



# Understanding the Clinical Research Process and Principles of Clinical Research

HIV/AIDS Network Coordination  
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## Participant Guide

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# INTRODUCTION

Welcome to this workshop about the clinical research process and the principles of clinical research. These are important topics to understand for those who are working to find new prevention technologies, improved treatment regimens, a vaccine, and a cure for AIDS (Acquired Immunodeficiency Syndrome).

Many people all over the world work very hard to find a cure for AIDS. In this workshop, you will learn about what happens to the people who participate in clinical research activities.

This workshop is designed to give you an opportunity to:

- Apply the information you learn in activities and discussions
- Ask questions about information you do not understand
- Practice what you learn

This Participant Guide includes information, facts, space to write your own notes, and a glossary. The glossary has many words, abbreviations, and definitions that you might not be familiar with.

Before we talk about clinical research, we need to talk about AIDS and some of the organizations that work on AIDS research all over the world.

## What Is AIDS?

AIDS stands for “acquired immune deficiency syndrome.” AIDS is caused by a virus called HIV (Human Immunodeficiency Virus). A person who is infected with HIV develops antibodies to fight the infection. A blood test for HIV looks for these antibodies. People who have HIV antibodies in their blood are called “HIV positive.”

Being HIV positive is not the same thing as having AIDS. AIDS develops over time as the HIV virus wears down the body’s immune system. The immune system is the body’s way to fight disease. A person can progress from simply being HIV positive to having an AIDS diagnosis when the body’s immune system is highly compromised by the effects of the virus.

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## What Is the History of AIDS?

The history of AIDS is quite short. There were cases of AIDS identified from stored samples from the 1950s. AIDS cases grew during the late 1970s and 1980s. AIDS is now a global epidemic. It has become one of the greatest threats to human health and development.

## What Are the Division of AIDS' (DAIDS) Top Scientific Priorities for HIV/AIDS Research Worldwide?

DAIDS has identified six important areas of research to:

- Foster research that unravels the fundamental processes governing host/virus interactions
- Identify and test ways to prevent HIV infection, treat HIV disease, and cure HIV infection based upon these findings

The National Institute of Allergy and Infectious Diseases (NIAID) is an organization that coordinates HIV/AIDS research around the world. NIAID's HIV/AIDS clinical trials networks have been designed to address one or more of NIAID's six high-priority areas of research:

<b>DAIDS Top Scientific Priorities</b>	<b>Network(s) Assigned to Address This Priority</b>
1. Vaccine research and development	HIV Vaccine Trials Network (HVTN)
2. Translational research/drug development	AIDS Clinical Trial Group (ACTG), International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT)
3. Optimization of clinical management, including co-morbidities	ACTG, IMPAACT, International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)
4. Microbicides	Microbicide Trials Network (MTN)
5. Prevention of mother-to-child transmission of HIV	IMPAACT
6. Prevention of HIV infection	HVTN, HIV Prevention Trials Network (HPTN)

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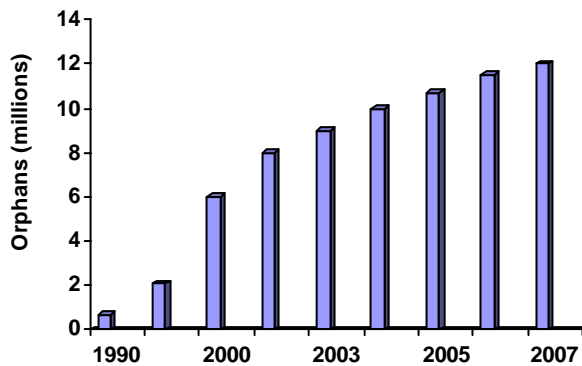
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## How Serious Is AIDS?

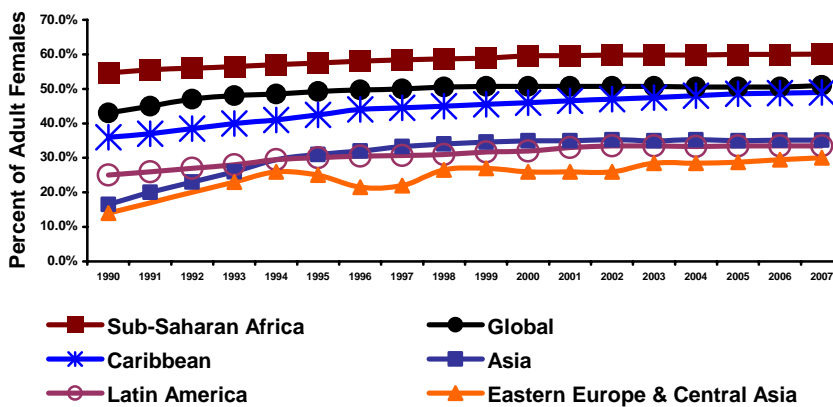
- At the end of 2007, approximately 33 million people were living with HIV<sup>1</sup>
- Every year, approximately 2.7 million more people become infected with HIV<sup>3</sup>
- Every year, approximately 2 million people die of AIDS<sup>2</sup>
- HIV is spreading most rapidly in Eastern Europe and Central Asia, where the number of people living with HIV increased 150% between 2001 and 2007<sup>3</sup>

Although HIV and AIDS are found in all parts of the world, some areas are more affected than others. The worst affected region is sub-Saharan Africa. In some sub-Saharan Africa countries, more than one in five adults is infected with HIV.<sup>4</sup>



This table shows the estimated number of children under 18 orphaned by AIDS in sub-Saharan Africa (1990-2007).<sup>5</sup>

Approximately 400,000 children under age 13 become newly infected with HIV each year. Most of these new infections are a result of mother-to-child transmission.<sup>6</sup> Without treatment, half of HIV-infected infants will die before the age of two.<sup>7</sup>



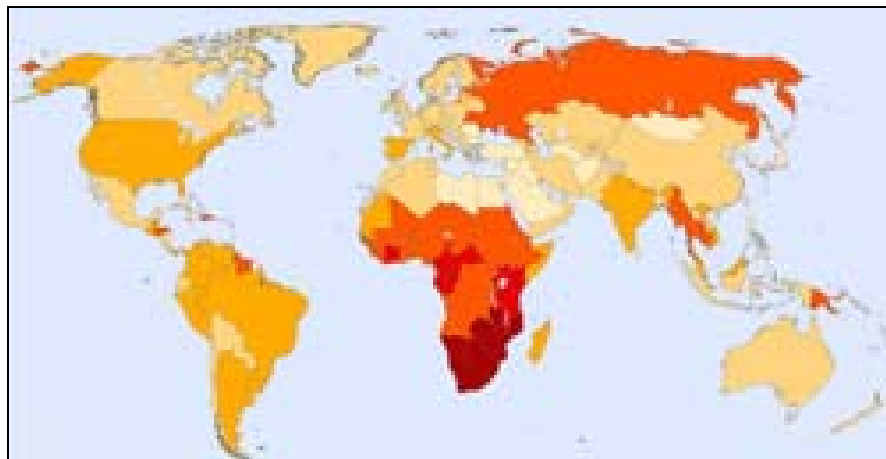
This table shows the percent of adults (15+ living with HIV) who are female, 1990-2007).<sup>8</sup>

Note: Current statistics used in this training are subject to change.



## Why Is Worldwide HIV Research Important?

HIV is transmitted by different routes in different people at different time intervals with different treatment options that lead to different outcomes. No single organization has the resources to complete the needed research.



The map shows a global view of HIV infection. The darker areas (Africa, Southeast Asia, Russia, and China) are most impacted.

In 2006, almost 40 million people worldwide were living with the HIV virus.<sup>9</sup>

## What Are the Millennium Development Goals (MDGs)?

In 2000, world leaders assembled at the United Nations to identify an action agenda for the new millennium. The agenda was agreed to by all the world's countries and included a set of ambitious development targets—the Millennium Development Goals (MDGs). One of the eight goals focuses on HIV/AIDS, which expressly calls on the world community to halt and begin to reverse the spread of HIV by 2015.

Ban Ko-moon, Secretary General of the United Nations said:

*The Millennium Development Goals can be achieved if immediate steps are taken to implement existing commitments. Reaching our goals for development around the world is not only vital to building better, healthier and decent lives for millions of people, it is also essential to building enduring global peace and security.*<sup>10</sup>

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## What Will We Do in This Workshop?

