Clinical Trials Explained

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Introduction

Would you feel comfortable going to a doctor and being prescribed a medicine that they had no idea of whether it was safe and worked in people? Probably not, and that is the value of clinical trials.

Clinical trials are the way new medicines or new doses/indications are tested on humans. They may not be a perfect system, but the results do help us understand how the treatments work, and how well or how safely they work. The treatment decisions a doctor makes for a particular individual in a given situation will usually be based on the evidence they are aware of, collected during clinical trials, and reviewed by regulatory authorities.

This document aims to help demystify the what, who and why of clinical trials, so you can be better informed should you or someone you know ever consider volunteering for a clinical trial. It was prepared by AccessCR's founder, Janelle Bowden (PhD), who is scientifically trained with over 10 years involvement in monitoring and managing clinical trials for pharmaceutical companies.

AccessCR is committed to making available information that helps the general public understand clinical trials and their pro's and con's, that they know how to find trials if interested in participating, and that they know their rights and how to question the researchers about the clinical trial they might be considering participation in.

While we believe this document to be an accurate reflection of the clinical trial process, we also advocate that readers do not rely on any one source for all their information. As such, we provide links to a number of other reliable sources of information on clinical trials on the Clinical Trial Information page of our website that we encourage you to review. If at any time you have feedback on the content of this document, please feel free to let us know at MoreInfo@AccessCR.com.au.

Where do clinical trials fit in to the process of developing a new treatment?

Developing a new medicine is a 4 step process:

- **Step 1:** Thousands of compounds are screened in the laboratory for their potential biological activity against different diseases. For those with activity, their chemical structure is determined, and perhaps altered to maximise the potential activity observed.
- **Step 2:** In the preclinical phase, compounds that were found to have activity in step 1 undergo further laboratory tests and animal tests to assess if the potential activity continues to occur, and if there are any initial signals to suggest the compound might be unsafe in humans.
- **Step 3:** Compounds that appear safe according to regulatory requirements, show good potential to treat a disease, have a stable chemistry and are able to be manufactured affordably in large quantities will usually go into the Clinical trial testing phase (described further below).
- **Step 4:** Once all required trials are completed, the data collected will be analysed and submitted to regulatory authorities (such as the FDA). Regulators will then review and determine whether they believe the compound is safe and effective (based on current data) to be approved to be used in the general population.

Only about 1 in 10,000 of the compounds that might have been originally tested in the lab will eventually be approved for use in the public after 10-15 years of testing, at a cost of up to $1 billion.

