CLINICAL TRIALS

WHAT YOU NEED TO KNOW

the CTN
CIHR Canadian
HIV Trials Network

le Réseau
Réseau canadien
pour les essais VIH des IRSC

Dedication

This document is dedicated to the memory of six people:

Claude Lachapelle, who died May 1, 1995.
Claude was general coordinator of Comité des personnes atteintes du VIH/sida du Québec (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 CIHR Canadian HIV Trials Network (CTN).

Kalpesh Oza, who died June 4, 1995.
Kalpesh, a pure scientist by training and activist by nature, was on the Board of Directors of CPAVIH in Montreal, and of the Canadian AIDS Society (CAS). He was also extremely active with both AIDS Action Now! and the CTN.

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.

Ben Kozak, who died March 18, 2005.
Ben was the Manager of Finance and Administration at CAS and was involved in the CTN as a member of the National Ethics Review Committee. He was an activist for AIDS and worked tirelessly at CAS as an advocate for people living with HIV.

Mark Creighan, who died April 24, 2006.
Mark worked at the CAS for many years as the Media Relations Officer. Mark was instrumental in the work carried out on behalf of CAS' members in advocating for additional funds to the Canadian Strategy on HIV/AIDS. He helped develop the third edition of this publication.

James Kreppner, who died May 14, 2009.
James was a hemophiliac treated during the 1980s' blood scandal from which he acquired HIV and hepatitis C — a tragedy that ignited his courageous battle for his own life and rights, and those of millions of Canadians. Amongst his national lobbying initiatives for human rights and people's right to health, he co-founded and served on the CTN's Community Advisory Committee from 1993-2007.

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.

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Ce document est également disponible en français. Pour obtenir une copie, veuillez vous adresser au Réseau canadien pour les essais VIH des IRSC, 1081, rue Burrard, bureau 620B Vancouver, C.-B., V6Z 1Y6. Tél: 1.800.661.4664.
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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 and 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 back.

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 presented here is still up-to-date, refer to the list of resources at the end of this handbook or contact the CIHR 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, therapeutic 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 and 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.

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 are not effective, and which drugs may cause unexpected side effects. Findings in clinical research, including studies on treatments, are helping people with HIV live longer, with improvements in quality of life that were not possible ten, five or even two years ago.

Planning and running a clinical trial involves teamwork. To find effective treatments, it's important that people living with HIV, 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 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 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 populations (women, Aboriginal people, people who use injection drugs and youth) 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 with people. There are many different kinds of research questions and they 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, microbicides** and **New Prevention Technologies** 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.

New prevention technologies are also known as biomedical interventions. This refers to a group of HIV prevention tools that employ medical interventions to reduce the risk of HIV infection. This category of HIV prevention includes male circumcision, microbicides, **PEP**, **PrEP**, **preventive** and **therapeutic vaccines**, and treatment as prevention.

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 new ways to administer the treatment.

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 repeatable and 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 on 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 problems such as 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 shows 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 effective it is at the same time.

Approval of a new treatment

New treatments are continually re-assessed for the benefits and risks observed at each stage of the clinical trial process. 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.

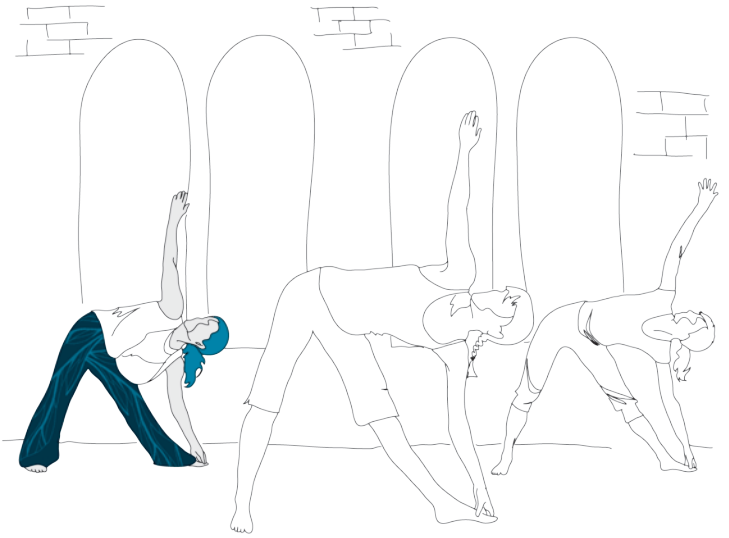
Federal government approval of a treatment doesn't necessarily mean that a particular treatment is effective or safe for all people at all times. It only means that the treatment has proven useful in enough people to be worth trying in a larger population and that, in most cases, its known side effects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

What do HIV trials test?