In this workshop, we will look at many important areas about AIDS research. We will learn important information and you will be able to ask questions. We will also do activities together to help you remember what you learn. The objectives of this workshop are to:

- Describe clinical research
- Describe the clinical research process
- Describe the principles of clinical research
- Define ethics
- Describe the role of a Community Advisory Board (CAB) in the research process
- List key partnerships
- Discuss issues affecting AIDS research for various stakeholders

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# CLINICAL RESEARCH

In this section, we will describe and discuss:

- Clinical trials
- The importance of research
- Where clinical trials take place
- The benefits of taking part in a clinical trial
- Possible risks when taking part in a clinical trial

## What Is Clinical Research?

Clinical research is an important tool to help develop solutions that will benefit people all over the world. Clinical research includes:

- Medical and behavioral research involving volunteer participants
- Investigations that are carefully developed and conducted with clinical outcomes recorded
- Identification of better ways to prevent, diagnose, treat, and understand human disease
- Trials that test new treatments, clinical management and clinical outcomes, and long-term studies
- Strict scientific guidelines
- Ethical principles to protect participants

Research is a systematic investigation to establish fact. Treatment is the care provided to improve a situation.

## What Is a Clinical Trial?

Following testing in laboratories and animal studies, the most promising treatments are moved into clinical trials. A clinical trial is sometimes called a clinical study. A clinical trial:

- Is a research study that tests how well an intervention works in a group of people
- Tests for new methods of screening, prevention, diagnosis, or therapy
- Is conducted in phases

During a trial, additional information is learned about an intervention, its risks, and its effectiveness and/or efficacy. Trials can only be conducted if there is an uncertainty about the outcome—trials cannot be conducted if the outcome is already known from a previous study.



## **Why Is Research Important?**

Research is important because:

- Clinical trials test how well new approaches and interventions work in people
- These approaches can be medical, behavioral, or management
- Each study answers scientific questions
- Each study helps scientists prevent, screen for, diagnose, manage, and treat a disease

People who take part in clinical trials contribute to the knowledge of how a disease progresses.

## **Where Do Clinical Trials Take Place?**

Clinical trials take place all over the world:

- Health care providers' offices
- Medical centers
- Community and university hospitals and clinics
- Veterans' and military hospitals

Clinical trials may include participants at one or two highly specialized centers. Or they may involve hundreds of locations at the same time.

Good clinical laboratory standards and practices are established by DAIDS. These standards and practices apply to lab facilities throughout the world. Research staff members receive training and certification to ensure the safety and security of the research.

Good Clinical Practice (GCP) is an international quality standard that governments can transpose into regulations for clinical trials involving human subjects. GCP guidelines include protection of human rights as a subject in clinical trial and assurance of the safety and efficacy of the newly developed compounds. GCP guidelines also include standards on how clinical trials should be conducted and a definition of the roles and responsibilities of clinical trial sponsors, clinical research investigators, and monitors.

Good clinical laboratory practice (GCLP) guidelines focus on good laboratory practice and good clinical practice guidelines/standards for medical testing laboratories conducting clinical trials in developing countries.



## **What Are Some Benefits of Taking Part in a Clinical Trial?**

Some benefits of taking part in a clinical trial are:

- Participants have access to promising new approaches often not available outside the clinical trial setting
- The drug, vaccine or other intervention being studied may be more effective and/or efficacious than the standard approach (although there is no guarantee that participants will receive the experimental drug, vaccine, or other intervention)
- Participants receive careful medical attention from a research team of doctors and other health professionals
- Participants may be the first to benefit from the study
- Results from the study may help others in the future

## **What Are Some of the Possible Risks Associated with Taking Part in a Clinical Trial?**

Some risks of taking part in a clinical trial are:

- New vaccines, microbicides, and other strategies under study are not always better than the standard care to which they are being compared
- New treatments may have unexpected side effects or risks that are worse than those resulting from standard care
- Health insurance and managed care providers may or may not cover all participant care costs in a study
- Participants may be required to make more visits to the doctor than they would if not in the clinical trial
- Participants in randomized trials are not able to choose the kind of intervention they will receive

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# CLINICAL RESEARCH PROCESS

In this section, we will describe and discuss the elements of the clinical research process.

## What Is the Clinical Research Process?

The clinical research process includes:

- Pre-clinical testing
- Investigational New Drug Application (IND)
- Phase I (assess safety)
- Phase II (test for effectiveness)
- Phase III (large-scale testing)
- Licensing (approval to use)
- Approval (available for prescription)
- Post-marketing studies (special studies and long-term effectiveness/use)

## What Is Pre-Clinical Testing?

Before a vaccine, microbicide, or other strategy can be tested in humans, pre-clinical testing is required. Pre-clinical testing is often conducted on animals. Many pre-clinical studies use a review committee to determine if the use of animals is warranted. The review committee also checks to see if the research can be improved by reducing or replacing animals. Laboratory and animal studies are conducted to:

- Find out if there is a potential benefit of the drug, vaccine, or other product
- Explore general safety concerns

After a vaccine, microbicide, or other strategy is found to have a potential benefit, it begins to be prepared for human testing.

Pre-clinical testing takes approximately three to four years.

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## **What Is an Investigational New Drug Application (IND)?**

For studies that involve a new vaccine, microbicide, or other strategy, after completing pre-clinical testing, an investigational new drug application (IND) must be filed:

- Describing the results of pre-clinical testing
- Clearly defining how future studies will be conducted

The U.S. Food and Drug Administration (FDA) has 30 days to review the IND. If the FDA approves the IND within 30 days, the vaccine, microbicide, or other strategy can proceed to a phase I trial.

## **What Is Phase I (Assess Drug Safety)?**

The goals of phase I clinical trials are:

- Assess safety for humans
- Select the dose to be used in future studies

During phase I, the study is designed to determine:

- How the human body reacts
- What side effects occur as dosage levels are increased

For the first time, the vaccine, microbicide, or other strategy is introduced to humans. Testing occurs in a small number of HIV-negative volunteers (20 to 100).

This initial phase of testing usually lasts several months to 1 year. About 70% of experimental drugs pass this initial phase.<sup>11</sup>

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## **What Is Phase II (Test for Safety and Effectiveness)?**

After a vaccine, microbicide, or other strategy has been shown to be safe, it must be tested for effectiveness and/or efficacy. A phase II study provides comparative information about relative safety and effectiveness and/or efficacy. Most phase II studies are randomized trials. This means:

- One group receives the experimental vaccine, microbicide, or other strategy
- A second "control" group receives the standard of care or placebo

Some phase II studies are "blinded." This means participants and researchers do not know who receives the experimental vaccine, microbicide, or other strategy. This testing may last from several months to 2 years. It may involve from 100-300 participants/volunteers. Only about 30% of experimental vaccines, microbicides, and other strategies successfully complete both phase I and phase II studies.<sup>12</sup>

## **What Is Phase III (Large-Scale Testing)?**

In a phase III study, testing involves 1,000-3,000 participants/volunteers. This large-scale testing provides a better understanding of:

- Effectiveness and/or efficacy
- Benefits
- Range of possible adverse reactions
- The comparison to standard of care treatment

Most phase III studies are randomized and blinded trials with specific entry criteria. Phase III studies typically last several years. 70-90% of vaccines, microbicides, and other strategies that enter phase III studies successfully complete testing.<sup>13</sup> After a phase III study is successfully completed, a company can request marketing approval from the FDA.

## **What Is Licensing (Approval to Use)?**

After all three clinical trial phases are complete and, if the research demonstrates that the vaccine, microbicide, or other strategy is safe and effective, a New Drug Application (NDA)/Biologics License Application (BLA) is filed with the FDA. This NDA/BLA must contain all scientific information compiled over the course of the trials.

The FDA is allowed at least 6 months to review the NDA/BLA. However, this review process can sometimes take up to 2 years, depending on specific country requirements.



## **What Is Approval (Available for Prescription)?**

After the U.S. Food and Drug Administration approves the NDA/BLA, the vaccine, microbicide, or other strategy becomes available for health care providers to prescribe.

Even if a product is approved, it must continue to comply with regulatory requirements over time. For vaccines, microbicides, and other strategies approved for use, reviews continue to ensure safety over time.

For example, all cases of adverse events caused by the vaccine, microbicide, or other strategy must be reported, and quality control standards must be met. Sometimes, the regulatory agency will also require post-marketing studies to evaluate long-term effects.

Accelerated approval<sup>14</sup> is when a vaccine, microbicide or other strategy that treats serious diseases (especially if they are the first available treatment or have advantages over existing treatments) is developed and made available more quickly. The process for serious diseases is designed to:

- Help development of treatments
- Speed review for serious diseases
- Fill an unmet medical need to get important new treatments to patients faster

Accelerated approval is based on these criteria if the treatment will have an impact on:

- Survival
- Day-to-day functioning
- Likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

AIDS is an example of a serious disease. Accelerated approval does not compromise the standards for the safety and effectiveness of the treatments that become available through this process.

## **What Are Post-Marketing Studies?**

Post-marketing studies (special studies and long-term effectiveness/use) are also called phase IV studies. They often have several objectives. These studies are often performed in special populations not previously studied (for example, children or the elderly). The studies are designed to monitor:

- Long-term effectiveness and/or efficacy
- The impact on a person's quality of life

Some studies help determine the cost-effectiveness of a therapy compared to other traditional and new therapies.





