

There is no Participant Guide page for this slide.

Welcome participants to the course. Tell participants to sit down anywhere they will be comfortable. Thank participants for coming to the workshop, if appropriate. Remind participants that the course will be more interesting and fun if they ask questions and share their experiences.


Tell participants to write their names on the Participant Guides. These Participant Guides are for them to keep and write notes in.

Explain that the Participant Guide contains a lot of information. Go through the Table of Contents to show participants what the course is about. Then show participants the Glossary at the end of the Participant Guide.

After everyone is settled, introduce a whole group activity (approximately 5 minutes): Introductions. Go around the room and ask each person to stand up and state his/her name, what they do, and why he/she is taking this workshop. Begin the introductions to provide an example. Feel free to use your own introductions activity (“ice breaker”), if desired.

This module will last approximately 50 minutes.

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).

A graphic on the left side of the slide features a stylized globe showing the Americas, set against a background of vertical blue and light blue bars. The globe is positioned at the top of a light blue bar, which is flanked by two darker blue vertical bars. Below the globe, there are some abstract blue shapes.

Introduction

This workshop will help those who work to find new AIDS:

- Prevention technologies
- Improved treatment regimens
- A vaccine
- A cure

In this workshop, you will:

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


Understanding the Clinical Research Process and Principles of Clinical Research, v1.0 2

Participant Guide, page 1

The Introduction should take approximately 50 minutes.

Review the content in the Participant Guide.

Tell participants they will see a lot of abbreviations in this course. The first time an abbreviation is used, there will be an explanation of what it stands for. The abbreviations are also included in the Glossary.



Agenda


- Morning:
 - Introduction
 - Clinical Research
 - Break
 - Clinical Research Process
- Lunch
- Afternoon:
 - Elements and Principles of Clinical Research
 - Break
 - Community Advisory Boards and the Research Process
 - Key Partnerships
 - Conclusion

Understanding the Clinical Research Process and Principles of Clinical Research 3

There is no Participant Guide page for this slide.

Review the agenda for the workshop. Be prepared to change this slide if the workshop is given with a different time structure.

Review the logistics of breaks and lunch, depending on the location.



Housekeeping

Instructions for:

- Fire drills
- Rest rooms/comfort rooms
- Messages
- Breaks and lunch
- Smoking


Remember to:

- Ask questions
- Share what you know
- Participate in all activities
- Have fun!

Understanding the Clinical Research Process and Principles of Clinical Research 4

There is no Participant Guide page for this slide.

Review housekeeping for the workshop. Be prepared to change this slide if the workshop location has specific housekeeping issues.



What Is AIDS?

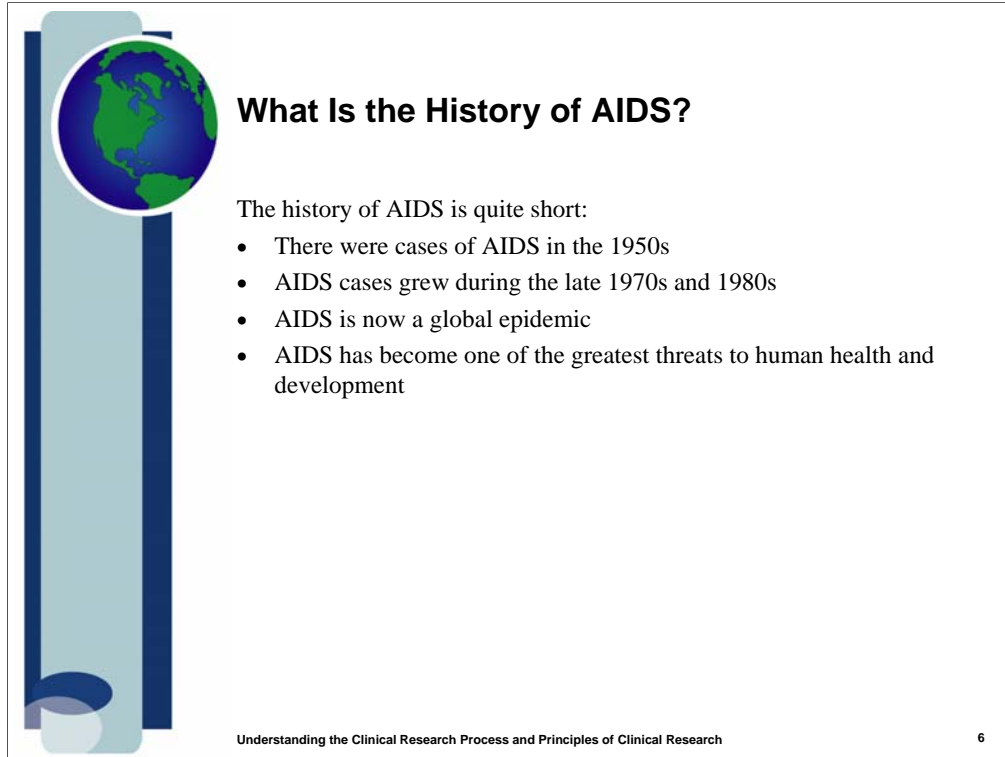
- AIDS stands for “acquired immune deficiency syndrome”
- It is caused by a virus called HIV (Human Immunodeficiency Virus)
- A person who is infected with the HIV virus develops antibodies to fight the infection—someone with the antibodies in their blood is called “HIV” positive
- HIV disease becomes AIDS when a person’s immune system is highly compromised by the effects of the virus

Understanding the Clinical Research Process and Principles of Clinical Research 5

Participant Guide, page 1

Review the content in the Participant Guide and on the slide.

