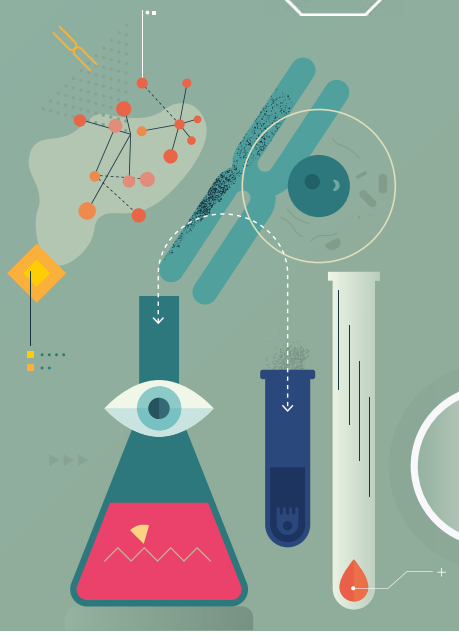
Clinical trials: your questions answered

A resource for people with Huntington's disease, their families and carers

To develop better treatments for diseases, we need well-run, reliable clinical trials. So it's vital that the most important people involved - the potential participants - are well informed about what clinical trials are, and how and why they are run. This is especially true in Huntington's disease, where research is increasing.



This leaflet has been produced by Roche, in consultation with Huntington's disease organisations, to provide basic information on clinical trials of medicines.

Trials may test more than medicines, for example lifestyle changes, surgical procedures, medical devices etc. For simplicity's sake, this pamphlet focuses on medicines.

What are clinical trials?

Clinical trials are medical research studies involving people. New medicines are first studied in a laboratory. Those that are promising are then submitted to quality health care committees for review and approval before any studies in people can begin.

Why are clinical trials needed?

To answer questions such as: Does a new medicine work? Does it work better than existing therapy options? Does it have side effects?

This is vital to help healthcare professionals understand which medicines are most suitable for any individual.

It is important to know that there is no guarantee that a clinical trial will find a better treatment.[1]

A trial medicine may turn out to not be an improvement on existing options or may be too limited by side effects.[1]

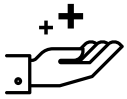
However, information gathered during any trial, successful or not, is still very useful, and may inform medication development in future trials.[1]

Who conducts clinical trials, and how are they regulated?

Various organisations, including governments, pharmaceutical companies, hospitals and universities may conduct clinical trials. Trials are regulated by laws, codes of conduct and ethical standards.

Before a trial can begin, it must be approved by the Ethics Committee of each hospital in which it is going to be run.

What are the benefits of participating in a clinical trial?



These may include:

- Contributing to the development of medication that could positively change the course of a disease and its impact on existing and future generations.
- Access to medication that is an advance on existing therapy.
- Access to medical experts and facilities.
- Comprehensive monitoring of participants' health while on the trial.

If you have more questions, please speak to a healthcare professional. A link to more information is on the back page

What sorts of clinical trials are needed in the development of medicines?

Clinical trials are divided into different phases: 1, 2, 3 and 4, often written as Phase I, Phase II, Phase III and Phase IV. A trial medication moves through these phases, in order, provided it meets the stipulated goals of each phase.

PHASE	AIM	IN WHOM
1	To understand the safety and effects of a medication, for example: how much is safe to give and how the body copes with it.[2]	A small number of people, usually healthy participants or very sick people with limited treatment options.[2,3] They often all receive the medication, usually beginning with small doses.[3]
2	To test how well the medication works in a disease; how to manage any side effects, and the best dose to use.[2,3]	Larger numbers of participants who have the disease.[2,3]
3	To confirm a new medication's safety and efficacy (how well it works).[2,3] This is generally the last step before approval can be sought from regulatory authorities for the medication to be available for more widespread use.[2,4]	Even larger numbers of participants, potentially thousands.[3] They may be split into groups, to compare one group vs another (see 'Randomisation' below).[3]
4	To monitor a medication's efficacy and safety in more people with the disease, and/or over an extended period of time.[3,5]	People using the new medication after regulatory authorities have approved it.[3,5]

How are clinical trials run to help ensure they are reliable and credible?

For a clinical trial to give a reliable, accurate answer to a question such as *"Does a new medicine work better than existing therapy options?"*, it has to be designed so it is balanced. The trial can't be biased either in favour of the new medication, or against it.

Ways to ensure trials are balanced include:

Randomisation

Trials often involve splitting participants into groups; one group receiving the new medication, the other group/s receiving an established treatment or a placebo (a substance resembling the medication but with no active ingredient).[6]

The aim is to compare what happens to the people in each group, and to see whether the difference between the two groups is large enough so that it is very unlikely to have happened by chance.[6]

The groups need to be as similar as possible, except for the medication received (or not received), so that any difference in outcome is due to the medication and not due to differences between the groups.[6]

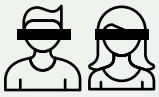
To ensure the groups are as similar as possible, in terms of age, gender (male/female) and other features, people are randomly allocated to them, like flipping a coin.[6]

Blinding

If a participant or a researcher knows which group the participant has been allocated to - new medication or placebo/comparator medicine - this can make them biased about the responses they observe, and how they report the effects of the treatments they are given.[6]

In a single-blind trial:
the participants do not know whether they are on the new medication or placebo/ comparator medicine.[6]

In a double-blind trial:
neither the participants nor the researchers know.[6]



This blinding approach therefore reduces the chance of bias.[6]

Clinical trials of new medicines may include a group of participants who do not receive the new medicine.[6]

What happens before a clinical trial?