# **ELEMENTS AND PRINCIPLES OF CLINICAL RESEARCH**

In this section, we will describe and discuss important elements and principles of clinical research, including:

- Protocols and protocol reviews
- Sponsors
- Eligibility criteria
- Informed consent
- Types of clinical trials
- What happens during clinical trials
- Who can participate in clinical trials, including inclusion and exclusion criteria
- The importance of ethics in clinical research

## **What Are the Elements and Principles of Clinical Research?**

The elements and principles of clinical research are:

- Protocol
- Protocol review
- Sponsor
- Eligibility criteria
- Informed consent
- Types of clinical trials
- Phases of clinical trials
- Activities during clinical trials
- Clinical trial participants



## **What Is a Protocol?**

Clinical research is conducted according to a plan (a protocol) or action plan. The protocol acts like a “recipe” for conducting the trial. The plan describes what will be done in the study, how it will be conducted, and why each part of the study is necessary. The protocol or plan is carefully designed to safeguard the participants’ health and answer specific research questions.

The same protocol is used by every doctor or research center taking part in the trial. A protocol describes:

- Who is eligible to participate in the trial
- Details about tests, procedures, medications, and dosages
- The length of the study and what information will be gathered

A protocol is led by a principal investigator. The principal investigator is often a doctor. Members of the research team regularly monitor the participants’ health to determine the study’s safety and effectiveness and/or efficacy.

## **What Is a Protocol Review?**

Clinical trials in the United States must be approved and monitored by an Institutional Review Board (IRB). The IRB ensures that the risks are minimal and are worth any potential benefits. An IRB is an independent committee. Physicians, statisticians, and members of the community belong to an IRB.

The committee ensures that clinical trials are ethical and that the rights of all participants are protected.

U.S. regulations require all research institutions in the United States that conduct or support biomedical research involving people to meet certain requirements. An IRB must initially approve and periodically review the research. Some research institutions have more than one IRB. During protocol reviews, networks review and assess what other networks are doing to see what information applies to what they are doing.



## What Is a Sponsor?

Clinical trials are sponsored or funded by various organizations or individuals, including:

- Physicians
- Foundations
- Medical institutions
- Voluntary groups
- Pharmaceutical companies
- Federal agencies such as the National Institutes of Health, the Department of Defense, Centers for Disease Control and Prevention (CDC), and the Department of Veterans Affairs

Trials can occur at sites as varied as hospitals, universities, doctors' offices, or community clinics.

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## What Are Eligibility Criteria?

Each study's protocol has guidelines for who can or cannot participate in the study. These guidelines, called eligibility criteria, describe characteristics that must be minimally shared by all participants.

The criteria differ from study to study. Criteria may include:

- Age
- Gender
- Medical history
- Current health status
- Lab values

Eligibility criteria for treatment studies often require that participants have a particular type and stage of a disease. Some HIV prevention studies may require that participants have certain risk factors for HIV infection.

Enrolling participants with similar characteristics helps to ensure that the results of the trial will be a result of what is under study and not other factors. In this way, eligibility criteria help researchers achieve accurate and meaningful results. These criteria also minimize the risk of a person's condition becoming worse by participating in the study.

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## What Is Informed Consent?

Informed consent is the process of providing potential participants with important facts about a clinical trial before they decide to participate. The process of informed consent, which means “providing additional information,” continues throughout the study. Members of the research team explain the details of the study. This explanation helps people make a decision that is right for them. Informed consent is not a contract or just a piece of paper—it is a process.

Informed consent must be provided:

- In the participants’ native language
- At an appropriate educational level

Translation or interpretive assistance can be provided for participants with limited language skills.

The research team provides an informed consent document that includes details about the study:

- Its purpose
- Duration
- Required procedures
- Who to contact for more information
- An explanation of risks and potential benefits

The participant then decides whether to sign the document

In many communities, illiteracy and mistrust exist toward anyone who asks for a signature as a commitment. Sometimes people fear their signatures may lead to unexpected obligations, because they attach great importance to legal formalities.

Volunteers are free to withdraw from a study completely or to refuse particular treatments or tests at any time (sometimes, however, this will make them ineligible to continue the study).

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## What Are Some Types of Clinical Trials?

Type of Clinical Trial	Description
Treatment	Test new treatments, new combinations, new approaches to surgery or radiation therapy, or clinical management strategies.
Prevention	Look for better ways to prevent a disease in people who have never had the disease. In the case of diseases other than HIV/AIDS, to prevent the disease from returning. Better approaches may include medicines, vaccines, and/or lifestyle changes.
Diagnostic	Determine better tests or procedures for diagnosing a particular disease or condition.
Screening	Test the best way to detect certain diseases or health conditions.
Quality of Life (or Supportive Care)	Explore and measure ways to improve the comfort and quality of life of people with a chronic illness.

For example:

- Anti-retroviral drugs (ARVs) are used to lower the risk of transmission of HIV from an HIV+ pregnant woman to her infant. Clinical trials have proven that ARVs are both safe and effective for this purpose.
- In a retrospective study, children known to be taking ARV treatment are enrolled. The researcher then reviews the medical record of each participant, checks the type of treatment received, and records information from the point of enrollment and looking backward at the 5 years *before* enrollment.
- In a prospective study, children enroll in the study and then started on ARV treatment. From the first visit, data are collected for 5 years going forward.

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## What Happens in a Clinical Trial?

Usually, clinical trials compare a new product, vaccine, management strategy, or therapy with another that already exists. This comparison helps to determine if the new one is as successful as, or better than, the existing one.

In some studies, participants may be assigned to receive a placebo (an inactive product that resembles the test product, but without its treatment value). Comparing a new product with a placebo can be the fastest and most reliable way to demonstrate the new product's therapeutic effectiveness and/or efficacy. Placebos are not used if a participant will be put at risk (standard of care)—particularly in the study of treatments for serious illnesses—by not having effective therapy. Potential participants are told if placebos will be used in the study before they enter a trial. For studies using placebos:

- Clinical trial investigators must be able to show that withholding active therapy from participants for a short time is unlikely to result in physical harm
- Participants must give voluntary, informed consent
- Investigators must closely monitor participants in these studies. For therapeutic trials, most studies compare new products or regimens with an approved therapy (for example, standard of care).

Randomization is when two or more alternative treatments are assigned to volunteers by chance instead of choice. The assigned treatment is administered with the highest level of professional care. The results of each treatment are compared at specific points during a trial, which may last for years. When one treatment is found superior, the trial is stopped so that the fewest participants possible receive the less beneficial treatment.

In single- or double-blind studies (also called single- or double-masked studies), participants do not know which medicine is being used, so they can describe what happens without bias. Blind studies are designed to prevent members of the research team or study participants from influencing the results. Therefore, scientifically accurate conclusions are more likely. Members of the research team are not told which participants receive which medication, so their observations will not be biased. If medically necessary, it must always be possible to find out what participants have taken:

- In single-blind studies, only the participant is not told what is being administered
- In a double-blind study, the *only* person who knows what is being administered is the pharmacist



## Who Can Participate in a Clinical Trial?

The main goal for using volunteers in a clinical trial is to prove, by scientific means, the effects and limitations of the experimental treatment on a wide variety of people. Research procedures with volunteers are designed to develop new knowledge, not to provide direct benefit to study participants. Before joining a clinical trial, a person must qualify for the study:

- Some research studies seek participants with illnesses or conditions to be studied in the clinical trial
- Some research studies need volunteers who do not have the disease being studied

A person with the condition being studied is called a “patient volunteer” and:

- Has a known health problem
- Participates in research to better understand, diagnose, treat, or cure that disease or condition
- Supports research procedures to help develop new knowledge (these procedures may or may not benefit the participant)

A person may also volunteer who is at risk for the condition being studied. A volunteer who does not have the condition being studied is called a “control” and:

- Participates in clinical research to test a new vaccine, microbicide, or other strategy or intervention
- Is needed when developing a new technique, such as a blood test or imaging device
- Helps define the limits of "normal"
- Serves as a control for participant groups and is often matched to participants on characteristics such as age, gender, or family relationship
- Receives the same test, procedure, vaccine, microbicide the participant group receives

Some volunteers serve as controls by not taking the test vaccines, microbicides, or other strategies. Or these volunteers may receive doses large enough only to show that it is present, but not at a level that can treat the condition. Investigators learn about a disease process by comparing how each kind of volunteer reacts to the trial.

Some studies require a major commitment in time and effort. Some studies may involve some discomfort. The research procedure may also carry some risk. The consent process for volunteers includes a detailed discussion of the study's procedures and tests.





