Clinical Trials

what you need to know

Dedication

This document is dedicated to the memory of three people:

- Claude Lachapelle, who died May 1, 1995;
- Kalpesh Oza, who died June 4, 1995; and
- Brian Farlinger, who died July 3, 1995.

Thanks to Brian, a lawyer and a leading activist with AIDS Action Now!, many restrictive federal and provincial government policies have changed and a great deal of progress has been made by the pharmaceutical industry for people living with HIV/AIDS.

Kalpesh, a pure scientist by training and activist by nature, was on the Board of Directors of the Comité des personnes atteintes du VIH/sida du Québec (CPAVIH) in Montreal, and of the Canadian AIDS Society. He was also extremely active within both AIDS Action Now! and the Canadian HIV Trials Network.

Claude was general coordinator of CPAVIH in Montreal for many years and a member of the administrative council of the Coalition des organismes communautaires québécois de lutte contre le sida (COCQ-sida) in Montreal. He was also an active member of the Community Advisory Committee of the Canadian HIV Trials Network.

These gifted and courageous activists are deeply mourned, and sorely missed. Their presence in our lives and contributions to the struggle will be with us always.

Third printing, May 2004

Acknowledgements

Clinical Trials: What you need to know was developed in collaboration by the Canadian HIV Trials Network (CTN) and the Canadian AIDS Society (CAS).

The Canadian HIV Trials Network and the Canadian AIDS Society would like to thank:

- AIDS Action Now! for permission to use material from its publication, AIDS and HIV Drug Trials in Canada, seventh edition.

- The Canadian AIDS Treatment Information Exchange (CATIE), and particularly Deirdre Maclean, for permission to excerpt information from the booklet, HIV Related Clinical Trials in Ontario.

CAS would also like to thank the following contributors: Fred Aoki, Russell Armstrong, Maggie Atkinson, Sharon Baxter, Raymond Beaulieu, Reeta Bhatia, Claudia Brabazon, Paula Braitstein, Constance Campbell, Suzanne Desbiens, Alain Descours, Pierre Desmarais, Marcel Dufour, Richard Lalonde, Catherine L'Homme, Megan MacLennan, Nancy Meagher, Wayne Moore, Wayne Rush, Kathy Sayers, Bob Shearer, José Sousa, Robyn Sussel, Darien Taylor, Emil Toma and Donald Zarowny.

CAS would like to thank Susan McCaron of the UpJohn Company of Canada for financial support.

This project was funded by the AIDS Care, Treatment and Support Program of Health Canada under the National AIDS Strategy, Phase II.

The opinions expressed in this document do not necessarily reflect the policies of Health Canada.

Copywriting
Maude Loignon

Editing
Jean Bacon (2nd edition: Robyn Sussel, Sophie Geeraerts)

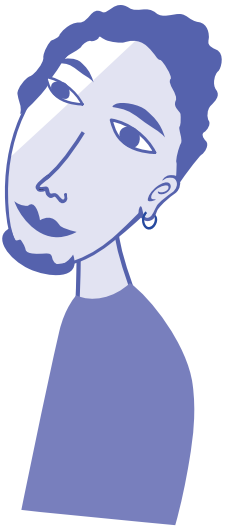
Third Edition Editing
Jim Boothroyd, Sophie Geeraerts and Wendy Soobis for the CTN, Marc-André LeBlanc, Anna Alexandrova, Kim Thomas, Mark Creighan, Maxxine Rattner, and Shaleena Theophilus for CAS.

Design and Illustration
Beverly Deutsch

Ce document est également disponible en français. Pour obtenir une copie, veuillez vous adresser au Réseau canadien pour les essais VIH, 620 – 1081 Burrard Street, Vancouver (Canada) V6Z 1Y6. Tél: 1.800.661.4664. Internet: www.hivnet.ubc.ca

Table of Contents

INTRODUCTION



About this Booklet

This booklet aims to give people living with HIV, their families, friends and others some basic information about **clinical trials**. Its purpose is not to endorse any particular trial or to try to persuade people to participate. Rather, it aims to shed some light on clinical trials: how and why they are conducted, how people can join a trial, and what they can expect if they decide to participate.

> Every effort has been made to keep the language understandable. Technical terms are in bold type the first time they appear, and are defined either in the text or in the glossary at the end.

HIV research continues to change rapidly. This means that clinical trial design — and the information in this booklet — may also change. To ensure the information here is still up-to-date, refer to the list of resources at the end or contact the Canadian HIV Trials Network.

Overview

The term "treatment" is used throughout this booklet to refer to a range of interventions or products being tested in clinical trials. These include drugs, food, supplements, treatment strategies, prevention methods, microbicides and vaccines.