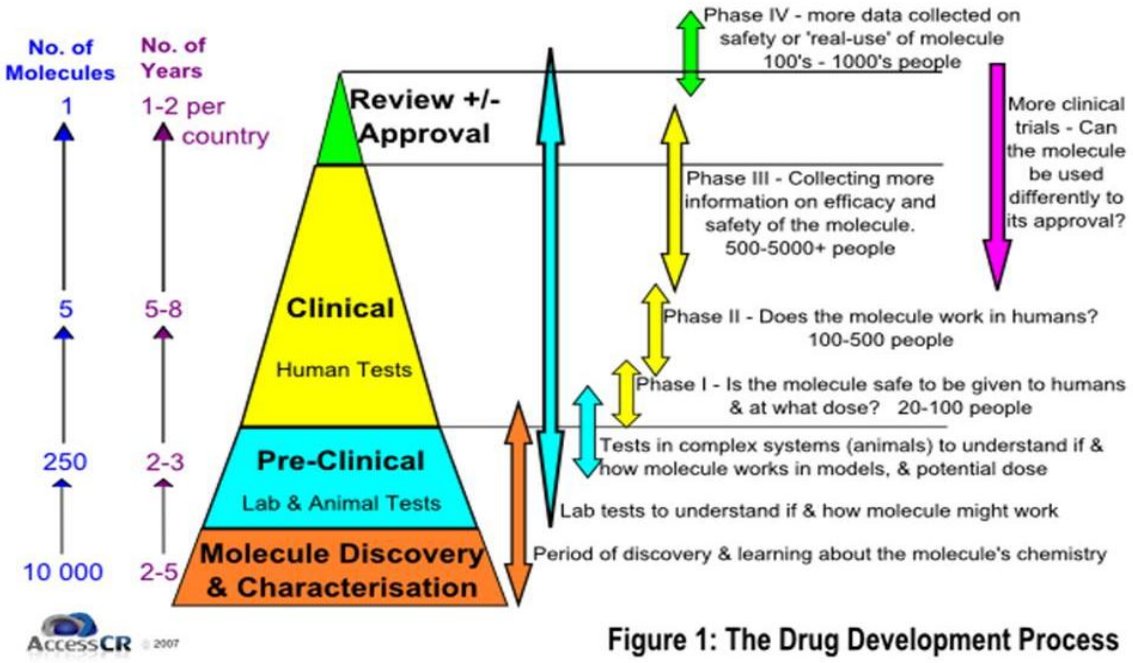

Figure 1: The Drug Development Process

Regulators will approve a medicine for use in a particular disease at a particular dose for a particular type of person. Many drugs however may work in more than one situation. So, an “approved medicine” may go back into the clinical research phase if it is thought it might work at a different dose or dosing schedule, or in the treatment of a different population or health condition.

The final point to note is that the different phases in the development process tend to overlap, and continue even after the approval of the new medicine as researchers, companies, governments and doctors try to understand everything they can about a new medicine.

Is the evidence from clinical trials perfect?

The wonderful things about humans is our individuality. The lottery that is our genetic make-up means that we are all unique, and this means we can react differently to medications.

It is not possible to test every new treatment on every person before approval, so researchers try to understand how a medicine works through testing in a clinical trial on only a sample of people. Researchers hope a sample will reflect how well and safe the intervention may be in general population, but it is not always perfect because of genetic variability, and human factors.

The size of the sample tested in clinical trials depend on how frequent, serious or chronic the condition being treated. For example, a medicine used to be used to treat high blood pressure, which lots of people have, will be tested on more people than a treatment for a rare disease for which there might only be 1000 people in the world affected. Or, there may be less people tested if there is thought to be an urgent need for a treatment, for example because people die from the condition and there is no other treatment. By the time a treatment is approved, it may have only been tested on 5,000-10,000 people worldwide.

Clinical trials are run under strict conditions with close medical monitoring in only a fraction of the population that may eventually receive the medicine. “Real-life” use of a medicine after it is approved can therefore uncover safety issues that were not previously found, or recognised as issues, in clinical trials. Clinical trials will continue after a medicine is marketed to collect further safety data. The new safety information collected can result in regulators sometimes taking approved medicines off the market.

What types of clinical trials are there?

There are lots of different types of clinical trials, and they are not all drug trials.

Treatment trials test the how well and how safe a new treatment or a new way of using a standard treatment is. The treatment being tested might be, for example, a device, a drug, herbal supplement, complementary or alternative therapy, or a new tool, procedure or surgical technique.

Diagnostic trials study new tests and procedures that might help identify a disease earlier or better. Screening trials might be done to identify people with, or at risk of, a health condition before there are symptoms.

Prevention trials may look at ways to reduce the risk, or chance of developing a condition.

Genetic studies are sometimes done as part of a clinical trial to help understand how genes may be linked to the detection or diagnosis of a condition, or the response to treatment.

What are Phase I, II, III, or IV trials?

The terms phase I, II, III and IV are usually used when there is an drug being tested. There can be multiple trials in each phase. The phases usually follow one another, but can sometimes overlap. Decisions will be made at the end of each trial whether to continue testing the treatment.

Let’s consider the treatment being test is called DrugABC.

Phase I

The first time DrugABC is tested in humans is called a FTIH (first time in human) or Phase I trial. The aim of Phase I trials is to find out what dose is safe in humans, how DrugABC should be given (by mouth, injected into a vein, or injected into the muscle), and how often. The researchers will watch closely for any possible side effects.

These trials are usually done on people staying in hospital so that the volunteers can be watched very closely, and there are doctors close by to help if there is a problem. These trials can take days to weeks to

finish, so can represent a big inconvenience for volunteers. This is why these are the only trials where volunteers are sometimes paid a small amount to participate.

Phase I studies are done in only a small group of 20-80 people, normally healthy people and usually men. This is because the possible effect on a women's reproduction system (which does not renew like the reproductive system of men) may not be well known at this early stage of development. Healthy volunteers are not used in phase I trials when a treatment is potentially toxic, such as for some cancer treatments, where it would be unethical to try these treatments on healthy people.