## What Are Inclusion/Exclusion Criteria?

All clinical trials have guidelines about who can participate—these are specified in the inclusion/exclusion criteria:

- Factors that allow someone to participate in a clinical trial are "inclusion criteria"
- Factors that exclude or do not allow participation in a clinical trial are "exclusion criteria"

These factors may include:

- Age
- Gender
- The type and stage of a disease
- Previous treatment history
- Specific lab values
- Other medical conditions

Inclusion and exclusion criteria are not used to reject people personally. The criteria are used to:

- Identify appropriate participants
- Keep them safe
- Help ensure that researchers can answer the questions they want answered

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## What Is Ethics?

Ethics means:

- Respect for persons
- Beneficence, which means to do good—in clinical research, beneficence means even more—to do no harm, or maximize possible benefits and minimize possible harm
- Justice, or fairness

Scientific research has produced many social benefits, but it has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments:

- During the Nuremberg War Crime Trials after World War II, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on prisoners. This code became the prototype of many later codes intended to assure that research involving human subjects would be carried out in an ethical manner.<sup>15</sup>
- The Tuskegee Study of Untreated Syphilis in the Negro Male (also known as the Tuskegee Syphilis Study, Public Health Service Syphilis Study, or the Tuskegee Experiment) was a clinical study, conducted between 1932 and 1972 in Tuskegee, Alabama by the U.S. Public Health Service. 399 poor, mostly illiterate African Americans with syphilis were recruited for research related to the natural progression of the disease if left untreated. The trial participants were not offered treatment for syphilis when it became available.<sup>16</sup>

The Belmont Report<sup>17</sup> was developed by The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research on April 18, 1979, to:

- Summarize the basic ethical principles identified by the Commission in the course of its deliberations
- State basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects

Ethical principles must guide all research activities including:

- All phases of research, including formation of research questions, design of the study, conduct of research, analysis of data, and interpretation of findings
- Dissemination of new knowledge in the forms of presentations and publications



## What Is Respect for Persons, Beneficence, and Justice?

<b>Respect for Persons</b>	<b>Beneficence</b>	<b>Justice</b>
People have a right to make their own choices	Researchers do everything possible to make sure the research does not harm participants in any way	There are more benefits for the participant than risks
All the facts about the research are presented to potential participants	The risks of the study will be kept as low as possible	Participants are fairly recruited as research participants
Volunteers must not be pressured to choose research over other options for care	The benefits of participating in the research study should be greater than the risks	
The community where research is being conducted is respected	It is more important to protect participants than to achieve benefits	
The community has a voice in what is done during the research (Community Advisory Boards help the research team do this)		

### Notes

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## Who Is Responsible for Ethics?

Everyone is responsible for ethics. An Ethics Committee (EC) or Institutional Review Board (IRB) must be trained to approve, monitor, and review research involving humans. Its purpose is to protect the rights and welfare of the research subjects to:

- Protect research participants
- Review protocols before trials may be conducted
- Ask researchers to change protocols, when needed
- Supervise a study from beginning to end
- Oversee scientific design
- Review community interests
- Review recruitment plans
- Enforce informed consent
- Enforce confidentiality

An EC/IRB is made up of people from different backgrounds not directly involved in the research. They must have no conflict of interest, include community representatives, and be trained. The EC/IRB ensures a study is ethical by ensuring:

- There are enough measures in place so the well-being of participants is protected
- Clear identification of how the study will be monitored to keep participants safe
- The study design is safe and appropriate
- The samples collected will support the design
- A description exists of how the community will benefit from the research
- Appropriate plans are identified to protect vulnerable populations and recruit fairly
- The informed consent process addresses all issues
- Members of the community understand informed consent
- Protection of the participants' privacy

Requirements for EC/IRB membership:

- Some members should have a background in science or research
- Some members should NOT have a background in science or research
- May include religious or other community leaders
- May include people who participated in earlier studies
- There are varied gender, age, ethnic, and cultural backgrounds
- There is a clear understanding of when to seek the help of outside consultants with specific expertise



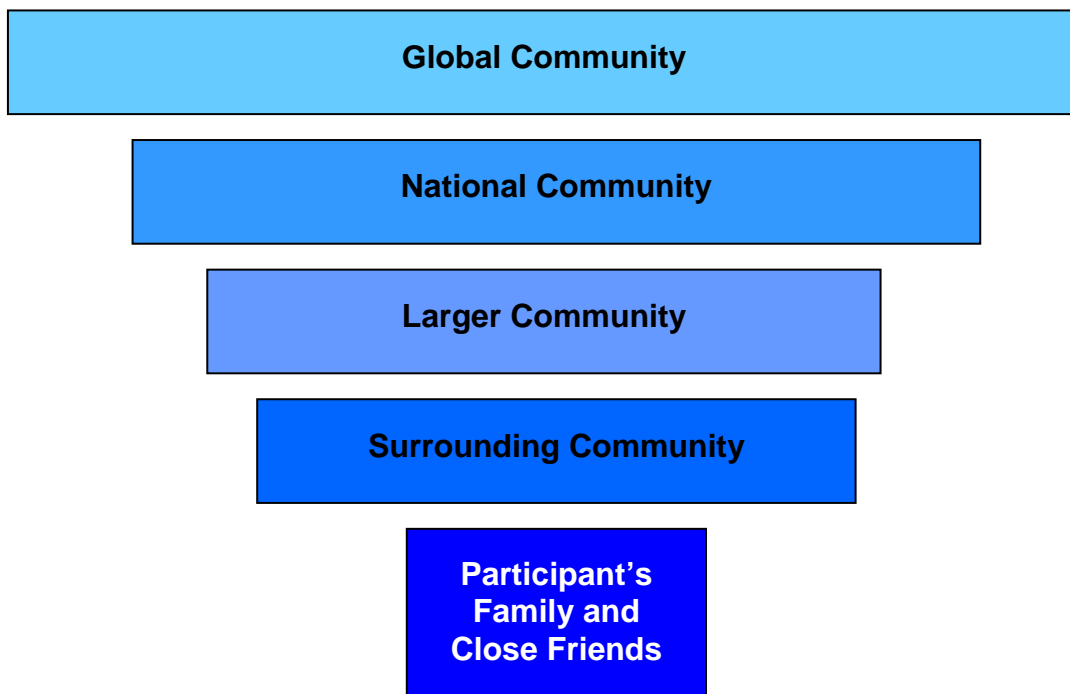
# COMMUNITY ADVISORY BOARDS (CABS) AND THE RESEARCH PROCESS

In this section, we will describe and discuss the role of a Community Advisory Board (CAB) in the research process, including:

- A definition of “community”
- The history of CABS
- CAB members
- How CABS are involved in a community
- How researchers and CABS interact

## What Is the Role of a Community Advisory Board (CAB) in the Research Process?

An AIDS trial participant is part of a large community. There is a wide range of external influences on an individual trial participant.





## **What Is a Community?**

A community shares common:

- Geography
- Racial or ethnic makeup
- Values, culture, beliefs, and interests

People can belong to many communities at the same time. Communities and the demographics of a target population are always changing.

## **What Is the History of CABs?**

In the 1980s, AIDS activists in the U.S. and Europe demanded that researchers and regulatory authorities move more quickly to find medications to fight HIV. With knowledge about scientific research and HIV, a group of activists looked for opportunities to review trial proposals. Through protests, letter-writing and by lobbying the U.S. government, they succeeded in changing the U.S. drug approval process.

This process resulted in creation of Community Advisory Boards (CABs) made up of non-scientists. These non-scientists review protocols, monitor trials, and help educate and inform the rest of the community. CABs were established to:

- Provide oversight and guidance for the protection of participants in clinical trials
- Help define research questions
- Communicate the interests and needs of the community to the research team
- Represent a specific community group infected with or affected by HIV

CABs were well established in the U.S. by the early 1990s. They were involved in some of the first U.S. HIV prevention and therapeutic networks. In the late 1990s, the first efforts to model an African AIDS prevention and therapeutic trial CAB took place in Uganda. The first CAB orientation meeting was organized there in July 1998. The first African HIV prevention and therapeutic trial CAB was launched in preparation for the trial the next year.