Clinical trials are carefully designed experiments that allow scientists to test their research questions on people. They are a logical, structured way to answer questions about how to prevent, treat and cure HIV or complications associated with HIV/AIDS. Clinical trials are the most effective way for scientists to assess whether the benefits of a particular treatment outweigh its risks, and if it will improve the lives of people living with HIV/AIDS.

Researchers have long used clinical trials to develop effective treatments for diseases, including many types of cancer and bacterial infections, as well as vaccines for many childhood illnesses. Over the last 20 years alone, clinical research in HIV has led to a greater understanding about the virus, aiding researchers to develop treatments for many **opportunistic infections** and treatments against HIV itself. Clinical trials have also shown which treatments aren't effective, and which drugs may cause unexpected side effects. This research and subsequent treatments are helping people with HIV/AIDS live longer, with a better quality of life than was possible ten, five or even two years ago.

Planning and running a clinical trial involves teamwork. To find effective treatments, it is important that people living with HIV/AIDS, scientists, doctors, drug companies and governments work together. Researchers, who are usually medical doctors, monitor the progress of people involved in the trial, ensure that the trials are of the highest scientific quality and analyze the results. Drug companies provide the drugs and usually fund trials testing new drugs. Governments and other funding bodies may pay for other trials. Government regulatory agencies are responsible for reviewing results of the trials and deciding, based on the scientific evidence, whether to approve an experimental treatment for wider use. Regulatory agencies also establish regulations and guidelines for clinical research to protect participants from unreasonable risks.

> People living with HIV/AIDS play a particularly key role in research: they help to ensure that researchers are aware of their needs and concerns, and as participants, they give researchers the scientific information required to develop treatments.

People living with HIV/AIDS also work closely with drug companies and governments to ensure that clinical trials reflect their concerns, and that policies and practices are fair and ethical.

However, for various reasons, certain groups have found it difficult to participate in clinical trials. Researchers and lobbying groups are making every effort to ensure that all populations are adequately represented.

ABOUT CLINICAL TRIALS

What is a clinical trial?

Clinical trials are carefully designed experiments that allow scientists to test their research questions in people. The research questions are many, and have evolved over time. In HIV, the early clinical trials tested new drugs for treatment of the disease and associated opportunistic infections. More recently, researchers have been testing potential **vaccines** and **microbicides** which could prevent infection or limit its effect. The goal is to determine if the treatment being tested is safe, how well it works, and if it should be approved for use in the general population.

How does a trial work?

A clinical trial is just one stage in the process of developing a new treatment. The entire process includes several steps: identifying a possible treatment, testing it on animals, getting approval for a clinical trial, running the trial, analyzing the results, applying for a licence and getting approval to use the treatment in the general population. This process can take many years: even when a treatment is put on the market, researchers may want to continue to investigate new ways of using it to reduce the frequency of dosage, to reduce side effects or to test it in novel treatment strategies.

Pre-clinical Testing: in vitro and animal studies

When a new treatment is developed, it must first be carefully tested before it can be given to people. These pre-clinical tests include in vitro studies and animal studies.

- In vitro studies are laboratory experiments that examine how a new treatment works on animal or human cells in test tubes. For example, the new treatment may be mixed with some healthy human cells and some HIV-infected cells to see if it will kill infected cells without damaging healthy ones. In vitro studies are repeated many times to ensure the results are dependable and not just due to chance. If in vitro studies show promise, researchers then proceed to the next stage: animal studies.

- Animal studies test new treatments in living animals. **Toxicity** studies are designed to determine if a treatment harms the body's organs. Some drugs can cause illnesses or reactions that don't show up unless the drugs are used for a long time. Other medications may be fine for the people taking them, but may cause birth defects in future generations.

Animals that reproduce quickly and have short life spans, such as mice and rats, are used to study both these problems. Other animals, such as monkeys, are used in certain studies because they are more like people and can have similar diseases. Testing new drugs or vaccines on these animals gives scientists a better idea of how they may affect people.

Clinical Trials: testing new treatments on people

If pre-clinical studies indicate that a treatment is useful and safe in animals, the treatment developer (pharmaceutical company, biotech company, university, etc.) asks Health Canada for permission to test it in people. To get approval for a clinical trial, a company must submit all the documentation and data from pre-clinical studies, including data that demonstrates the treatment is safe enough to be tested in people. The company must also provide a detailed written plan or **protocol** for the trial. A protocol is a researcher's description of why and how a study will be conducted.

Testing in people is done in four phases of trials:

Phase I: Researchers give the treatment to a small number of people (with or without HIV) to see what dose is safe, starting with single administration. Different participants receive different doses to determine which dose is safest. Phase I trials are riskier than later phases, because typically little is known of the treatment's effects on humans. These trials are short, usually no more than two or three months, and generally involve 20 to 80 participants.