Volunteers are usually divided into smaller groups, called cohorts. Each cohort is treated with an increased dose of DrugABC and the highest dose with an "acceptable" level of side effects will usually be used for Phase II studies.

Phase II

In phase II trials, DrugABC will be tested for the first time in people with the health condition the medicine is hoping to treat to find out if it has the desired effect, and to collect more safety information. There might also be some early comparisons with other products on the market to see if it is at least as good and safe as other medicines available. Typically these trials will involve 100-500 people in at least 2 different trials.

Phase III

If DrugABC appears to work in Phase II and still has an "acceptable" safety profile, it will be tested in larger groups (from 500-5000+ people) with the target health condition. The aim of these studies is to show that DrugA works, and how safe and well it works compared with other treatments available. Researchers will continue to monitor for side effects and collect information that will allow the treatment to be used safely. Once all phase III trials are completed, if the treatment looks good, companies will submit the data to the regulatory authorities for review, and hopefully approval.

Phase IV

Once DrugABC is approved, regulatory authorities usually require the company to perform additional clinical studies under more "real-life" conditions to collect more information on DrugA's risks, benefits, and optimal use. These are called Phase IV or "post-marketing" trials.

Who runs clinical trials?

Clinical trials are run by researchers, also called investigators, who could be trained as scientists, medics, nurses, complementary or alternative medicine practitioners, or other health professionals, like physiotherapists.

The researcher with primary responsibility for looking after the trial at a particular centre (called the principal investigator) should have relevant qualifications and experience to run the trial and care for the safety of the people in the trial. Those qualifications will usually be reviewed by the ethics committee and sponsors of the trial before the trial and investigator are approved to start.

The principal investigator is allowed to delegate responsibilities to their research team, but the team must be trained for the tasks they are delegated. The principal investigator will always have the final responsibility for the way the trial is run and the quality of the data collected.

Who pays for (sponsors) clinical trials?

Clinical trials may be funded by a range of organisations, including:

- private and/or commercial enterprises (for example biotechnology, device or pharmaceutical companies);
- not-for-profit organisations (for example the Cancer Council);
- philanthropists (like the Bill and Melinda Gates Foundation);
- government agencies and research councils who are interested in better or more cost effective treatments or ways to prevent, screen, or diagnose health conditions.

Ethics committees will review the funding arrangements for a trial before deciding whether to approve the trial to begin. It is not ethical to start a trial that will not have enough money to finish. They will also check that volunteer payments (if any) are ethical, and the payment to the clinical trial site and researchers is appropriate for the amount of work being performed.

Who regulates and approves clinical trials?

There are alot of rules around how to run clinical trials, based on international guidelines and local country regulations. The International guidance for how clinical trials are run is known as Good Clinical Practice (ICH-GCP). These guidelines set out the responsibilities of ethics committees, researchers, sponsors and monitors of trials, the records that should be kept and the details around documentation like safety information, study protocols and the information given to volunteers.

All trials that carry any type of risk will be reviewed and approved by a Research Ethics Committee /Institutional Review Board before they start. In some countries, the regulatory authority may also need to provide some type of approval before clinical trials can start.

Where do clinical trials take place?

Clinical trials are usually conducted in clinics where the researchers work. This might be GP or primary care physician offices, hospital clinics or departments, specialist clinics, and may be private or public institutions.

Trials can be “single-centre” (run at only one clinic), or “multicentre” (run at many clinics at the same time). Multicentre trials may be done in just one country, or multiple countries around the world.

Clinical trials vs Treatment – Therapeutic Misconception

Trials are conducted to find out if a new medicine or new use of an approved medicine is safe. You should therefore not take part in a clinical trial thinking the treatment you get will ‘treat you’ – it is still only being research to see if it will treat you. Sometimes you will do better, and sometimes you will not. The hope will be that the treatment will do good, but there is no guarantee when you are receiving a compound still being researched. This is something you must understand before you agree to take part in a trial. Always make sure the researchers tell you all the possible risks and benefits before you take part.

Is it safe to be in a clinical trial?

There is no guarantee of 100% safety by taking part in a clinical trial, because the purpose of clinical trial is to establish safety and whether the treatment works for a particular condition.