Most treatments that are tested fall into the following categories:

- Drugs that fight the HIV virus, called **antiretrovirals** (ARVs).
- Treatments that prevent or treat side effects of antiretrovirals (e.g., high blood fat levels).
- Treatments for co-infections such as hepatitis B or C, or HPV (human papilloma virus).
- 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).
- **Pre-exposure prophylaxis** (ARVs that, when taken daily by HIV-negative individuals, prevent the acquisition of HIV).

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 at present 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, we consider it unethical in Canada to give a placebo to trial participants if a standard treatment is available. Currently, placebos are used when the drug being tested is added to a 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, while 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 treatments. 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.

Pilot Studies

Pilot studies are small-scale investigations focused on gathering and assessing data to determine if larger randomized clinical studies are feasible.

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.

Observational studies

A type of study in which individuals are observed or certain outcomes are measured. No attempt is made to affect the outcome (for example, no treatment is given). An observational study observes characteristics of a subset of a population or a cohort.

Prevention-based studies

Prevention studies test methods of preventing or reducing disease transmission. They can be either behavioural or biomedical. Behavioural prevention studies, such as risk reduction counselling, test methods of preventing high-risk behaviours (for example, unsafe sex, needle sharing) and exposures to disease. Biomedical prevention studies investigate the efficacy of drugs in preventing or reducing disease transmission.

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 (Canadian Foundation for AIDS Research (CANFAR), for example). 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 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, called 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. Over the last 20 years, more community-based clinics specializing in HIV care have also 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 of 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, microbicides, and PrEP, 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.

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 her/his 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 doctor 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 CIHR Canadian HIV Trials Network (CTN) and CATIE collaborate to produce a registry of enrolling HIV clinical trials in Canada. The registry is published on a poster and each trial is posted on the websites of both organizations.

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

CATIE offers treatment information, helping people living with HIV 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 are still interested in participating, it's 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 organization. Ask to talk to previous clinical trial participants. When making a decision, it's 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, microbicides and New Prevention Technologies, and helps other people living with HIV.

Risks

- Having no guarantee of a personal benefit from the trial.
- Experiencing side effects that could be dangerous or make your health worse, including being admitted to hospital.
- Having to stop other medications that are working well.
- Not being eligible for specific trials in the future.
- Not knowing who is receiving the experimental drug.
- Making changes in lifestyle, such as taking medication at 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 your consent. 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.

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?

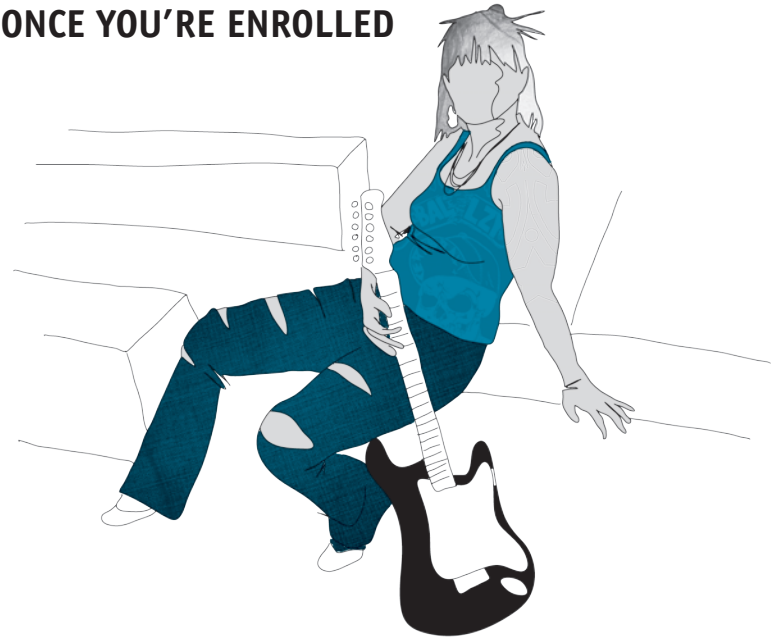
All trials examine a specific aspect of a treatment, which means that participants must meet strict entry requirements called **inclusion** and **exclusion criteria**. While broad criteria can be assessed during the preliminary screening interview, an in-person screening visit is necessary to assess 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-positive" (or "must be HIV-negative" for studies on prevention methods) and "must have a specific CD4 cell count."