Phase II: Researchers give the treatment to a larger number of participants (several hundred) over a longer period of time to determine the most effective dose, to see if it is working and to learn whether it has any medium-term side effects. These trials normally span a few months to a year.

Phase III: Researchers give the treatment to a much larger group of people over several months or years to determine whether the treatment remains effective or has any side effects that only show up after a longer period of time. Researchers also compare new treatments with treatments that are already in use. If a treatment is successful at this point, it may be approved for general use.

Phase IV: Researchers often continue to study a treatment after it has been approved in what are called "post-marketing" trials. They watch for any side effects or problems that may show up only after several years of use, or test the treatment in different prevention and/or treatment strategies.

Today, many clinical trials combine phases. For example, Phase I/II trials might study a treatment dose and how it works, while Phase II/III trials might study both how the treatment works and how well it works at the same time.

Approval of a new treatment

New treatments are continually re-assessed for their effectiveness, benefits and risks at each stage of the clinical trial process and a trial can only proceed to the next phase of testing with approval from Health Canada. Once a treatment has been tested successfully in the first three phases of clinical trials, the manufacturer can apply to Health Canada for formal approval to market or sell the treatment.

Federal government approval of a treatment doesn't necessarily mean that a particular treatment is effective or safe for all people at all times. It only means that the treatment has proven useful in enough people to be worth trying in a larger population and that, in most cases, its known side effects do not outweigh its benefits.

What do HIV/AIDS trials test?

Most treatments that are tested fall into the following categories:

- Drugs that fight the HIV virus, called **antiretrovirals**
- Treatments that prevent or treat side effects of antiretrovirals (e.g. high blood fat levels)
- Treatments that prevent or treat HIV-related illnesses (opportunistic infections such as thrush or *pneumocystic carinii pneumonia* (PCP))
- Drugs that treat cancers
- Treatments that reinforce the immune system, known as immunostimulators or **immunomodulators**
- Vaccines that could prevent, limit the effects of, or cure HIV infection (**preventative** or **therapeutic vaccines**)
- **Gene therapies**
- Microbicides (products that, when applied topically, are able to prevent the sexual transmission of HIV and other sexually transmitted diseases)

Clinical trials are designed to answer a variety of questions, such as: Is the new treatment safe? Does it work? Are there any long-term side effects?

What are the different types of trials?

Most HIV trials nowadays compare a new treatment with something else to discover which, or what combination, is better and safer. The different types of trials described here allow researchers to answer different medical questions:

Placebo trials

In the early days of the HIV epidemic, many trials compared a drug with a **placebo**. A placebo is something that looks, smells and tastes like the drug, but has no drug, or active agent, in it. In these trials, one group of people is given the drug, another group the placebo. Both groups are then studied to compare their reactions. Placebo trials are a quick, accurate way to assess whether the treatment is better than doing nothing. However, with the current information we have about HIV treatment, in Canada we consider it unethical to give a placebo to trial participants if a standard treatment is available. Nowadays, placebos are used when the drug being tested is added to the standard treatment, or when there is no existing standard treatment.

Comparison trials

Most trials are comparison trials that compare one treatment with another.

The following are examples of different types of comparison trials:

- New treatment vs. standard treatment: In these trials, one group receives a commonly used treatment, another group the new treatment. Scientists compare the two to see which works better.

- New treatment and standard treatment vs. standard treatment: In these trials, both groups receive commonly used treatments, but one group also receives the new treatment. Researchers then consider whether adding the new treatment has a positive effect on health and/or quality of life.
- Dose comparisons: These trials compare the use of a new treatment at different doses. Researchers then assess which dose works best and has the fewest side effects.
- Management trials: As more HIV treatments become available, many researchers are focusing on treatment strategies rather than solely on the safety and efficacy of particular treatment. In these trials, researchers may study when is the best time to start HIV treatment, while others may compare a new treatment strategy with a common treatment strategy.

Controlled trials

Researchers use measures or controls to ensure accurate results. These are the specific rules that researchers and participants must follow to reduce the effect of any bias (emotions, attitudes or personal beliefs) that could distort the results. For example, clinical trials are randomized and/or double-blinded.

Randomized controlled trials

In randomized, controlled trials participants are assigned randomly (like the flip of a coin) to one of several treatment groups. This is usually done using a computer. This helps to remove any bias when deciding which participants receive the new treatment.

Double-blind controlled trials

Double-blind, controlled trials ensure that neither the participants nor the doctors know who has received which treatment. The trial remains blinded until the last person to volunteer has completed the trial.

Who conducts trials?