Some of the first CABs, especially in the U.S., were made up mostly of people living with HIV and AIDS. In some communities, this is still the case. Now most CABs are comprised of individuals representing various parts of the community, such as religious groups, schools or universities, media and NGOs/CBOs.<sup>18</sup>



## Who Participates on a CAB?

CAB participants include volunteers from a broad range of backgrounds representing different groups within a community. Some volunteers are paid, but usually they are not. CABs can set their own guidelines. CAB participants are a group of people from a local community (research site) who:

- Bring community concerns about the research to the research team
- Teach members of the community about the research
- Are the point of communication and education between researchers and the community members who might be affected by the research
- People who want to contribute their knowledge and skills to the work of the CAB with a sensitivity and respect for different points of view and willingness to work together towards common goals
- People with a direct interest in the prevention and treatment of HIV
- People who have the ability and desire to communicate well
- People who have the ability to listen and learn with a desire to help others learn
- People who work well with others, especially those from different communities or with different points of view
- People with a strong commitment to the prevention, treatment, and control of HIV
- And, ideally, people who hold the belief that one person can make a difference

CAB members are diverse in gender, age, race, and risk group, including:

- Trial participants/target group
- Community members and opinion leaders
- Religious leaders
- Press/media
- HIV-positive and affected individuals

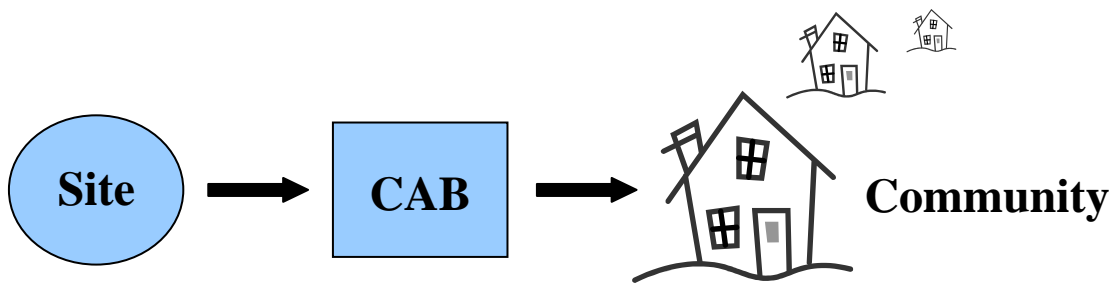
Ideally, 40% of the CAB's members are from the target population of a site's trials.

Regional CABs (where applicable) reflect the diverse regional community and report to sites about regional activities. They also bring information from the region, the site CABs, and the broader community to the international CAB.



## How Are CABs Involved in the Community?

CABs are now a significant piece of prevention and therapeutic trials in both developed and developing countries. They serve as primary liaisons between the community and the trial researchers. For example, a CAB member might tell a doctor: “I am concerned that this trial is too demanding for the participants. Four visits in one month is a lot to expect of people in our community.”



Often a senior scientist or physician and/or other member of the trial staff will attend CAB meetings. CAB members take on active roles in planning for and implementing AIDS prevention and therapeutic trials. Examples of their activities include:

- General community outreach and education
- Sharing with the community information about the ongoing work of the research team and the results of the research (investigators give the information to the CAB members and the CAB members communicate the information to the community)
- Helping to get community members to voice their thoughts, suggestions, or opinions about the study or about research in general
- Support for volunteer recruitment
- Providing feedback on trial protocols, including criteria for participation, informed consent forms and processes, and volunteer recruitment and retention
- Advising investigators regarding potential participants' perspectives about the trial, including strong negative reactions or specific changes to a protocol
- Providing a safeguard (with the institutional ethics review committee) for participants' rights
- Representation at important national, regional and international meetings and conferences
- Identifying the needs of all members of the community
- Reviewing HIV prevention and education tools to be used in the community (i.e., brochures, videos, etc.)
- Discussing new research protocols, informed consent forms, and provide feedback to the Principal Investigator (PI) and Research Coordinator
- Providing a forum where persons receiving services at a hospital or clinic can voice concerns and share experiences



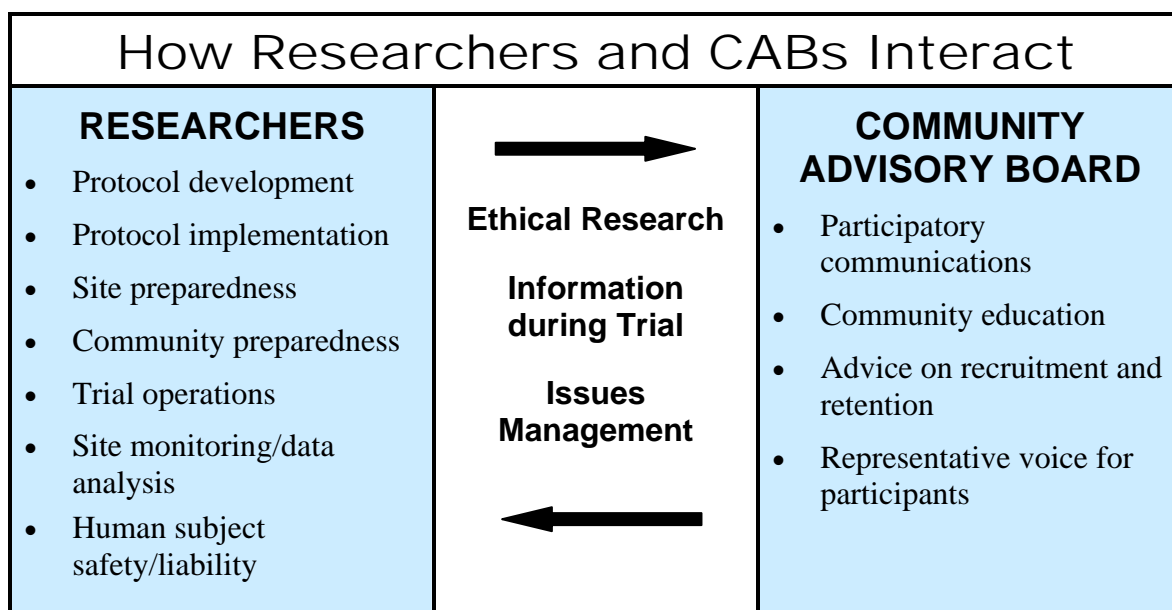


## How Do Researchers and CABs Interact?

Researchers and CAB members cooperate to ensure ethical research, share scientific and community information during a trial, and manage their activities collaboratively. Researchers know it is important to have general support from the communities that will be involved in the research for a trial to be successful.

As the CAB acts as a liaison between the researchers and the community, researchers may hold consultations with CABs or other community groups about an upcoming trial. Although they are not responsible for finding participants, CABs can help researchers find participants. CABs might help design a flyer and provide input on how and where to best reach potential participants, but they would not distribute the flyer.

CABs give feedback to researchers. CABs may have the opportunity to provide feedback on the actual trial protocol, the informed consent document, and any educational materials to be used in the community. Researchers may make changes to the trial protocol and other documents so that they reflect community input. Cooperation helps ensure that communities receive the right information, that their concerns are addressed, and that the trial will run smoothly in the community. The CAB, research team, and site staff must strengthen their own collaboration BEFORE reaching out to the community.



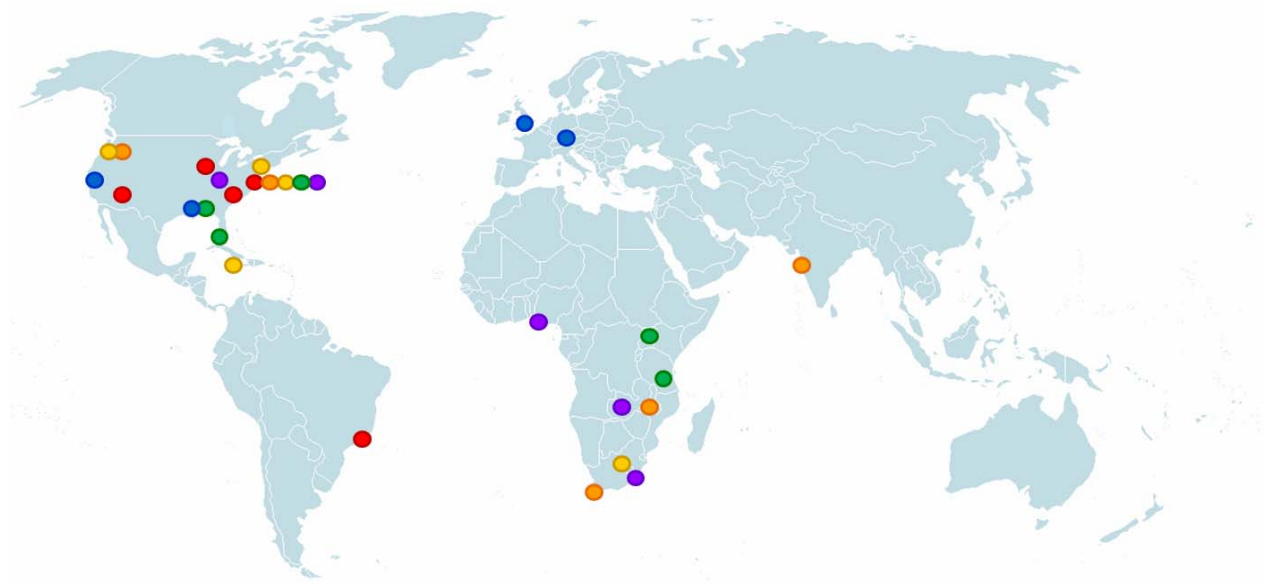


## KEY PARTNERSHIPS

In this section, we will describe and discuss:

- The clinical trials network
- The Community Partners (CP) organization

NIAID conducts and supports research to better understand, treat, and prevent infectious, immunologic, and allergic diseases. For more than 50 years, NIAID research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the U.S. and around the world. There are six clinical trials networks funded by NIAID.<sup>19</sup>





## What Is a Clinical Trials Network?

A clinical trials network is made up of researchers from hospitals and clinics in different areas of a country or parts of the world that cooperate to answer the same research questions. Each clinic in the network is a clinical research site (CRS). Representatives from different networks and institutes work together to keep each other informed of the work of their networks.