Exclusion criteria protect people who might be harmed by the study drug. For example, anyone who is being treated for an active illness, 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 their 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're ready to move on to the clinical trial itself.



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're 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. A study may be ended early if the risk affecting one of the treatment groups is determined to be too great.

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 won't 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 isn't 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's 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 not all volunteers are enrolled at the same time, so 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's 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, and childcare. 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 CIHR 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 may be eligible to be reimbursed for travel and childcare expenses.

It is illegal for anyone to sell a drug that has not been approved by the Health Products and Food Branch of Health Canada.

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.

Always 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 emergency room 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 (for example, 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)

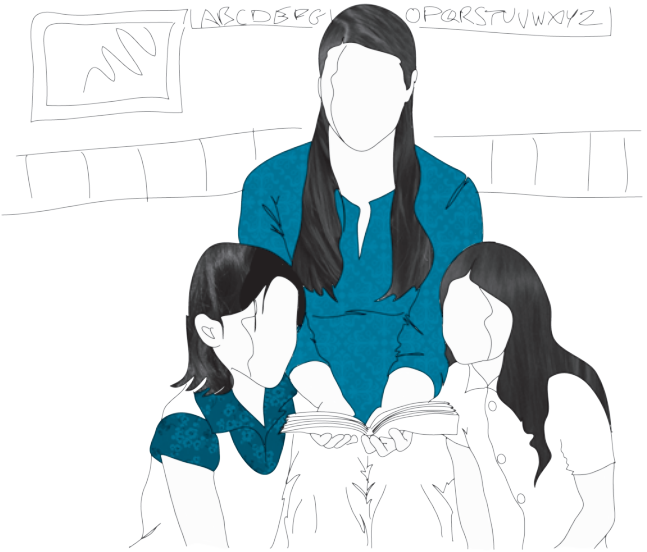
Health Canada can authorize a manufacturer to release any drug that has not yet been approved for sale in Canada on an emergency basis — including drugs in clinical trials. To receive a drug that is not yet licensed but has been listed in the **Special Access Programme** (formerly the Emergency Drug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

Drug companies are not required to provide the 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. 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



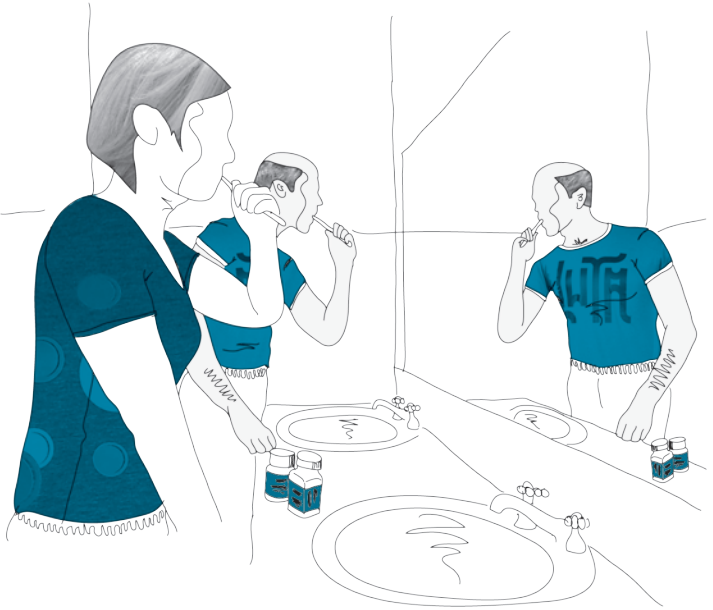
To better understand HIV and how HIV treatments and preventative methods work, it's important that all populations be represented in clinical trials.

> However, for a variety of reasons, certain populations of Canadians have more difficulty than others in gaining access to clinical trials. This includes Aboriginal people, women, youth and people who use injection drugs.

As a result, trial participants are not representative of certain populations of people living with HIV and trial results can be undermined by this shortcoming.

Researchers and community organizations know this and strive to ensure that all populations are adequately represented. In addition, many of the member organizations of the Canadian AIDS Society (CAS) 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 38).

