UNDERSTANDING CLINICAL TRIALS AND DRUG DEVELOPMENT
A short guide
## CONTENTS

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>What are clinical trials?</td>
</tr>
<tr>
<td>3</td>
<td>Why do we have clinical trials?</td>
</tr>
<tr>
<td>4</td>
<td>How do clinical trials work?</td>
</tr>
<tr>
<td>5</td>
<td>How do clinical trials help the development of new medicines?</td>
</tr>
<tr>
<td>5</td>
<td>What kind of people take part in clinical trials?</td>
</tr>
<tr>
<td>6</td>
<td>How are people recruited on to clinical trials?</td>
</tr>
<tr>
<td>6</td>
<td>What are the risks?</td>
</tr>
<tr>
<td>7</td>
<td>What happens if something goes wrong?</td>
</tr>
<tr>
<td>7</td>
<td>Why do I get paid?</td>
</tr>
<tr>
<td>8</td>
<td>Can I change my mind?</td>
</tr>
<tr>
<td>8</td>
<td>How do you keep my personal information confidential?</td>
</tr>
<tr>
<td>8</td>
<td>What types of trials do Covance Leeds run?</td>
</tr>
<tr>
<td>9</td>
<td>What happens at the clinic during a trial?</td>
</tr>
<tr>
<td>9</td>
<td>How can I find out about trials I can take part in?</td>
</tr>
<tr>
<td>9</td>
<td>Where can I find out more about clinical trials?</td>
</tr>
<tr>
<td>10</td>
<td>Glossary of clinical trials terms</td>
</tr>
</tbody>
</table>

## INTRODUCTION

Covance is one of the biggest Contract Research Organisations (CROs) in the world with over 10,000 employees in over 60 countries, working with Pharmaceutical and Biotechnology companies from across the globe to develop new and better medicines. It takes 12-15 years and around £100 million to develop just one new medicine.

The UK is a world leader in clinical research, supported by an established healthcare system, world-renowned training and the highest quality regulations and the Covance clinic in Leeds encompasses all of these virtues.

Currently, public knowledge of clinical trials and the benefits they can bring to people’s health are not well known which hinders participation. Covance hopes the information provided in this booklet can help raise awareness of medicine development and the part clinical trials play in this process. Hopefully in turn, this will encourage more people to consider taking part in clinical trials and contributing to the discovery of tomorrow’s medicines.
WHAT ARE CLINICAL TRIALS?

Clinical trials are a type of medical research that involves both people with a medical condition and healthy people to test new medicines and treatments. They are used to collect scientific data to answer specific questions like if the medicine works as expected, what doses are needed and if there are any side effects. The more trials that are run, the more can be understood about the medicine.

The treatments could help people to survive a life threatening illness, for example a blood infection, or improve the quality of life for people with long term conditions, such as chronic pain, perhaps by offering a medicine with less side effects than the current options.
WHY DO WE HAVE CLINICAL TRIALS?

Clinical trials are the only sure way to understand how new medicines will work in people and are required by governments around the world. The information from the clinical trials is used to help the Doctors and Scientists develop the most effective treatment. All new medicines have to go through a number of different stages of development called ‘phases’ to get the approvals needed for patients to receive it. These are:

**Discovery** - In this phase pharmaceutical and biotechnology companies identify a potential new medicine. These are chemicals that are either made by scientists or they already exist in microbes, plants or animals. Some well known examples are:

- Paracetamol - is a “man made” pain killer
- Penicillin - is found naturally in some moulds
- Aspirin - was first discovered in the bark of the willow tree
- Insulin - is a hormone found in most animals

**Pre-clinical** - Any new drug must be tested in animals before it even reaches a person. Animals are used to identify any potential side effects and see how the medicine might affect the body.

**Phase 1** – Early stage testing in a small number of healthy volunteers to assess how long the medicine stays in the body for, if it is working as expected and to look for side effects. Participation in these studies lasts anywhere from a few days to 2 or 3 weeks.

**Phase 2** – Early stage testing in a small number of patient volunteers to see if the new medicine works in the patient group. These studies usually run over a period of months to sufficiently assess the effects.

**Phase 3** – Late stage testing in large numbers (sometimes thousands) of patient volunteers usually from across the world to compare the effects with the standard treatment, see how well the drug works and how long its effects can last, find out more about any side effects including how common certain ones are. The studies can last for years to investigate any possible longer term effects.

**Phase 4** – This is testing after the drug has been approved for use, to monitor the long term use and effectiveness as well as investigating any rare side effects.

The Covance Leeds clinic performs Phase 1 and 2 clinical trials to decide whether it is appropriate to develop the medicine further. If it has no health benefits or has unwanted side effects it may not be developed further.