Clinical trials that test new treatments in Canada are usually designed and paid for by the company that has developed the new treatment. Universities and other research organizations may also be involved in the design of new treatments. Their research is usually sponsored through public granting agencies or existing foundations (for example CANFAR). Trials are a mandatory part of the process for approving treatment products, and provide the data that regulatory agencies require to determine if a treatment is safe and beneficial.

> Every trial has a principal investigator (PI), the researcher who is supervising the trial. Usually the PI is a doctor with a lot of experience in the area that is being studied.

The trial may take place at several locations across the country or across several countries. Each of these locations is called a trial site and has an investigator in charge of the trial at the site, the study site investigator. Most HIV-related clinical trials in Canada take place in cities that have university teaching hospitals with clinics specializing in HIV disease. Over the last 10 years, more community-based clinics specializing in HIV care have begun to run clinical trials.

As more treatments for HIV become available, independent researchers are also developing clinical trials that further test common treatments. These investigator-driven clinical trials are generally sponsored by granting agencies such as the Canadian Institutes for Health Research (CIHR).

How do researchers assess results?

Investigators use certain tests and measurements, often called **surrogate markers**, to quickly assess the effect of a trial treatment on the health of participants. Two of the most common surrogate markers are a **viral load** test and a **CD4 cell count**. In the case of drugs and therapeutic vaccines, researchers may take blood or tissue samples and measure the amount of virus present (the viral load test) before participants take the trial drug, while they are taking the drug, and after. If a viral load is high, it means the virus is replicating quickly in the body. If a viral load is low, it suggests the body, by itself or with a treatment, is keeping the virus in check.

The CD4 cell count is a blood test that measures the number of immune system cells that have CD4 receptors. A low or falling CD4 cell count may indicate that HIV disease is progressing, since HIV infects and destroys CD4 cells.

In the case of preventative vaccines and microbicides, researchers may look at the rate of new infections in trial participants.

Throughout the clinical trial, researchers test for these and other surrogate markers, hoping to see signs that the treatment is having a positive effect on the health of participants.

To study long-term effects of a treatment or treatment strategy, researchers rely on other markers, such as quality of life, adherence to treatments, side effects, disease progression and death.

Who protects participants?

Participants in clinical trials must be protected and trials must be scientifically valid.

The conduct of clinical trials is regulated by Health Canada, which has adopted the **Good Clinical Practice** (GCP) guidelines developed by the International Committee of Harmonization. The Health Canada publication *Good Clinical Practice: Consolidated Guidelines* gives a detailed list of the responsibilities of investigators, sponsors and Research Ethics Boards (REBs).

Research Ethics Boards (REB), whether institutional or independent, safeguard the rights, safety and well-being of all trial participants. Before a trial can start at a hospital, clinic or doctor's office, the Principal Investigator must submit a detailed application to his/her REB for approval. Another name for these is Institutional Review Board (IRB).

In 2003, Health Canada started conducting routine inspections to ensure that clinical trials are conducted according to good clinical practices.

PARTICIPATING IN CLINICAL TRIALS

Where can I find information about trials?

If you are living with HIV and interested in clinical trials, talk to your doctors or local AIDS organization about possible alternative treatments and trials in your area. On page 37, you will find a list of organizations and their contact information.

The Canadian HIV Trials Network (CTN) and the Canadian AIDS Treatment Information Exchange (CATIE) collaborate to produce a registry of enrolling HIV clinical trials in Canada. The registry is published quarterly on a poster and each trial is posted on the web sites of both organizations.

The Canadian HIV Trials Network is a federally funded organization whose mandate is to develop treatments, vaccines, and a cure for HIV disease and AIDS through the conduct of scientifically sound and ethical clinical trials.

CATIE offers treatment information, helping people living with HIV/AIDS and their caregivers make informed healthcare decisions.

There are several steps to take before you can participate in a clinical trial, but anyone can apply.

If you find a particular trial in which you are interested, contact your family doctor. He or she can refer you to the site investigator or you can call the site directly. A telephone screening interview with the trial nurse or another member of the trial staff will likely provide enough information for you to see whether you can participate, according to the entry criteria. Anyone who meets the initial criteria and is interested can make an appointment for a screening visit, the next step in the qualifying process.

How do I make a decision?

At the end of the screening interview, you may be asked if you want to enter the trial. At this point, you will receive a detailed information package, including an **informed consent** form.

Once you've reviewed the information and if you're still interested in participating, it is often helpful to discuss with the trial nurse and/or doctor what the trial will mean to you, and how it will impact your health and lifestyle. They will also explain the known, and potential, benefits and risks.

Take all the time you need to make your decision about participating: discuss the trial with your doctor, partner, friends, family or your local AIDS group. Ask to talk to previous clinical trial participants. When making a decision, it is important for you to consider all factors: the time commitment, the benefits and the possible risks.