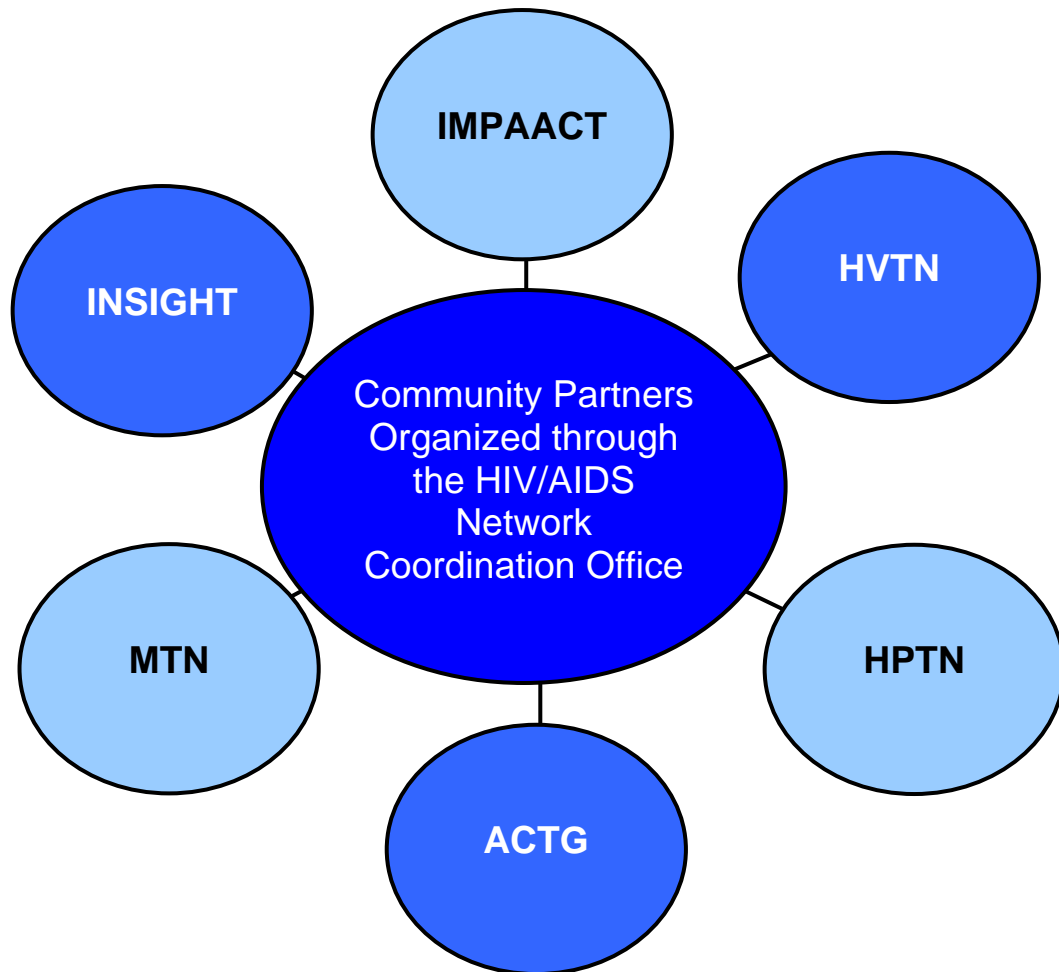
These six networks are important partners:

AIDS Clinical Trial Group (ACTG)	The largest therapeutic clinical trials group in the world, including many sites in resource-limited countries. These investigators and units serve as the major resource for HIV/AIDS research, treatment, care, and training/education in their communities.
HIV Prevention Trials Network (HPTN)	The HPTN is a worldwide collaborative clinical trials network that develops and tests the safety and efficacy of primarily non-vaccine interventions designed to prevent the transmission of HIV.
HIV Vaccine Trials Network (HVTN)	An international collaboration of scientists and educators searching for an effective and safe HIV vaccine. The HVTN's mission is to facilitate the process of testing preventive vaccines against HIV/AIDS by conducting all phases of clinical trials, from evaluating experimental vaccines for safety and the ability to stimulate immune responses, to testing vaccine efficacy.
International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT)	IMPAACT focuses on significantly decreasing the mortality and morbidity associated with HIV disease in children, adolescents, and pregnant women.
International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)	INSIGHT develops strategies for the optimization of treatment (anti-retroviral and immunomodulatory therapies and interventions to prevent and treat complications of HIV and anti-retroviral therapies) to prolong disease-free survival in a demographically, geographically, and socioeconomically diverse population of individuals infected with HIV.
Microbicide Trials Network (MTN)	The MTN brings together international investigators and community and industry partners who are devoted to reducing the sexual transmission of HIV through the development and evaluation of products applied topically or administered orally, working within a unique infrastructure specifically designed to facilitate research required to support licensure of these products for widespread use.



## What is Community Partners?

Community Partners is made up of community representatives from all six of the HIV research networks funded by the National Institutes of Health (NIH) through the Division of AIDS.





## What Are Some Cross-Network Activities?

Cross-network activities include:

- Community involvement to facilitate effective community engagement in research design, development, and implementation and provide community input at the cross-network leadership level
- Data management, such as the harmonization of data collection processes and coordination of site infrastructure changes
- Evaluation metrics, including the development and application of consistent standards of performance evaluation
- Training development and distribution, including the development and distribution of training modules that apply across organizations and communicating training opportunities to site and network staff
- Scientific leadership to advance optimal collaborative clinical trials research activities within the networks and drive collaborative efforts among the networks and other research partners
- Laboratory processing, including specimen collection and processing, laboratory training, repository utilization, quality assurance and proficiency testing
- Research site management and clinical trials logistics and issues identification and resolution
- Behavioral science to ensure that the networks benefit from state-of-the-science methods and procedures that optimize adherence to product and risk reduction counseling, minimize the risk of confounding user and product failures, and that the best quality behavioral science is integrated into clinical trials

### Notes

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## Which Organizations Support the Six Clinical Trials Networks?

The following organizations support the clinical trials networks:

- The National Institute of Allergy and Infectious Diseases (NIAID) created the Division of Acquired Immunodeficiency Syndrome (DAIDS) in 1986 to develop and implement the national research agenda to address the HIV/AIDS epidemic
- The HIV/AIDS Network Coordination (HANC) project works with the six HIV/AIDS clinical trials networks funded by DAIDS of the U.S. National Institutes of Health (NIH) with the intent of creating a more integrated, collaborative and flexible research structure<sup>20</sup>
- Statistical and operations centers
- Central laboratories
- Contract Research Organizations (CROs)

## Who Are the Primary Partners with the NIH?

The National Institute of Health is made up of 27 institutes and centers. Each focuses on specific research areas. More than 80% of NIH research activities are conducted by scientists around the world.<sup>21</sup>

Important NIH organizations that focus on AIDS-related research are:

- National Institute of Allergy and Infectious Diseases (NIAID)
- National Institute of Child Health and Human Development (NICHD)
- National Institute of Mental Health (NIMH)
- National Cancer Institute (NCI)
- National Institute on Drug Abuse (NIDA)
- National Institute of Dental and Craniofacial Research (NIDCR)
- Office of AIDS Research (OAR)

## Notes

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## Who Are Other Network and NIAID Partners?

NIAID alone cannot manage all of the complex issues associated with HIV/AIDS treatment and prevention research. NIAID also partners with the Centers for Disease Control and Prevention (CDC) and other organizations to address the complex global research needs, including:

- The Bill & Melinda Gates Foundation works to stop the spread of HIV by expanding access to successful prevention strategies. It also identifies and researches new ways to prevent HIV transmission.
- The International AIDS Vaccine Initiative (IAVI) works to ensure the development of safe, effective, accessible, preventive HIV vaccines.
- The Center for HIV/AIDS Vaccine Immunology (CHAVI) works to solve major problems in HIV vaccine development and design.
- William J. Clinton Foundation works with governments and other partners to increase the availability of high-quality AIDS care and treatment for people in need, lower the cost of essential tests and treatments, and strengthen health systems in the developing world.
- The Global Fund to Fight AIDS, Tuberculosis and Malaria is an international financing institution that invests the world's money to save lives. To date, it has committed US\$ 15.6 billion in 140 countries to support large-scale prevention, treatment and care programs against the three diseases.
- The Joint United Nations Programme on HIV/AIDS (UNAIDS), through a series of goals, resolutions and declarations adopted by member nations of the United Nations, has a set of commitments, actions and goals to stop and reverse the spread of HIV and scale up towards universal access to HIV prevention, treatment, care and support services.