Those medicines that do show potential to help patients will enter the later phases of development to provide the risk and benefit information to the Doctors who will decide if the treatment is right for their patient. This information also helps the government decide if the medicine is suitable for use in the NHS. In the UK a committee called NICE (National Institute for Health and Clinical Excellence) decides which new medicines can be prescribed by NHS doctors in the UK. You have probably heard about them on the news when they decide whether or not to recommend a new medicine.
HOW DO CLINICAL TRIALS WORK?

Highly trained and experienced Doctors, Scientists and Statisticians design a clinical trial to answer specific research questions. They will look at other trial designs that have been previously conducted to generate the most efficient design to collect data to answer the research questions.

This design is known as the ‘protocol’ which is the instruction document to explain how the trial will run. In order to conduct the study the protocol must be approved by both:

• A government regulatory body - in the UK this is the Medicines and Healthcare products Regulatory Authority (MHRA)
• An NHS ethics committee, an group consisting of medical staff like doctors and nurses as well as members of the public

What do the MHRA do?

For all trials in the UK, a Clinical Trial Authorisation (CTA) application must be made to the MHRA for approval to run the trial here. The MHRA will review the information provided and approve the trial if they feel that it is the most appropriate and safe design to collect the required data and that the information will be helpful in the development of the medicine.

What do the ethics committee do?

For Phase 1 and Phase 2 trials, the ethics committee determine if the trial is ethical by deciding if there is a real benefit to the potential new treatment and that any risks of side effects are minimal. In addition they check the information given to volunteers is clear and unbiased so they can decide for themselves if they would like to take part, the payment is appropriate for the time commitment for the trial and there is sufficient compensation for people in the trial in the unlikely event that something goes wrong. The committee can refuse to provide approval for clinical trials that do not meet these criteria and prevent the trial from going ahead.
HOW DO CLINICAL TRIALS HELP THE DEVELOPMENT OF NEW MEDICINES?

Each new medicine must be approved by the government of each country in which it is intended to be used. The government departments that make this decision need to be provided with evidence that the medicine is safe and has a health benefit. Conducting scientifically designed clinical trials is the only way that this information is generated to enable the approval of a new medicine for use. A new medicine will only be approved for use if:

- It is safe and works effectively
- It is a brand new treatment for a particular disease or it is a better treatment than the ones that already exist
- It causes fewer unwanted side effects in patients

WHAT KIND OF PEOPLE TAKE PART IN CLINICAL TRIALS?

Different people take part in different Phases of clinical trials. The early development studies often involve healthy volunteers and the later phase studies involve people with medical conditions (generally with the condition the medicine is intended to treat). The people who can take part are defined in the trial protocol in the eligibility criteria section. As these inclusion and exclusion parameters, such as age or medical history, ensures that the trial is safe and no volunteers are exposed to avoidable risks, it may limit the trials that you can take part in.

By undertaking screening tests, we can understand which of the trial criteria are a match for you. For example, if a potential side effect of a new drug is that it increases blood pressure you may have your blood pressure assessed to check if the trial will be safe for you. For Phase 1 clinical trials, women are often not able to take part if they are pregnant as the risk to the unborn baby is not known.

However, if you do not qualify for a particular study it doesn’t mean that you are unhealthy; it is just that particular trial is not right for you.

Healthy
Post Menopausal
65 Years Young
Smoker
Diabetic
Asthmatic
Obese

7000 people took part in a healthy clinical trial last year in the UK
HOW ARE PEOPLE RECRUITED ONTO CLINICAL TRIALS?

Covance Leeds has a dedicated team of volunteer recruitment specialists based at the clinic who manage our database of potential volunteers so we can contact them when a suitable trial is available for them. Our team is aware of all the trials that are available at the clinic and can answer any questions you might have about taking part in a clinical trial or refer you to one of our Covance Doctors if you require specific medical information.

We encourage people to join our database through general advertising, for example on the radio or via newspaper adverts. We maintain our volunteer website with up to date information about what it is like to take part in a trial and also have an online and social media presence, for example Facebook and Twitter, to enable our volunteers to communicate with us and allow us to let people know about new studies that may be coming up. All information is held on a voluntary basis so if at any point you would like to no longer be contacted, just let us know and we can update our database.

WHAT ARE THE RISKS?

Like most things in life, participating in clinical trials can carry some risk that no one can really predict. While any predictable risks are minimised through careful planning and design, there may be side effects that the doctors and scientists were not anticipating. These are often short-lived feelings such as nausea or headaches. As part of the clinical trial process, you will be given all the information that the researchers know about potential risks or the likelihood of sides effects.

