment being tested is responsible for patient improvement instead of other factors.

A new drug must demonstrate a benefit over an existing drug or a placebo before it is approved. The trial is said to be *controlled* when there is a **treatment** group that receives a new drug, and a **control** group that receives a placebo or standard drug. The **placebo** group receives an inactive product that has no pharmacological effect (in studies dealing with serious or life-threatening illnesses, the currently accepted treatment is used instead of a placebo). The comparison between the control and treatment groups allows scientists to determine whether the new drug is effective.

To remove any factors or biases that could weaken the study, clinical trials are **randomised**, which means subjects are randomly assigned to the treatment or control group. Clinical drug trials are **double-blind**, meaning neither participants nor doctors know who has been given the new treatment and who has been given the placebo or standard treatment. This is to avoid subconscious biases which could interfere with the results. Blinding can be broken in emergencies.

Some vitamin and mineral supplements are recognised as low risk by the Australian Register of Therapeutic Goods. This means they are rigorously tested for safety and quality, but may not be tested for effectiveness in the same way as drugs. Find out more about supplements and mitochondrial disease here.

Phases of a Clinical Drug Trial

Drug Discovery

- A promising new drug is discovered

Preclinical Studies

- In vitro testing - the drug is studied in laboratory cell models
- Animal testing - the drug is studied in animals for safety and efficacy

Ethical Review

- The drug passes extensive review by the Australian Human Research Ethics Committee (HREC)

Phase I

- A small group of healthy volunteers are given small doses of the drug. Researchers evaluate safety, looking closely for any adverse reactions

Phase II

- A large group of volunteers who suffer from the condition that the drug aims to treat receive the drug. Researchers assess whether the volunteers have an improvement in their disease or symptoms

Phase III

- Multiple large groups are established. One group receives the new drug, while the other groups receive a placebo or existing treatement. Researchers compare outcomes between the two groups

Government Review

- The Australian Therepeutic Goods Administration (TGA) analysis the data and, if the drug is demed safe and effective, approves the drug

Phase IV

- Data collection continues after the drug has been approved, to better understand how the drug works and how it should be used

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Trial Vs Study: What's the Difference?

A clinical trial is a specific type of study that researchers use to learn about medical treatments. The other main type of study is an **observational study.** Observational studies occur when researchers monitor patients over the course of their usual treatment and analyse their outcomes at the end of treatment. Observational studies are useful for learning more about the condition itself.

Clinical trials on the other hand are much more complex. They involve setting very specific conditions beforehand and maintaining these conditions throughout the course of the trial. Before a drug can be approved, it must be tested in a clinical trial and not simply an observational study. After approval, researchers may use observational studies to gather more information about the drug.

Getting Involved in a Clinical Trial

Researchers seek volunteers who are representative of the overall population the drug is designed to treat. All trials have strict inclusion and exclusion criteria which must be met before subjects can join the trial.

- **Inclusion Criteria** – may include different subtypes of the disease, or having/not having a genetic diagnosis
- **Exclusion Criteria** – elderly people and pregnant women are generally excluded from trials as they are particularly vulnerable to side effects

Volunteers must demonstrate **informed consent.** This means they understand the trial, the risks and benefits, and their personal responsibility as participants. Confidentiality is strictly maintained, and no identifiable information tying participants to the trial will be released.

Risks

Most drugs have side effects, and a few people may suffer serious allergic reactions or even death. Treatment is not guaranteed in clinical trials. However, trials can offer treatment options to people for whom no treatment currently exists. Trial participants make extremely valuable contributions to medical knowledge and to other patients with their condition.

There are often restrictions such as not being able to travel, eat certain foods, exercise vigorously, or take other drugs at the same time. Clinical trials are purely voluntary, and subjects may withdraw at any time. There is no cost to join a clinical drug trial.

Individuals interested in joining clinical trials for mito should join the Mito Foundation Mito Registry to be the first to learn of relevant clinical trials being conducted in Australia.

Who Sponsors Trials?

Clinical trials are paid for and conducted by three different kinds of organisations:

- Drug companies – privately held companies that make money by developing and selling drugs and therapies.
- Private organisations - under grant from National Health & Medical Research Council grant or donation.
- Public organisations – for example, a university or teaching hospital.

Due to the risks associated with clinical trials, federal regulations control how a trial can take place. Researchers must submit detailed plans to governing bodies for approval before a trial can take place. The main governing bodies involved are the Therapeutic Goods Administration (TGA) and the Human Research Ethics Committee (HREC).

- The HREC works with research groups to advise them on protocol and ethics as they conduct clinical trials on goods that have not yet been approved The TGA controls the supply and licensing of approved therapeutic goods in Australia.

Find out more about these groups: https://www.tga.gov.au/sites/default/files/access-hrec.pdf