A researcher would never ask you to take part if they thought the risks outweighed the benefits, nor would an ethics committee approve the trial. Ethics committee review the safety data to make sure the expected risks don’t outweigh the expected benefits and that the trial is scientific and appropriately conducted. During the trial the researchers will pay extra special attention to make sure your health is being looked after.

There is more information below to help you work out the level the risk of a clinical trial and whether it is right for you.

Why would I take part in a clinical trial?

Different people have different reasons for volunteering for clinical trials. You might like to take part to have a more active role in your own health, get personal medical attention from the researchers, obtain expert medical care, gain access to new treatments early, or help others in the future by contributing to the advancement of medical knowledge.

One potential benefit of being in a clinical trial is the extra attention you will receive from the medical research team than you wouldn’t get as an regular patient. The research team need to make sure you are safe during the trial, so they will be checking your well-being far more thoroughly than usual. Any tests involved with the trial will usually be at no cost to you.

The negative of all this extra attention is the extra responsibilities you will have in following the trial procedures and the inconvenience you may have of visiting the clinic more often for trial visits.

You may not be interested in a particular trial because you don’t like the possible side effects, you don’t have the time or willingness to follow the procedures and attend the study visits, or you think you’d prefer to take an approved medicine already available.

Ultimately, taking part in a trial is your own decision and you should never feel pressured to go into a trial. If you do agree to take part, you can withdraw your participation at any time without consequence to your future medical care.

Will I get paid for taking part in a clinical trial?

Normally, it is only volunteers hospitalised for phase I trials that are offered payment. This is because they are usually healthy people, confined to a clinic non-stop for days to weeks and can't expect any medical benefit from the treatment being researched.

Payment is not usually considered ethical for other types of trials, as it might induce people to take part for money. The information sheet on the trial for volunteers will specify any reimbursement that the ethics committee have approved. This might include re-imbursement for travel expenses getting to and from the clinic, or a snack if you are at the clinic for long visits (of a few hours or more). For very long trials (that are many years long), you might sometimes receive a gift during the trial, that is perceived in some way relevant to the conduct of the trial or health condition you have.

The indirect financial benefit of participating in a trial is the medical care and tests performed specifically for the purposes of the trial will be free to you. Anything that is considered standard care and not being done only for the trial you will usually still need to pay for.

How do I know if I might be suitable for a trial?

Every trial has a list of eligibility criteria that outlines who will be suitable (or eligible) to take part. You may see this list referred to as the "Inclusion/Exclusion Criteria". These lists are important for the safety of the volunteers, and reliability of the data from the trial.

The clinical trial registers available online will usually list the main trial inclusion/exclusion criteria. However, only the researchers will be able to make the final decision as to whether you are eligible after reviewing your health and screening test results against the inclusion/exclusion criteria. The research can only perform this review after they have explained the trial and you have decided to consent (agree) to take part.

What is Informed Consent? What is the process and how should I prepare?

The very first step for someone considering taking part in a study is the discussion they will have with the researcher to introduce and explain the trial. This discussion is a process called '**Informed Consent'**. The use of the word 'consent' doesn't mean that you have to agree to the trial. Rather it is about making sure you understand everything you need to know about the trial and the treatment so you can decide if the trial is **right for you**, before you consent.

If you know in advance that you are going to discuss a trial with a researcher, it can be a good idea to prepare for that meeting. It is likely that you will hear alot of new information, and it can be hard to remember it all and absorb it all at one. Therefore you might like to:

- Write down a list of possible questions to ask to bring to the meeting (but don't be afraid to ask new questions if you think of new one's during the meeting).
- Ask a friend or relative to come along for support and to hear the responses to the questions.
- Bring paper to write down the answers to your questions during the meeting, or bring a tape recorder to record the discussion for later. (Note: For privacy reasons, you should ask the researcher if they mind you recording the conversation).

The researcher will usually provide a written information sheet that tells you the reason the trials is being run, what is being tested, what you will need to do, the potential side effects and benefits, your rights and protections in the trial, what happens to the data collected, and contacts for more information. Sometimes a researcher may (unintentionally) forget to tell you something about the trial in their discussion with you, so it is very important that you read this information, in addition to talking to the researcher.