Checking eligibility: Just because someone has a disease, it doesn't mean that they will automatically be eligible for a trial of a medication for that disease.

Inclusion criteria:
Trials are designed for a specific group of people with a disease, based on factors such as:

- A defined age range.
- Gender - for example only men or only women.
- Type and stage of disease - for example only people with disease above or below a threshold of severity.

Exclusion criteria:
A trial may also have exclusion criteria - characteristics that disqualify people from participating - such as:

- Presence of other medical conditions - for example people with conditions that might make them particularly vulnerable to the trialled medication's side effects.
- Use of other medications - for example people using medications that could mask the trialled medication's effect.

These inclusion and exclusion criteria are critical because they typically identify a group of people in which it is hoped that the medication will have a positive effect.

While exclusion criteria can result in disappointment for people, it is very important that healthcare professionals stick accurately to them.

Eligible, but still not enrolled in the trial: People may also be excluded from a trial if it has already recruited enough participants.

When trials are planned, they will generally have a target number of participants.

The aim is to have enough people involved so that the results are due to a real effect of the medication, and not chance.

For example, if two out of three people improve while on a new medication, this may be due to chance. But if 200 out of 300 improve, this is more likely to be a real effect.

The researchers will use a formula to calculate the target participant number, and when it is reached the trial closes recruitment.

Informed consent: The decision about whether to volunteer for a trial rests with the participant.

Issues to be considered include what the trial is aiming to show; any possible benefits and risks involved, and what taking part will involve.

Participants acknowledge they understand the trial by signing a form saying they have given their 'informed consent' to take part.

Importantly, informed consent is not a contract obliging participants to remain in the trial; they can withdraw at any time.

What happens during a clinical trial?

How and where participants take the treatment depends on the trial. They may be able to take it at home. In some cases, it may have to be in a hospital or clinic.

Participants may also need regular assessments and tests to monitor the medicine's effects.

Because a participant's commitment to the trial may last many months, and it can be disruptive to their normal life, they need to consider entering a trial very carefully, as it is important for the results that as many participants as possible complete the trial.

This is especially true considering that some participants may have to leave the trial early because of side effects.

To ensure the trial results are as reliable as possible, it is important that participants take the medication as instructed.

For example, at the correct dose, frequency, and time of day, and with or without food, as necessary.

What happens after a clinical trial?

Depending on results, participants are sometimes given the opportunity to enrol in an extension study, in which they are guaranteed to receive the active medication.

From the point of view of the trial researchers, the results will lead to a decision about what to do next, for example:

- To proceed to another trial phase.
- To stop the research.
- Or to seek regulatory approval for the medication to be available for use.

They may also decide on research in other stages of the disease, or even entirely different diseases. This broadens the medication's use, so more people benefit.

Often the anonymised results will be presented at medical conferences and published in scientific journals.

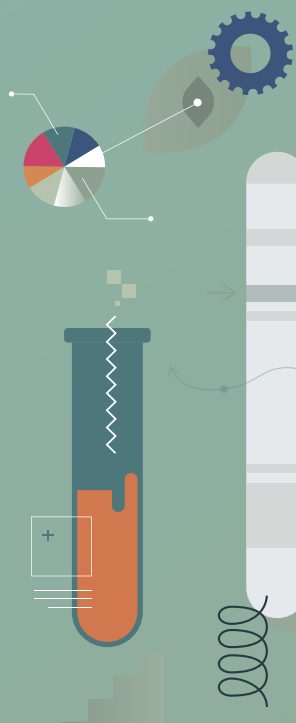
What if someone misses out on a place in a clinical trial?

Being excluded from one trial does not mean that a person will be excluded from another trial.

Being excluded also does not necessarily mean that they will not be eligible to receive the trial medication, if and when it is approved.

For more information

visit www.australianclinicaltrials.gov.au



This leaflet is an educational initiative, proudly sponsored by Roche. It is not intended as a substitute for advice from a qualified medical professional, nor it is considered a comprehensive and exhaustive source of information.

References: 1. Consumers Health Forum of Australia. Consumer Guide to Clinical Trials. Available at: https://www.australianclinicaltrials.gov.au/sites/default/files/content/18239%20NHMRC%20-%20CHF%20Fact%20Sheet-v1-0-accessible.pdf Accessed July 2020. 2. Medicines Australia. Clinical Trials. Available at: https://medicinesaustralia.com.au/policy/clinical-trials/ Accessed July 2020. 3. Cancer Research UK. Phases of clinical trials. Available at: https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/what-clinical-trials-are/phases-of-clinical-trials Accessed July 2020. 4. Therapeutic Goods Administration. Australian clinical trial handbook. Clinical trial phases and stages. Available at: https://www.tga.gov.au/book-page/clinical-trial-phases-and-stages Accessed July 2020. 5. National Health and Medical Research Council. Phases of clinical trials. Available at: https://www.australianclinicaltrials.gov.au/what-clinical-trial/phases-clinical-trials Accessed July 2020. 6. National Health and Medical Research Council. How clinical trials work. Available at: https://www.australianclinicaltrials.gov.au/what-clinical-trial/how-clinical-trials-work Accessed July 2020. Roche Products Pty Limited, ABN 70 000 132 865, Level 8, 30-34 Hickson Road, Sydney NSW 2000. Medical Information: 1800 233 950. EMVRAD0003 EC-AU-9969 PreparedSep20