The benefits and risks of participating in clinical trials include:

Benefits

- Being among the first to benefit if an experimental therapy is effective
- Having your health monitored more often, which may be beneficial
- Being part of a process that develops new treatments, vaccines or microbicides and helps other people living with HIV/AIDS

Risks

- Having no guarantee of a personal benefit from the trial
- Experiencing side effects that could be dangerous or make health worse, including being admitted to hospital
- Having to stop other medications that are working well
- Not being eligible for other trials in the future
- Not knowing who is receiving the experimental drug
- Making changes in lifestyle, such as taking medication at very regular intervals, or not eating certain foods
- Facing stigma and discrimination

What is an informed consent?

Informed consent is a process in which the risks, benefits, and requirements of a trial are clearly explained to volunteers.

If you meet the preliminary study entry criteria and are strongly considering taking part in a trial, you will be asked to give your informed consent. The informed consent form should fully explain in plain language the trial as well as the possible risks or dangers. Informed consent forms usually require the participant's signature, the signature of a witness and the signature of the principal investigator or designated study staff.

Giving your informed consent means that you understand the trial. In other words:

- You understand that the trial is a scientific experiment, and there may be risks and dangers to your health
- You have been told the specific reasons for doing the trial, the drugs you might be given, the number of visits and the kinds of lab tests required
- You have the information you need to decide whether to take part in the trial
- You understand your rights and responsibilities.

If you are concerned about any of the trial requirements, talk to trial staff before giving informed consent. They may be able to make some exceptions, or you may decide not to take part in the trial after all.

You will receive a copy of the signed informed consent for your records. However, remember that signing the form is not the end of the process. Informed consent is an ongoing process. Investigators have a responsibility to continue to inform you of any new information about the drug you are taking, or any information that would influence your decision to participate in the trial. In fact, the investigator needs your consent that you wish to continue to participate.

As a participant, you have the right to leave a clinical trial at any time.

Leaving a trial will not affect your regular health care or your ability to participate in other trials for which you meet the entry criteria.

Once you sign the informed consent form, you are considered enrolled in the trial. However, before you can participate, you may first be asked to come to the study site for a screening visit to ensure you meet the more detailed study entry criteria.

What happens at the screening visit?

All trials examine a specific aspect of a treatment, which means that participants must meet strict entry requirements called **inclusion** and **exclusion criteria**. While broad criteria can be assessed during the preliminary screening interview, an in-person screening visit is necessary to assess detailed criteria, which may include a physical exam and testing.

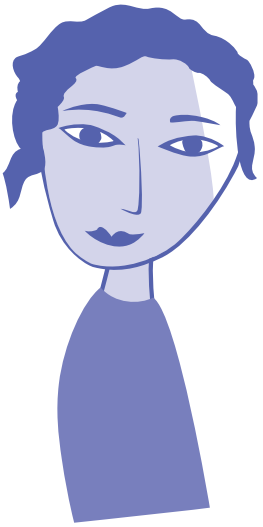
Inclusion criteria ensure that relatively similar people take part in a trial. This allows researchers to make reliable comparisons about the way the experimental treatment works. Some examples of inclusion criteria might be that a participant "must be HIV+" (or "must be HIV-negative" for studies on prevention methods) and "must have a CD4 cell count between 100 and 300."

Exclusion criteria protect people who might be harmed by the study drug. For example, anyone who is being treated for an active illness, such as pneumocystic carinii pneumonia, or who is pregnant will likely be excluded from a trial. Until recently, pregnant women have seldom been allowed to enter drug trials in case the drug harms the fetus. However, recent guidelines in the United States and Canada have made it increasingly acceptable to include pregnant women in particular circumstances.

At the screening visit, you will be asked a variety of questions about your health, your medical history as well as the drugs and treatments you use. You will also have an extensive physical exam, along with lab tests, such as blood tests or x-rays.

Once researchers are satisfied that you meet all the entry criteria, you are ready to move on to the clinical trial itself.

ONCE YOU'RE ENROLLED



What are the stages of trial participation?

Clinical trials have many different stages. Depending on the type of trial, you will take part in all or some of the following stages:

Randomization
You are randomly assigned (like the flip of a coin) to a study treatment group.

Waiting period
You may have to wait before starting the study treatment. During this time, investigators observe your health before treatment begins.

Washout period
Before starting the study treatment, you may be asked to stop taking a medication and wait for a period of time. This allows the body to get rid of all traces of the medication and avoid harmful treatment interactions.

Treatment period
The length of time that investigators plan to have you on a treatment before they evaluate its effect. This is usually 12, 24 or 48 weeks.

Follow-up visits
Before and during the treatment period, you will be asked to come to the clinic for regular visits. The frequency of these visits is usually higher than for routine care. The follow-up may be once a month for the first six months. Sometimes, you will be asked to come after the end of the study treatment period.