Unless the trial is for an emergency treatment that needs to be given quickly, you will usually be able to take as much time as you need to read this information, ask questions and understand the trial. This means you can take the information home to read if you would prefer to read more slowly, ask your regular GP or family members for their opinions, or think more slowly about the trial. It is OK to ask other people for their opinions about the trial, so long as your remember those opinions are given for lots of different reasons, and may not necessarily be informed with all the facts on the trial or your health. The choice whether to take part in the trial or not should always be your own decision.

Sometimes researchers may have trouble explaining a scientific term easily in writing, so while they try to write the information in an easy to understand way, if there are words you do not understand, or you have difficulty reading or communicating in the language the information sheet is written in, you should ask the researcher, ethics committee or other people you rely on.

You have every right to say no if you are uncomfortable, feel rushed, don't understand or don't want to take part in a trial, and it should not affect your future treatment. You also should report if you feel you have felt heavily pressured or coerced to take part in a trial, to the ethics committee.

What are some questions I might ask the researcher about a clinical trial?

It is important to ask questions before deciding to join a clinical trial. Researchers expect that you will have questions, so you should not be worried about asking. **No question is a silly question**. It would be far worse to take part in a trial that you did not fully understand. Some questions people might like to ask the researchers include:

The Study

- What is the purpose of the study?
- What health conditions must I have? Are there any particular conditions that would exclude me?
- Why do you think the approach being tested may be effective? Has it been tested before?
- How will it be decided which treatment I get in the trial? Do I have a choice?
- How many volunteers will be in the trial?
- Who is sponsoring the study?
- Who has reviewed and approved the study?
- What are the medical credentials and experience of the researchers and other study personnel?
- How will the study results and my safety be monitored?
- How long will the trial last?
- How will the results be shared?

Possible Risks and Benefits

- What are the possible short-term and long term benefits?
- What are the short-term risks, such as side effects, or possible long-term risks?
- What other treatment options are available?
- How do the possible risks and benefits of the trial compare with my current treatment, or other options?
- What will happen if I suffer a serious side effect as a result of the trial? Can I withdraw from the study at any time?

Participation and Care

- What will be my responsibilities if I take part?
- What kinds of treatment, medical tests, or procedures are involved? How often will I receive the treatments, tests, or procedures?
- How often will I need to visit the researchers and what will I need to do between visits?
- Is there anything I am not allowed to do while I am in the trial? Are there any medications or supplements I shouldn't take while I am in the trial?
- Will treatments, tests, or procedures be uncomfortable or painful? If so, how can I be made more comfortable or have the pain controlled?
- How do the tests in the study compare with what I might receive outside the study?
- Will I be able to take my regular medications while in the clinical trial?
- Where will I come for my medical care? Will I need to be hospitalised? If so, for how long?
- Who will be in charge of my care? Who should I contact if I have a problem?
- Will I be able to see my own doctors?
- How long will I need to stay in the study? Will there be follow-up visits after the study?
- Will I have access to the medicine after the trial is over?

Personal Issues

- How might the trial affect my daily life?
- Will participating in a trial affect my life insurance and medical insurance status? Am I covered by insurance if something goes wrong because of the trial?
- Who will get to see my medical records, and how is my privacy protected?
- Do I need to tell my GP about the trial, or do you do that?
- What support is available for me and my family?
- Will I be paid to take part in the trial? Will any of my expenses be covered?
- Can I talk with people already enrolled in the study?

These questions are also available as separate document to download on the AccessCR website.

How do I put the risks of a trial in context?

Everyone has different ideas of what are acceptable risks. Some people choose to sky-dive, race fast cars or bungee jump, whereas others would feel too uncomfortable with the risks to ever try them. In that sense, assessing the risk of taking part in a clinical trial will also be an individual decision, because different types of trials have different levels of risk.

Some people are quite happy to take part in phase I trials because their perception is that level of risk (the drug has never been tried in humans before) is lower than the potential benefit for themselves (financial reward). Others would not be comfortable with that decision.