GLOSSARY OF TERMS



Antiretroviral: A substance that stops or suppresses the activity of a retrovirus.

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

CIHR 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 coordinate 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 already-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 and AIDS.

Immunotherapies: The treatment that controls HIV by boosting the immune system rather than attacking HIV directly.

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.

Inflammatory biomarkers: Molecules, often found in the blood, that signal inflammation in the body. They can be used to measure the level of inflammation in tissues and organs.

Informed consent: A process in which the risks, benefits, and requirements of a trial are explained to potential participants. 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.

New prevention technologies: Also known as biomedical interventions. This refers to a group of HIV prevention tools that employ medical interventions to reduce the risk of HIV infection. This category of HIV prevention includes male circumcision, microbicides, PEP, PrEP, preventive and therapeutic vaccines, and treatment as prevention.

Opportunistic infection: An illness such as pneumoncystis jiroveci pneumonia that people with HIV and 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.

Post-exposure prophylaxis (PEP): The temporary use of anti-HIV drugs by an HIV-negative person immediately after a known or suspected exposure to HIV, to reduce the risk of infection.

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.

Pre-exposure prophylaxis (PrEP): The daily use of ARVs for the prevention of HIV in people who are HIV-negative.

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 isn't 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.

Treatment: A range of interventions or products being tested in clinical trials. These include drugs, food, supplements, therapeutic strategies, prevention methods, microbicides and vaccines.

Vaccine: A substance that teaches the 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 cleared from the body.

WHERE TO FIND HELP

The following list includes organizations or programs engaged in the HIV response and/or who provide information on HIV treatments, clinical trials, and drug access.

Treatment/Clinical Trial Information

CIHR Canadian HIV Trials Network
620B - 1081 Burrard Street
Vancouver, BC V6Z 1Y6

Tel: 1.800.661.4664 or 604.806.8327
ctninfo@hivnet.ubc.ca
www.hivnet.ubc.ca

CATIE
555 Richmond Street West, Suite 505
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
Many of CAS's member organizations have locally-based treatment information programs. A list of these organizations can be found on their website (www.cdnaids.ca) or by contacting CAS by phone (see over).

National Community Organizations

AIDS Action Now!
info@aidsactionnow.org
www.aidsactionnow.org

Canadian Aboriginal AIDS Network (CAAN)
6250 Salish Drive
Vancouver, BC V6N 2C7

Tel: 604.266.7616
kenc@caan.ca
www.caan.ca

Canadian AIDS Society (CAS)
190 O'Connor, Suite 800
Ottawa, ON K2P 2R3

Tel: 613.230.3580
1.800.499.1986
CASinfo@cdnaids.ca
www.cdnaids.ca

CAS is a national coalition of more than 120 community-based AIDS organizations across Canada. A list of these organizations can be found on its website or by contacting CAS by phone or fax. Many of the member groups of the Canadian AIDS Society represent special populations.

Canadian Foundation for AIDS Research (CANFAR)
165 University Avenue, Suite 710
Toronto, ON M5H 3B8

Tel: 1.800.563.CURE (2873)
www.canfar.com

Canadian HIV/AIDS Legal Network
1240 Bay Street, Suite 600
Toronto, ON M5R 2A7

Tel: 416.595.1666
info@aidslaw.ca
www.aidslaw.ca

Canadian Treatment Action Council (CTAC)
Box 203, Suite 1109B
555 Richmond Street West
Toronto, ON M5V 3B1

Tel: 416.410.6538
ctac@ctac.ca
www.ctac.ca

Canadian Working Group on HIV and Rehabilitation (CWGHR)
1240 Bay Street, Suite 600
Toronto, ON M5R 2A7

Tel: 416.513.0440
info@hivandrehab.ca
www.hivandrehab.ca

Drug Access Information

Therapeutic Products Directorate
2nd Floor, Holland Cross, Tower A
11 Holland Avenue, A.L. 3002C
Ottawa, ON K1A 0K9

Tel: 613.941.2108
SAPdrugs@hc-sc.gc.ca
www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index-eng.php

Reference

National Council on Ethics in Human Research (NCEHR)
240 Catherine Street, Suite 208
Ottawa, ON K2P 2G8

Tel: 613.233.5445
office@ncehr-cnerh.org
www.ncehr-cnerh.org