During a trial, your wellbeing is the number one priority to Covance Leeds staff. You will be monitored regularly throughout the trial and will have constant access to our experienced and friendly medical team who will perform routine assessments to check on your health during your stay.

In addition to the payment you receive in return for the time you commit to the trial, you undergo a free thorough medical check up which is reassuring and could be of real benefit to your health if something is picked and treated quickly. However most importantly, you are helping to develop new medicines for people who really need them.

Taking part in a clinical trial is a great thing to do, both for yourself and for the benefit of future patients. However like most extraordinary things, clinical trials aren’t for everyone. What you need to think about is whether the potential risks outweigh the benefits to you.
It is highly unlikely that anything will go wrong.

**WHAT HAPPENS IF SOMETHING GOES WRONG?**

It is highly unlikely that anything will go wrong when taking part in a clinical trial, however every trial must have arrangements in place in the rare event that something does. Some people do react badly to some medicines, including those already prescribed by doctors. No one is really sure why, and it cannot be predicted, but it is very rare and with the right staff and equipment present the symptoms can easily be treated. In such cases immediate medical care is provided by the clinic and the local hospital if necessary.

**WHY DO I GET PAID?**

The early stages of drug development need healthy volunteers to provide accurate information about the properties of a new medicine. If people with a medical condition were used at this stage, their condition often affects the quality of the study data therefore making it hard for the Doctors and Scientists who are developing the drug to make the right decisions. Healthy people don’t need to take a medicine, so we pay you for the time you spend on the trial and the inconvenience it causes to your normal daily lifestyle.

Each clinical trial will have different requirements in terms of the assessments performed; how long you need to stay in the clinic and the restrictions you might need to adhere to, for example refraining from strenuous exercise and drinking alcohol for a week before the study or following our detailed timetable of assessments and activities like the times you can eat and go to bed.

You are paid for this inconvenience and commitment of your time i.e. the more complex and the longer the trial lasts, the more you are paid because you have to commit more time to the trial and be inconvenienced for longer. It is important to note that you are not being paid because the trial or the new medicine is “risky”, the scientists and clinicians designing the trial do so with aim to reduce any risk as much as possible. The study payment is simply to compensate you for the time and inconvenience you will experience by participating in a clinical trial.

By contrast, in the later clinical trials such as in Phase 3, it is normal for patients not to be paid for their participation because their health can benefit.
**CAN I CHANGE MY MIND?**

Yes. Clinical trials are entirely voluntary so you can stop your involvement at anytime. However, if you do decide you no longer want to take part, your payment may be affected.

**HOW DO YOU KEEP MY PERSONAL INFORMATION CONFIDENTIAL?**

If you register on our volunteer database, we will need to collect personal information, such as contact details and an address, as well as information about your medical history. We will also request a copy of your medical records from your GP, but only with your prior consent. All this information will be kept confidential. Only limited staff within the clinic have access to the database and all trial information is anonymised. We like to inform your Doctor that you have taken part in a clinical trial, but again only with your consent. If any clinical trial data is published in medical journals or presented at scientific conferences, the results are always anonymised and no names or any identifying information will be used in any reports about the trial.

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**WHAT TYPES OF TRIALS DO COVANCE LEEDS RUN?**

Covance Leeds run two types of trials:

- **First-in-Human (FIH) trials** - the first time a test medicine is given to people
- **Labelling trials** - providing information on the medicine label or to help the prescriber, for example if the medicine should be given with food, if the age of the patient will affect the amount of medicine needed or if it might affect any other medication the patient might be taking at the same time.

The clinical trials in the Leeds clinic tend to run from a few days to a few weeks. Occasionally we have studies that may last a couple of months, however as the clinic performs mainly early stage development trials in small numbers of healthy volunteers or patient groups, they tend to be quite short in comparison to the later stage trials which look at long term benefits of a medicine.
WHAT HAPPENS AT THE CLINIC DURING A TRIAL?

The collection of information about the new medicine is the reason for conducting a clinical trial, so there will be a number of tests and assessments performed such as measuring your blood pressure, taking blood samples or filling in questionnaires. We will also want to look out for any potential side effects so you will be asked how you are feeling at regular intervals while on the trial. As these assessments are performed to a detailed timetable, you will need to stay at the clinic either overnight or for a set amount of time during the day so these can be performed. A clinical trial is a very complex scientific experiment in which we ask our volunteers to live their lives whilst in the clinic, to a very detailed timetable of assessments and activities (we even tell you when you can eat and go to bed!). However, in between these assessments you will have lots of free time to use our entertainment facilities.

HOW CAN I FIND OUT ABOUT TRIALS I CAN TAKE PART IN?