End of study
The study usually ends when all participants have completed the study treatment or follow-up period. This means that if you are one of the first participants in the study, you will be in the study for a longer period than if you are one of the last participants to enroll in the study.

What are my responsibilities?

Your main responsibility is to be sure that you understand the rules of the trial and are realistic about your ability to follow them. If you feel that you will not be able to keep appointments or follow the schedule, talk to trial staff. There may be ways to work around your schedule. Given the strict guidelines of trials, participants who do not follow the trial rules will be withdrawn.

Remember: you can also leave a trial at any time, for any reason.

What is the role of my family doctor?

As a clinical trial participant, your health will be monitored at the trial site. However, you should also continue to see your own doctors – those responsible for your overall health — for regular check-ups and lab tests. It is not ethical for the trial doctors to take over general medical care of participants. To avoid having the same tests repeated, family doctors and site investigators usually work out a way to share test results.

When family doctors are also trial investigators, they ask another doctor to review the trial protocol and informed consent with their patients. In addition, they often recommend that their patients who are participating in the trial see another doctor for regular care during the trial. This is one way to ensure that the doctor's interest in enrolling volunteers for the trial does not conflict with his/her obligation to provide the best possible patient care.

What happens after the trial?

When your time in a trial ends, you will be asked to participate in an exit interview. During this interview, you may be told what treatment you were receiving (if you don't already know). Since the code in double-blind trials is not broken until everyone has completed the trial, participants in those trials may not find out what treatment they were getting until some time after they finish the study.

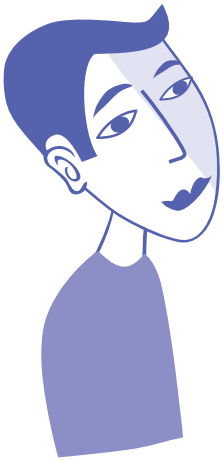
You should expect to receive the results of the trial when it is finished. Ask the study nurse or doctor for information about how results will be given to you if this is not explained in the informed consent form. Also, keep in mind that because enrollment is staggered, a two-year trial may take several years

to reach its conclusion — the last person enrolled must have been in the study for a full two years.

It is important for you to stay in touch with investigators after a trial ends, so that you can report any recurring symptoms or side effects. Investigators can also pass on any new information about the treatment to you and other participants.

As noted earlier, if any new information about the trial treatment becomes available during the trial, the sponsors and the investigators must tell all trial participants.

OTHER THINGS TO CONSIDER



Are there any costs?

In Canada, provincial health insurance and the treatment manufacturer usually cover the cost of treatments and lab tests. However, you may have other expenses, such as loss of wages, time off work, transportation costs, babysitting or daycare. If you need help with childcare or transportation costs, talk to the trial staff: in some cases, funds are available to assist you. Trial organizers can explain what can be reimbursed, how, and when.

In 2003, the Canadian HIV Trials Network (CTN) formally established funding to cover reasonable costs of this kind, so if you are participating in a trial supported by the CTN, you can expect to be repaid for travel and childcare expenses.

Although it is illegal for anyone to sell a drug that hasn't been approved by the Health Products and Food Branch of Health Canada, you may have to pay a dispensing fee if you receive your trial drug through a hospital or local pharmacy.

What if I become ill?

If you become sick while in a trial, tell the trial staff immediately. You may be experiencing side effects of an experimental treatment, or have caught an illness that a study treatment could make worse.

Also, keep your informed consent form and trial information package. Here you will find a 24-hour toll-free number to call for advice if you have problems with the study treatment. Because the treatment being tested is experimental, doctors in emergency rooms may not be able to help participants who become ill. However, if you are very ill, go to the emergency department of a hospital and take your informed consent form with you. This will give the ER doctors more information about the treatment you are taking and help them contact your trial doctor.

Can I take other drugs?

While in the trial, you will likely not be permitted to take certain medications, particularly if the trial treatment interferes with other drugs. The trial treatment might also cause a reaction that another drug could make worse.

To protect yourself, keep a list of all the medications you take, including over-the-counter drugs like cold tablets or cough syrup, and complementary therapies, such as herbal and vitamin supplements — you can never be too careful. You should also be aware that the potential for interactions with street drugs (e.g. heroin, cocaine and ecstasy) is unknown for most experimental HIV drugs.

OTHER OPTIONS

If you are not accepted into a trial or don't want to participate, you may still be able to get experimental treatments by other means:

Compassionate access

Drug manufacturers sometimes make a limited amount of an experimental drug available through a less restrictive **compassionate access** trial. Participants must still meet certain requirements, such as having a CD4 cell count below a specified level or being intolerant to standard treatment.