It is the hope of the community and DAIDS that all of the networks collaborate and share their studies and resources to build the best and most productive HIV/AIDS clinical trial science in the world.

### Notes

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## CONCLUSION

In this workshop, we:

- Described clinical research
- Described the clinical research process
- Described the principles of clinical research
- Defined ethics
- Described the role of a Community Advisory Board (CAB) in the research process
- Listed key partnerships
- Discussed issues affecting AIDS research for various stakeholders
- Applied the information you learn in activities and discussions
- Asked questions about information you do not understand
- Practiced what you learn

On the next page, you will find the Workshop Evaluation. Please complete this evaluation to provide feedback to your instructor. Your comments are important to us, so please answer all questions.

Thank you for your participation in this workshop.

*This project has been funded in whole with a grant from the United States Government Department of Health and Human Services, National Institutes of Health, National Institute of Allergy and Infectious Diseases (U01 AIO68614).*





## Workshop Evaluation

Name \_\_\_\_\_ Date \_\_\_\_\_

**Directions:** Please check the box that best represents your opinion.

### Program Content

	Strongly Agree	Agree	Disagree	Strongly Disagree
1. I understood the workshop objectives.				
2. The content provided me with new information.				
3. The activities and discussions helped me understand the content.				

### Instructional Materials

4. The instructional materials were logically sequenced.				
5. The course materials will be useful on the job.				

### Instructional Presentation

6. The pace of the course was appropriate.				
7. The time given to complete activities was appropriate.				

### General Evaluation

8. The knowledge and skills gained will help me.				
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Please explain any ratings of "Disagree" or "Strongly Disagree"

What information was most valuable to you?

What information was least valuable to you?

Comments



## GLOSSARY

### A

**ACTG** AIDS Clinical Trial Group

**Acquired Immunodeficiency Syndrome** AIDS

**Adverse reaction** Harm associated with the use of medication at a normal dose.

**AIDS** Acquired Immunodeficiency Syndrome. The late stage of HIV disease, characterized by a deterioration of the immune system and a susceptibility to a range of opportunistic infections and cancers.

**AIDS Clinical Trial Group** See ACTG

**Antibodies** Found in blood or other bodily fluids. Used by the immune system to identify and neutralize foreign objects, such as bacteria and viruses.

**Anti-Retroviral drugs** ARV

**ARV** Anti-retroviral drugs

### B

**Beneficence** To do good. In clinical research, means to do no harm, or maximize possible benefits and minimize possible harm.

**Blinded or blinding** A method used in a clinical trial to prevent participants and/or researchers from knowing whether the patient is receiving the experimental or control treatment in a trial. Also referred to as "masking." Single blinding is when only the patient does not know which treatment he or she is receiving.

**Blinded study** A clinical trial in which participants are unaware whether they are in the experimental or control arm.

### C

**CAB** Community Advisory Board

**CBO** Community Based Organization

**CDC** Centers for Disease Control and Prevention

**Centers for Disease Control and Prevention** CDC



**Center for HIV/AIDS Vaccine Immunology** Works to solve major problems in HIV vaccine development and design.

**CHAVI** Center for HIV/AIDS Vaccine Immunology

**Chronic illness** An illness that is long lasting.

**Clinical research site** CRS

**Clinical trial** A research study that tests how well an intervention works in a group people. It tests for new methods of screening, prevention, diagnosis, or therapy.

**Cohort** Groups of individuals who share one or more characteristics in a research study and who are followed over time. For example, a vaccine trial might include two cohorts, a group at low risk for HIV and a group at higher risk.

**Community Advisory Board** CAB

**Community Based Organization** CBO

**Community Partners** CP

**Consent** A patient's oral and written agreement to participate in a clinical trial. Consent is based on full disclosure about the treatment, its potential risks and benefits, alternative treatments, and any other information the patient needs to make the decision. Patients enrolling in clinical trials must sign a consent form that explains what will happen in the trial.

**Contract Research Organization** CRO

**Control** An inactive substance (also known as a placebo) sometimes given to trial participants. In a vaccine trial, the control group is compared with one or more groups of volunteers given experimental vaccines.

**Control group** In a clinical trial, the patient group(s) that does not receive the experimental treatment. The control group receives the standard treatment, placebo, or no treatment in accordance with the trial design, and the results of the control group(s) are compared to the results from the experimental group.

**Controlled trial** A prospective clinical trial comparing two or more treatments, or placebo and treatment(s) in similar groups of patients or within patients. A controlled trial may or may not use randomization to assign patients to groups, and it may or may not use blinding to prevent them from knowing which treatment they get.

**CP** Community Partners

**CRO** Contract Research Organization

**CRS** Clinical Research Site



## D

**DAIDS** Division of Acquired Immunodeficiency Syndrome

**Data and Safety Monitoring Board DSMB**

**Double-blind study** A clinical trial in which neither the study staff nor the participants know which participants are receiving the experimental vaccine and which are receiving placebo. Double-blind studies are thought to produce the most objective results.

**DSMB** Data and Safety Monitoring Board.

## E

**EC** Ethics Committee

**Effectiveness** The degree to which a test or treatment produces a desired result in patients in the daily practice of medicine.

**Efficacy** The degree to which a diagnostic test or treatment produces a desired result in patients under the idealized circumstances of a clinical trial.

**Endpoint** The final results of an intervention, such as vaccination, compared among different groups in a clinical trial. In early vaccine trials, common endpoints are safety and specific types and levels of immune responses.

**Entry criteria** Definition of a target population that is appropriate to the research question. An accessible population that is practical to study.

**Ethics** Respect for persons, beneficence, and justice.

**Ethics Committee** EC

**Exclusion criteria** See Inclusion/exclusion criteria.

**Experimental** Investigational, unproven.

**Experimental treatment group** The group that receives the investigational treatment in a trial. The group to which the control group results are compared.

## F

**FDA** Food and Drug Administration

**Food and Drug Administration** FDA

**Funder** The organization that provides the money to conduct research.



## **G**

**GCLP** Good Clinical Laboratory Practice

**GCP** Good Clinical Practice

**Good Clinical Laboratory Practice GCLP**

**Good Clinical Practice GCP**

## **H**

**HANC** HIV/AIDS Network Coordination

**HIV** Human Immunodeficiency Virus

**HIV/AIDS Network Coordination HANC**

**HIV Vaccine Trials Network HVTN**

**Host-virus interaction** How the body interacts when a virus is present.

**HPTN** HIV Prevention Trials Network

**Human Immunodeficiency Virus HIV**

**HVTN** HIV Vaccine Trials Network

## **I**

**IAVI** International AIDS Vaccine Initiative

**Immune Deficiency** A breakdown or inability of certain parts of the immune system to function, which makes people susceptible to diseases they would not ordinarily develop.

**Immunity** Natural or vaccine-induced resistance to a specific disease. Immunity may be partial or complete, specific or nonspecific, long-lasting or temporary.

**Immunization** The process of inducing immunity by administering a vaccine, thereby "teaching" the immune system to recognize certain antigen(s) and thus prevent infection or illness when it subsequently encounters the infectious agent.

**IMPAACT** International Maternal Pediatric Adolescent AIDS Clinical Trials Group

**Inclusion/exclusion criteria** The medical or social reasons detailing the grounds by which a person qualifies for participation in a clinical trial. For example, some trials may exclude people with chronic liver disease or certain drug allergies.



**IND** Investigational New Drug Application

**Informed Consent** An agreement signed by all volunteers participating in a clinical research study, indicating their understanding of: (1) why the research is being done; (2) what researchers hope to learn; (3) what will be done during the trial and for how long; (4) what risks are involved; (5) what, if any, benefits can be expected from the trial; (6) what other interventions are available; and (7) the participants' right to leave the trial at any time.

**Immune system** A biological process that protects against disease. It detects and distinguishes harmful viruses from healthy cells and tissues in order to function properly.

**Immunomodulatory therapy** A method to treat disease by modulating an immune response.

**Inclusion criteria** The factors used to judge a participant's eligibility for inclusion in a trial. There is an underlying rationale for the criteria selected. The rationale relates to the questions that the researchers are trying to answer by conducting the trial.