Covance Leeds provides ‘trial listings’ to our volunteers on the database. You can register for the volunteer database online or call our recruitment team on 0800 591 570 or 0113 394 5200. We also detail our current studies on our website at www.covanceclinicaltrials.com/browseourstudies

WHERE CAN I FIND OUT MORE ABOUT CLINICAL TRIALS?

If you wish to find out more about clinical trials, there are a number of places you can visit for further information:

Medicines and Healthcare products Regulatory Agency (MHRA)
www.mhra.gov.uk
All clinical trials in the UK are approved by the MHRA and their website contains further information regarding their role in UK clinical trials.

European Medicines Agency (EMA)
www.ema.europa.eu
The EMA also provide advice on how to conduct clinical trials in Europe and the UK and their website holds information such as policies and guidance documents.

National Research Ethics Services (NRES)
www.hra.nhs.uk
NRES is a branch of the National Patient Safety Agency and all studies conducted in the UK must have approval from NRES to start the trial. This is a great source of publications and information about ethical research.

Current worldwide trials
www.clinicaltrials.gov
This is an American website that details ongoing trials around the world, although mainly for patients, the site provides some useful information on the background of clinical trials.

Applied Clinical Trials Magazine
www.appliedclinicaltrialsonline.com
A trade press magazine that is published monthly and available in digital or print format. Applied Clinical Trials magazine contains information about everything from clinical trial data management, to risk mitigation.
for one trial, you might be fine to take part in another.

Inclusion and exclusion criteria (Eligibility criteria) - These criteria define who can take part in clinical trials. They are based on all the information known about the test medicine and are used to minimise any risks to those taking part in the trial. They vary for each clinical trial so while you may not meet the criteria for one trial, you might be fine to take part in another.

Check-in - Prior to the start of the clinical trial, the volunteers attend the clinic for ‘check-in’ so we can show you to your study room and further explain what will happen on the trial. There are some extra checks and assessments to perform before you are given the test medicine. Check-in is usually in the afternoon before you are given the test medicine to ensure any test results needed before dosing can be available in time.

Informed consent - Clinical trials are entirely voluntary and thus the Doctors involved need to explain the trial information to allow you to decide for yourself whether you would like to take part or not. You are provided with an information leaflet to read prior to speaking with the Doctor so you can ask questions to help you understand further before making a decision. If you do not freely provide your consent, you cannot take part in the trial. If you are happy with all the information provided, both you and a Doctor will sign a form that shows you have decided to take part of your own free will. By signing the informed consent, it does not mean you have to take part in the trial, you can still decide not to take part at any point, and you will not need to provide a reason for your decision. In the event that new information or changes to the trial design are made then you will be re-consented to allow you to re-think your decision in light of the new information and even decline to take part if you want to.

Double-blind - Trials where both the volunteers and the Doctors are not aware of who is given a placebo or the test medicine to avoid any influence this information might have on the Doctors assessments as well as the volunteers.

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Dosing - This is the term used when giving a volunteer the test medicine.

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Drug trial - A trial testing the effectiveness and safety of a new medicine or drug.

Dose - The amount of medicine that is given to a volunteer.

Efficacy - The ability of the test medicine to produce a beneficial outcome.

Pharmacodynamic data - Type of data that looks at the effect the test medicine has on your body e.g. does it lower your cholesterol levels or reduce your blood pressure.

Pharmacokinetic data - Type of data that looks at the effect your body has on the test medicine e.g. does it break it down? where does it go in the body? how quickly is it removed?

Placebo - A replica of the test medicine, which looks exactly like the real drug so they cannot be told apart, but has no active ingredient. Using placebos allows the data collected from people taking the placebo and the real medicine to be compared so the researchers can understand the affect of the real medicine. For example, sometimes on a clinical trial if someone has a headache other people in the group may also feel like they have a headache. If all people taking both placebo and the real medicine have this feeling, it is unlikely to be related to the test medicine.

Protocol - The design of the clinical trial is written in a guide or manual which is called the Protocol. This explains all aspects of the clinical trial including the type of participants, what and when assessments will be performed and how to report the data.

Stand-by - To ensure that the clinical trial collects enough data, more people are recruited for the study than are needed to take part. This is because sometimes people cannot take part at the last minute, or may catch a cold. In this situation, the stand-by would then ‘replace’ the person who can no longer take part. Stand-by status is allocated at random prior to the trial starting.

Residential stay - When you need to stay overnight in the clinic during a clinical trial, this is referred to as a residential or “over night” stay.
Got a suggestion? We’re listening.

Covance Leeds encourages feedback to help improve the information provided to our potential research volunteers.

Please provide any comments by email to volunteer.leeds@covance.com or visit www.covanceclinicaltrials.com