Special Access Programme (SAP)

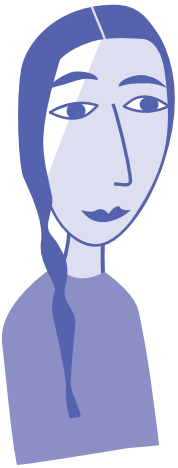
Health Canada can authorize a manufacturer to release any drug that has not yet been approved for sale in Canada on an emergency basis — including drugs in clinical trials. To receive a drug that is not yet licensed but has been listed in the **Special Access Programme** (formerly the Emergency Drug Release Programme - EDRP), you must ask your doctor to contact the programme.

Drug companies are not required to provide a drug through the Special Access Programme. Each request is reviewed on an individual basis. Drug companies may charge a fee for the drug, including full retail cost.

Buyers' Clubs

Buyers' Clubs, which are more common in the United States than in Canada, are co-operative organizations that provide easier access to treatments for people living with HIV/AIDS. They may be able to provide access to some experimental drugs, although they usually deal more with vitamins and other complementary therapies. For more information about Buyers' Clubs, contact your community-based AIDS organization.

ACCESS TO CLINICAL TRIALS



To better understand HIV and how HIV treatments and preventative methods work, it is important that all populations be represented in clinical trials.

> However, for a variety of reasons, certain groups of Canadians have more difficulty than others in gaining access to clinical trials: for example, Aboriginal people, women, youth and injection drug users.

As a result, trial participants are sometimes unrepresentative of the wider population of people living with HIV/AIDS and trial results can be undermined by this shortcoming.

Researchers and HIV/AIDS community organizations know this and make every effort to ensure that all populations are adequately represented. In addition, many of the member groups of the Canadian AIDS Society represent special populations and may be able to help you get into a clinical trial. Check the CAS website or call CAS for the group in your community (see page 37).

GLOSSARY OF TERMS

Antiretroviral: A substance that stops or suppresses the activity of a retrovirus such as HIV: AZT and ddI for example.

Buyers' Club: Cooperative organizations that provide easier access to treatments for people living with HIV.

Canadian HIV Trials Network (CTN): A non-profit organization funded by the Canadian Institutes of Health Research to encourage and coordinate HIV clinical trials in Canada. The CTN has a Community Advisory Committee that reviews every proposed clinical trial submitted to the Network.

CD4 cell count: A measure of the number of the immune system cells that have CD4 receptors. A CD4 cell is a type of T cell. These cells normally orchestrate the immune response (defence) to infections.

Clinical trial: A carefully designed experiment that allows scientists to test their research questions in people.

Compassionate access: A trial that allows people who do not participate in the research study (because they do not meet the inclusion criteria or for other reasons) to have access to the drug or treatment being tested. Most compassionate arms are restricted (for example, to those with CD4 cell count below specified amount, intolerant to standard therapy, etc.).

Controls: Specific measures that researchers and participants must follow to reduce any bias that could affect the results of a trial.

Controlled, comparison trials: Trials in which one group gets an experimental treatment and another gets either a placebo or an approved therapy. Participants do not usually know which group they are in.

Dose comparison trial: A trial that compares different amounts of the same drug. Sometimes different doses are tested against a placebo.

Double-blind trial: Participants in this type of trial are divided into two or more groups: one gets the experimental treatment; the other gets the standard treatment or a placebo. Neither the researchers nor the participants know who is taking which drug until the trial is over.

Gene Therapy: An approach to preventing and/or treating diseases by replacing, removing, or altering key genes, or otherwise manipulating genetic material.

Good Clinical Practice (GCP): An international ethical and scientific quality standard for designing, conducting, recording and reporting clinical trials.

Immunomodulators: Drugs that strengthen the immune system and help the body to fight off infections or other diseases that attack people living with HIV/AIDS.

Inclusion/exclusion criteria: Conditions that determine why a person may or may not be allowed to enter a trial. For example, most trials do not allow pregnant women to join. Others do not allow people to take certain drugs, and others exclude people with certain illnesses.

Informed consent: A process in which the risks, benefits, and requirements of a trial are explained to volunteers. Before entering the trial, participants must sign an informed consent form, which should include a plain-language description of the benefits, risks, and basic structure of the trial.

Microbicides: Products that when applied topically are able to prevent the sexual transmission of HIV and other sexually transmitted diseases.

Opportunistic Infection: An illness such as Pneumoncystis carinii pneumonia (PCP) that people with HIV/AIDS can get and which can be potentially life-threatening. People with healthy immune systems do not usually get these illnesses, even though most people already have the organisms that cause these illnesses in their bodies. When the immune system is damaged, the organisms take advantage of the "opportunity" to cause illness.

Placebo: Something that looks, smells and tastes like the drug, but has no drug in it. This is sometimes referred to as a "sugar pill".