You will need to assess each trial on its own merits according to your own risk profile. Here are 13 things you might like to consider:

1. Is this a phase I, II, III or IV trial? Is it a screening, treatment, or prevention trial? What types of trials am I be happy to take part in?
2. What is an "acceptable" level of side effects? This will be different for every new treatment. Before an ethics committee approve a study they will have made their professional opinion on whether the trial has an acceptable level of risk, based on what the expected benefits of the treatment are compared with the known or anticipated risks or side effects. The ethics committee would never approve a trial if it considers the risks outway the benefits. If you are not sure what the ethics committee has reviewed, you should contact them using the details provided in the patient information sheet, or through the institution that the researcher works for.
3. What do you know about the side effects of the treatments you would be taking if you weren't in the trial? How new are those other treatments and how many people have used them in order to collect the safety information on those treatments? Think about how many people you would feel comfortable knowing had used the treatment, before you'd be comfortable with the amount of safety information known and therefore willing to use the treatment yourself.
4. Is this a new treatment being tried, or is it a different use for a treatment that has already been approved?
5. What is my chance of getting the test treatment in this trial, rather than the approved comparator?
6. Is there a placebo arm, and if so, would I be willing to risk no treatment compared to some type of treatment? As background, you should know that ethics committees look very closely any trial that has a placebo arm. While it is the best way to find out if a treatment works is to compare it to no treatment, it is considered unethical to give no treatment if there is what is considered to be a "good" treatment currently on the market. If there are treatments on the market, trials might still have a placebo arm if current medical thinking suggests the impact of those treatments is not great.
7. What types of side effects might I be willing to put up with compared to the benefits if the new treatment works? As an example, you might think that feeling sick for a few weeks while you receive a cancer treatment is OK if that treatment might slow down or stop the cancer. However, you might not be prepared to feel sick every day taking an arthritis medication whenfor you, feeling sick is worse than having to put up with the arthritis pain.
8. What is the chance you will get any of the side effects listed in the patient information sheet? Early in the life of a new treatment, it is hard to know how often particular side effects occur. Researchers may have some limited data, but may also need to guess at the types of side effects that might occur based on experience with other drugs that work in a similar way.
9. For example, if they have only tested 200 people, the side effect that will happen in only 1 in 10,000 people may not yet have appeared. Or it may have appeared, but because only 200 people have been tested, they don't know it will happen less often than 1 in 200 people. You might like to look at other similar drugs to see how often the side effects happen. You might also like to see how often the same types of side effects happen the treatments you would get outside of the trial to see if there is much difference between the trial treatment and your other choices.
10. What is the impact of some of the side effects on my health? For example, if swelling is a listed side effect, what is the cause for that? Is the treatment causing fluids to be retained that I could take a pill to relieve or is it likely to have a more serious effect such as causing congestive heart failure that I could get hospitalised for? This is something you should discuss with the researcher who should be able to provide you with more information if you need it.
11. Does the trial have any risks that are not associated with the treatment itself, but with some of the procedures that take place? For example, taking blood can cause bruising, regular X-rays expose you to radiation, or some people can be allergic to the contrast agents used in MRI or CT scans. You might be comfortable with the blood draws or CT scans because you have had them before and didn't have a problem, or the procedures are not often enough for you to be worried, or these may be risks you aren't prepared to take.

12. Do you feel that the research team have the time, experience and qualifications to look after your safety while you are in the trial? One advantage of being in a trial is the close medical attention you should receive from the research team, but you need to be confident they have the resources and experience to look after you.
13. Finally, do you have a good rapport with the research team and do you feel they have been open and up-front with you about the risks? If you feel comfortable with the research team, it is more likely that you will comfortable with the risks of the trial as you will have confidence in their expertise and ability to take care of you in the case of a problem.

At the end of the day, only you can decide whether you are happy to accept the risk of taking part in a particular trial. You should feel confident to ask the researcher if you need any help getting more information to help you decide on the risks.

How do I confirm for myself that I understand a trial before I decide yes or no?

After you have read the information sheet and discussed the trial with the researchers, you should ask yourself these questions to make sure you understand what the trial is about and what you will need to do if you take part:

- why the study is being done ?
- why am I suitable or being asked to take part?
- who is running the study and who is funding the study?
- what are the treatments being tested and what is the chance of receiving each treatment?
- Who pays for the treatments and tests done for the trial?
- Why do the researchers think the treatment being tested might work and has it been tested before?
- what are the risks and benefits of being in the trial compared to my current or alternative treatment/s?
- who would I contact with any questions before or during the study?
- who is looking after me during the trial and how do I contact them if I had any questions or problems during the study?
- How long will I be in the trial?
- how often and how regularly I would need to visit the researcher?
- Will I need to be hospitalised?
- how long do the visits to the researcher take?
- What tests will I need to do when I visit the researcher (for example blood tests, or other tests that might make you uncomfortable)?
- What do I need to do between visits to the researcher? (For example, take tablets at a particular time(s) of the day, take a certain number of tablets, give injections, make phone calls, fill in a diary or questionaires)
- How might this trial affect my daily life, and am I happy with that?
- how is my identity and data being protected?
- how do I withdraw if I don't want to stay in the trial?
- for what reasons might the trial get stopped or the investigator withdraw me from the trial?
- Is there any follow-up care after the study?
- Will I get the results and when?

These questions are also available as a separate document on the AccessCR website.

I've been asked to consent for my child or someone else I care for. Is this OK?

Not everyone who is suitable to take part in a study are able to consent for themselves. Reasons for this might include they are too young, they have a mental health condition or they might be incapacitated in some way, for example, unconscious when a decision needs to be made.

The rules surrounding the ability of children to consent for themselves to take part in a trial are quite grey, and the decision is usually based on the researcher's confidence that the child understands what the trial is about and what might or will happen during the trial. Typically however, a researcher will ask a child to agree to a trial (assent), as well as the parents to agree for their child to take part in a trial (consent).

The USA regulatory agency, the FDA, have written an article to explain the reason for including children in clinical trials that might help you make a decision about whether you are interested in having your child take part in a trial.

The approach for consenting adults that may not be able to understand a trial or consent for themselves is similar to that for children. If local regulations allow, a carer/guardian might be able to consent on behalf of the potential volunteer. In emergency situations, where an immediate decision is necessary and no carer or guardian is available, doctors may be able to consent on behalf of a volunteer, although the volunteer would be asked to re-consent when they are able. There will be strict guidelines in place as to who can make these decisions and the process they need to follow.

What happens when I agree to take part in a trial?

If you agree to take part in the trial, you will be asked to sign a consent form. This form documents who had the discussion with you about the trial, when and that you agree to take part, knowing you can withdraw at any time.

You should be given a copy of the information sheet and consent form with copies of all the signatures for your reference. You should keep this document so you can be reminded what to do during the study and who to contact if you have any questions.

The next step is to be screened for the study to see if you are eligible to take part. Depending on the trial, the screening period may be minutes, days or weeks. You might be asked questions about your medical history, your family's medical history, your current medical conditions, any medications you are taking (which includes any herbal or vitamin supplements, creams or drinks), and/or you might be asked to fill in some questionnaires. Researchers might do some basic medical checks (such as height, weight, blood pressure, pulse rate), collect blood or urine samples, or do more thorough tests like X-rays, MRIs, CT scans, lung function or exercise tests.

If you aren't able to continue in the trial, the researcher will discuss with you what your future treatment options are. Some people feel disappointed when they are not suitable for a trial. That is understandable if there are not lots of other treatment options for you, or there is great hope in the new treatment. However, you should take comfort in the fact that the researcher hasn't let you go in the study because the screening tests suggested the treatment may not have worked for you or it wasn't going to be safe for you based on the information currently known about the treatment. And remember, a trial of a new treatment is only an investigation of what might work – there is no guarantee the test treatment will work.

If you do continue in the trial, you will get one of the treatments under investigation. Every trial is very different, so the number of visits, what happens at each visit, what you will need to do between visits to the research team and the length of the study will vary. It is very important you follow all the researcher's instructions during the trial, as these are there to try and keep you safe, and make sure the trial is run properly. A clinical trial is the one time when the rules are NOT meant to be broken.

I've signed the consent form, and have started the trial, but have now changed my mind about taking part. What can I do?

It is OK to withdraw from a trial at any time, and it should have no impact on the medical care you will receive after taking part in the study.

Signing the consent form is your commitment that you **plan** to finish the trial. You shouldn't agree to take part if it is not your intention to try to be in the trial to the end, as this wastes your time on unnecessary clinic visits and study procedures, other people miss out on taking part that might have wanted to, and the researchers may not be able to use the data collected because it is incomplete.

Having said that, there are going to be times when unforeseen things happen and you make a decision that you would like to withdraw from the study.