**INSIGHT** International Network for Strategic Initiatives in Global HIV Trials

**Institutional Review Board** IRB

**International AIDS Vaccine Initiative** IAVI

**International Maternal Pediatric Adolescent AIDS Clinical Trials Group** IMPAACT

**Intervention study** Subjects are selected from one population with a particular characteristic present. Then the total study group is divided into two groups: one group receives the intervention and one group does not (the control group). The comparison of the outcomes of the two groups at the end of the study period is an evaluation of the intervention.

**Investigational** Experimental, unproven.

**Investigational New Drug** IND

**IRB** Institutional Review Board

## **J**

**Justice** There are more benefits for the participant than risks. Participants are fairly recruited as research participants.

## **L**

**Lab values** Measurements of cellular and clinical components of the body. The values from the measurements are based on averages of a survey of presumably healthy people. The concept of individual normal values is based on an acceptable response compared with known evidence of a disease.



## **M**

**MDG** Millennium Development Goals

**Microbicide** A compound or substance used to reduce the infectivity of viruses.

**Microbicide Trials Network** MTN

**Millennium Development Goals** MDG

**Monitoring Activities** To check patients' health status during a trial. Activities to oversee the progress of a trial to ensure a researcher's compliance with the protocol and regulatory requirements.

**MTN** Microbicide Trials Network

## **N**

**National Cancer Institute** NCI

**National Institute of Allergy and Infectious Diseases** NIAID

**National Institute of Child Health and Human Development** NICHD

**National Institute of Dental and Craniofacial Research** NIDCR

**National Institute of Mental Health** NIMH

**National Institute on Drug Abuse** NIDA

**National Institutes of Health** NIH

**NCI** National Cancer Institute

**New drug application (NDA)** An application made to FDA that requests a license to market a new pharmaceutical in the United States. The application must include all appropriate clinical data from phase I through phase III clinical trials.

**NGO** Non-government organization

**NIAID** National Institute of Allergy and Infectious Diseases

**NICHD** National Institute of Child Health and Human Development

**NIDA** National Institute on Drug Abuse

**NIDCR** National Institute of Dental and Craniofacial Research



**NIH** National Institutes of Health

**NIMH** National Institute of Mental Health

**Non-government organization** NGO

**Nuremberg Code** A code of human research ethics devised in 1947 after World War II. This code forms the foundation for current law and ethics on consent.

## O

**OAR** Office of AIDS Research

**Office of AIDS Research** OAR

**Outcome** - The ultimate result of a medical test or treatment given to a patient. General, patient-oriented outcomes are overall survival rates, disease-free survival rates, treatment-related morbidity, and mortality.

## P

**Patient characteristic** The medical (for example, disease, stage of disease, hormone receptor status, prior treatments) or demographic (for example, age, gender, marital status, race) qualities or traits of a patient.

**Patient volunteer** A volunteer subject who participates in research to test a new drug, device, or intervention.

**Phase I** A Phase I vaccine trial is a clinical trial with a small number (usually 60 or less) of healthy volunteers, typically at low-risk for HIV infection. Phase I trials test a vaccine's safety in humans, including its metabolic and pharmacologic actions and any side effects seen with increasing doses.

**Phase II** A Phase II vaccine trial is a controlled clinical study to identify common short-term side effects and risks associated with the test vaccine and to collect expanded information on its immunogenicity. Phase II trials enroll some volunteers with characteristics similar to potential participants of an efficacy (Phase III) trial. They enroll up to several hundred participants and generally have two or more arms.

**Phase III** A Phase III vaccine trial is a large controlled study to determine the ability of a vaccine to produce a desired clinical effect on the risk of a given infection, disease, or other clinical condition at an optimally selected dose and schedule. These trials also gather additional information about safety needed to evaluate the overall benefit-risk relationship of the vaccine. Phase III trials usually include several hundred to several thousand volunteers.

**Placebo** An inactive substance given to some study participants, while others receive the test substance (for example, a vaccine). Placebos provide a basis for comparison.





**Prospective study** Participants enroll in the study and then started on a treatment. From the first visit, data are collected going forward.

**Protocol** The detailed plan for a clinical trial, outlining its rationale, purpose, methodologies (such as vaccine dosages, routes of administration, length of study, eligibility criteria) and other aspects of trial design.

## R

**Randomized Trial** A study in which participants are assigned by chance to one of two or more arms of the trial. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms.

**Recruitment** Processes used to find, attract, and enroll trial participants according to eligibility criteria.

**Regulations** With respect to clinical research, the federal statutes, codes, and laws that govern the conduct of federally funded clinical trials and privately sponsored clinical trials for new drugs, devices, biologics, and procedures.

**Research team** In clinical trials, the group of healthcare professionals who conduct the trial. It typically includes a principal investigator and a clinical research coordinator.

**Respect for persons** People have a right to make their own choices. All the facts about the research are presented to potential participants. Volunteers must not be pressured to choose research over other options for care. The community where research is being conducted is respected. The community has a voice in what is done during the research.

**Results** Analysis of the data collected during a trial.

**Retrospective study** Participants already taking a specific treatment are enrolled. The researcher then reviews the medical record of each participant, checks the type of treatment received, and records information from the point of enrollment and looking backward *before* enrollment.

**Risk** In a clinical trial, the probability of discomfort or harm to participants.



## S

**Side effect** Undesired effect of a treatment. Investigational new drugs and devices are evaluated for immediate and long-term side effects.

**Single-blind study** A term used to describe a study in which either the investigator or the participant, but not both of them, is unaware of the nature of the treatment the participant is receiving. Also called single-masked.

**Sponsor** An individual, company, institution, or organization that initiates, manages, and/or finances a clinical trial.

**Standard of care** Treatment that experts agree is appropriate, accepted, and widely used. Health care providers are obligated to provide patients with the standard of care.

**Standard treatment** The treatment that is currently thought to be effective.

## U

**UNAIDS** United Nations Programme on HIV/AIDS

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## V

**Vaccine** A mixture that is given to help stimulate the body's own immune system to produce antibodies to fight a certain disease. The mixture contains weakened or killed microbes (bacteria or viruses) or microbe parts. It is the antibodies and other immune responses that are created in response to the vaccine that protect against a future infection by the target disease.

**Virus** A microorganism composed of a piece of genetic material surrounded by a protein coat. To replicate, a virus must infect a cell and direct its cellular machinery to produce new viruses.

**Voluntary** Free of coercion, duress, or undue inducement. In a clinical trial, voluntary refers to a participant's decision to enroll.



## ENDNOTES

- <sup>1</sup>[http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008\\_Global\\_report.asp](http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp)
- <sup>2</sup> [http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008\\_Global\\_report.asp](http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp)
- <sup>3</sup> <http://www.unaids.org/en/KnowledgeCentre/HIVData/EpiUpdate/EpiUpdArchive/2007>
- <sup>4</sup> [http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008\\_Global\\_report.asp](http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp)
- <sup>5</sup> IAVI Insights, Policy Brief #17, September 2008
- <sup>6</sup> [http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008\\_Global\\_report.asp](http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp)
- <sup>7</sup> [http://www.unicef.org/nutrition/index\\_24808.html](http://www.unicef.org/nutrition/index_24808.html)
- <sup>8</sup> IAVI Insights, Policy Brief #17, September 2008
- <sup>9</sup> <http://www.aidsmap.com/en/news/2371742D-B68C-48AC-8E23-2449F2AD5B56.asp>
- <sup>10</sup> IAVI Insights, Policy Brief #17, September 2008
- <sup>11</sup> [http://www.genzyme.com/research/clinical\\_trials/trialprocess.asp](http://www.genzyme.com/research/clinical_trials/trialprocess.asp)
- <sup>12</sup> [http://www.genzyme.com/research/clinical\\_trials/trialprocess.asp](http://www.genzyme.com/research/clinical_trials/trialprocess.asp)
- <sup>13</sup> [http://www.genzyme.com/research/clinical\\_trials/trialprocess.asp](http://www.genzyme.com/research/clinical_trials/trialprocess.asp)
- <sup>14</sup> <http://www.fda.gov/oashi/fast.html>
- <sup>15</sup> <http://ohsr.od.nih.gov/guidelines/nuremberg.html>
- <sup>16</sup> <http://www.tuskegee.edu/global/story.asp?s=1207598>
- <sup>17</sup> <http://ohsr.od.nih.gov/guidelines/belmont.html>
- <sup>18</sup> [http://www.communityconsortium.org/about/about\\_history.html](http://www.communityconsortium.org/about/about_history.html)
- <sup>19</sup> Map from the HANC Community Partners website.
- <sup>20</sup> <http://www.hanc.info/Pages/index.aspx>
- <sup>21</sup> [www.nih.gov/about/organization.htm](http://www.nih.gov/about/organization.htm)