Preventative Vaccine: A vaccine designed to prevent a disease in a person.

Protocol: Detailed written plan of a study.

Randomized trial: A trial in which participants are assigned to one of the study treatment groups randomly (as by the flip of a coin). Usually a computer is used to randomly allocate participants to the arms of such a study. This helps remove any bias when deciding which participants receive a particular treatment.

Special Access Programme: Health Canada can authorize a manufacturer to release any drug that has not yet been approved for sale in Canada on an emergency basis — including drugs in clinical trials. To receive a drug that is not yet licensed but has been listed in the Special Access Programme (formerly the Emergency Drug Release Programme - EDRP), you must ask your doctor to contact the programme.

Surrogate markers: A surrogate is a substitute. If something under study is not readily measurable because it takes a long time to show up, researchers may use a surrogate to predict the eventual measurement. Viral load counts and CD4 cell counts are examples of HIV surrogate markers.

Therapeutic Vaccine (or treatment vaccine): A vaccine designed to boost the immune response to HIV in people already infected with the virus.

Toxicity: The unwanted effects or damage caused by a drug.

Vaccine: A substance that teaches the body immune system to recognize and/or protect against a disease caused by an infectious agent (virus or bacteria).

Viral Load: Amount of HIV in the blood.

Washout period: A period during which participants do not take certain drugs, so that all traces of those drugs can be washed out of the body.

WHERE TO FIND HELP

The following list includes organizations or programmes engaged in HIV treatment advocacy and/or who provide information on HIV treatments, clinical trials, and drug access.

Treatment/Clinical Trial Information

Canadian HIV Trials Network
National Office
620 - 1081 Burrard Street
Vancouver, BC
V6Z 1Y6
Tel: 1.800.661.4664 or 604.806.8327
ctn@hivnet.ubc.ca
www.hivnet.ubc.ca

Canadian AIDS Treatment Information Exchange (CATIE)
555 Richmond Street West, Suite 505
Box 1104
Toronto, ON
M5V 3B1
Tel: 1.800.263.1638 or 416.203.7122
info@catie.ca
www.catie.ca

Local Canadian AIDS Society Member Groups
Also, many of CAS' member organizations have locally-based treatment information programmes. A list of these organizations can be found on their web site or by contacting CAS by phone (see under Advocacy).

Advocacy

AIDS Action Now!
Box 25, Station F
Toronto, ON
M4Y 2L4
Tel: 416.977.5903

Canadian Aboriginal AIDS Network (CAAN)
602-251 Bank Street
Ottawa, ON
K2P 1X3
Tel: 613.567.1817
1.888.285.2226
info@caan.ca
www.caan.ca

Canadian AIDS Society (CAS)
309 Cooper Street, 4th Floor
Ottawa, ON
K2P 0G5
Tel: 613.230.3580
1.800.499.1986
CASinfo@cdnaids.ca
www.cdnaids.ca

A national coalition of more than 115 community-based AIDS organizations across Canada. A list of these organizations can be found on its web site or by contacting CAS by phone or fax. Many of the member groups of the Canadian AIDS Society represent special populations (e.g. Positive Women's Network, Africans in Partnership Against AIDS, Asian Community AIDS Services, etc.)

Canadian HIV/AIDS Legal Network
417 Saint-Pierre Street, Suite 408
Montreal, Quebec
H2Y 2M4
Tel: 514.397.6828
info@aidslaw.ca
www.aidslaw.ca

Canadian Treatment Action Council (CTAC)
Box 116, Station F
Toronto, ON
M4Y 2L5
Tel: 416.410.6538
ctac@ctac.ca
www.ctac.ca

Drug Access Information

Special Access Programme (SAP)
Therapeutic Products Directorate
Finance Building 2nd Floor
Tunney's Pasture P.L. 0202C1
Ottawa, ON
K1A 1B6
Tel: 613.941.2108
SAPdrugs@hc-sc.gc.ca
www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_sap_drugs_e.html

Reference

American Foundation for AIDS Research (amfAR)
120 Wall Street, 13th Floor
New York, NY
10005-3902
Tel: 212.806.1600
txdir@amfar.org
www.amfar.org
Publisher of the *HIV/AIDS Experimental Treatment Directory.*

Canadian HIV/AIDS Information Centre
1565 Carling Avenue, Suite 400
Ottawa, ON
K1Z 8R1
Tel: 613.725.3434
1.877.999.7740
aidssida@cpha.ca
www.aidssida.cpha.ca

National Council on Ethics in Human Research (NCEHR)
774 Echo Drive
Ottawa, ON
K1S 5N8
Tel: 613.730.6225
office@ncehr-cnerh.org
www.ncehr-cnerh.org