Always discuss withdrawing from a trial with the research team. This is not so they can talk you out of it, but so that they can make sure you withdraw safely. You shouldn't just stop the treatment. The research team will want to watch you carefully when you come off the study treatment, as they will be looking for any side effects that might be caused by stopping the treatment, just as they were looking for what happened while you were on the treatment.

What happens if there is new information or I have questions during the study?

Even though you signed the consent form at the start of the study, the process of informed consent is ongoing throughout the trial.

There might be times when you forget what you were told at the start of the study, or have thought of new questions you didn't have before. Any time you have questions about the trial or treatment, you should ask the researchers, and you don't necessarily have to wait until your next clinic visit to ask. The information sheet for the trial should provide the phone numbers of who to contact if you have any questions and don't want to wait until your next study visit.

There may also be times when new information becomes available that might make you change your decision to continue in the study, such as additional study visits or tests being requested, or new safety information, or a change in the researcher or sponsor of the trial. Any time you are provided with new information that might affect your decision to continue in the trial, you will be asked to sign an additional 'consent' form to indicated you received the information and agree to continuing taking part in the study.

Regulations require researchers to get any written information given to patients reviewed by an ethics committee before it is provided. For new information that is not considered urgent, you will receive the information once the ethics committee have approved the new information.

For information that is considered urgent for you to know, the research team may first tell you about the update before the ethics committee have approved the form and document your verbal agreement to continue in the study. They will then follow up with you at a later date with the paperwork once it is approved by the ethics committee. This process is allowed for urgent information because regulators understand that your safety must come first, ahead of making sure the paperwork is complete.

What does randomisation mean?

Randomisation is the method that researchers use to try to prevent bias in results that could be introduced if a patient or researcher could choose which treatment group to assign a volunteer to. The theory is that by randomly assigning volunteers to different treatment groups, where each treatment is theoretically as good as each other, you reduce the chance of bias in the results.

In simple terms, the chance you will be randomised to one treatment arm or another is like the chance of a women falling pregnant with a boy or girl. There is basically the same chance of both options, and neither option is better than the other in theory (although you might still have a preference).

What happens to the information collected about me in a trial? Is it kept confidential?

While you are in the study, the research team will be collecting information (data) about you to work out what effect the treatment having on you and your health condition. The information sheet and researcher should inform you how this data will be handled and how your confidentiality will be protected.

What happens at the end of a trial?

The information sheet should also explain what will happen at the end of the trial. If you have any questions, you should ask the researchers. Typically, you will need to return any trial medications or study supplies, and the doctor will perform a final medical review. The researcher will discuss your future treatment options.

You might be finished with the trial visits, but there might still be other people going through the trial, so the results may not be immediately available. If you didn't know what treatment you were taking during the trial, you normally won't be told until everyone has finished the trial and results have been analysed. The reason for this is that the researchers don't want to bias their interpretation of the results by knowing who received what treatment too early.

Once the results have been analysed, which can take months, the results should be published and the researchers should be able to tell you what treatment you received and what the overall results of the trial suggest. At your last visit, you might like to ask when/how you will receive the results.

Where can I find out what clinical trials are available?

The AccessCR website has a list of international registers you can search for clinical trials. Your local doctor, hospital or research clinics may also have information on clinical trials available in your local area. Occasionally, you may see trials advertised online, on TV or radio or in posters.

Where can I get more information?

A number of other reliable sources of information on clinical trials are listed on the Clinical Trial Information page of our website. Your doctor may be able to help, although many doctors do not participate in clinical trials, or know much about them. Many online disease associations and community groups also provide information about clinical trials. Never rely on just one source of information, and when it comes to health information online, be careful to assess whether the information looks to be from a reliable source.

The last word

If you are ever considering taking part in a clinical trial, always make sure:

- **you understand** what the trial is about, the procedures you will have to follow, how your rights and identity will be protected, that the risks and benefits have been properly explained and that the trial has appropriate ethical approval;
- you know that **it is OK to say no** to taking part;
- that **you can ask questions** at any time if you have them;
- that you **must consent** before a researcher conducts any tests;
- you **don't assume that you will always do better** by participating in the clinical trial;
- that if you agree to take part, **you can withdraw at any time;**
- **you know who to contact** if you have questions or need help.

If you still have questions about the clinical trial process, please do not hesitate email us at MoreInfo@AccessCR.com.au, and we will do our best to help.