Allow for questions and discussion.



What Is the History of AIDS?

The history of AIDS is quite short:

- There were cases of AIDS in the 1950s
- AIDS cases grew during the late 1970s and 1980s
- AIDS is now a global epidemic
- AIDS has become one of the greatest threats to human health and development

Understanding the Clinical Research Process and Principles of Clinical Research 6

Participant Guide, page 2

Review the content in the Participant Guide and on the slide.

Allow for questions and discussion.



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
 - Cure HIV infection

Participant Guide, page 2

Review the content in the Participant Guide and on the slide.

Depending on the experience level of participants, review the content in the table.



How Serious Is AIDS?

- At the end of 2007, approximately 33 million people were living with HIV
- Approximately 2.7 million more people become infected with HIV every year
- Approximately 2 million people die of AIDS every year
- HIV is spreading most rapidly in Eastern Europe and Central Asia
- Approximately 400,000 children under age 13 become newly infected with HIV each year
- Without treatment, half of HIV infected infants will die before the age of two



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 needed HIV/AIDS research.



What Are the Millennium Development Goals (MDGs)?

The United Nations identified an action agenda for this millennium: eight millennium development goals.

One of the eight MDGs focuses on HIV/AIDS.

The HIV/AIDS millennium development goal calls on the world community to halt and begin to reverse the spread of HIV by 2015.



What Will We Do in This Workshop?

We will look at many important areas about AIDS research. We will learn important information and ask questions. We will also do activities 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 the Community Advisory Board (CAB) in the research process
- List key partnerships
- Discuss issues affecting AIDS research for various stakeholders

What Do You Know?

Answer 10 questions about clinical research.

Understanding the Clinical Research Process and Principles of Clinical Research

12

There is no Participant Guide page for this slide.

This activity functions as a pre-test to find out how much participants already know about the information presented in this workshop.

Avoid mentioning the word “test” so participants do not become stressed. This activity should be a low-key method of getting to know the participants, what each is capable of, and find out how much they know in a non-threatening way.

See the Instructor Guide for various options to deliver this activity. It can be delivered by using a handout or reading aloud the questions and asking for participant’s to provide the answers.

As specific questions are covered in the workshop materials, there will be a reminder inserted in these notes to remind participants of the questions and answers. This technique helps participants remember answers for the post-test at the end of the workshop.

Answers to the questions are:

1a, 2a, 3c, 4b, 5g, 6a, 7a, 8a, 9e, 10c



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

Participant Guide, page 6

This module will last approximately 50 minutes.



What Is Clinical Research?

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.

Participant Guide, page 6

Note: Depending on the level of knowledge of the workshop participants, a discussion of cohort studies (as prospective clinical trials) vs. clinical trials can be discussed.

Allow for questions and discussion.



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.

Participant Guide, page 6

Note: Emphasize the text in italic on the slide: "...trials cannot be conducted if the outcome is already known from a previous study."

Allow for questions and discussion.



Why Is Research Important?

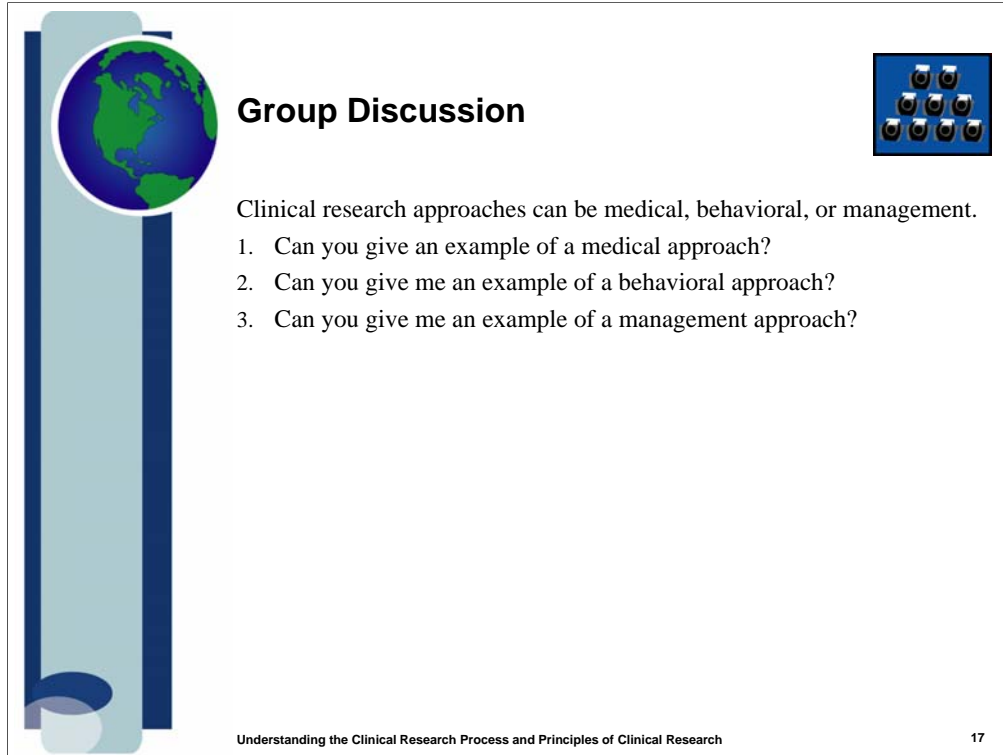
Research is important because:

- 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.

Participant Guide, page 7

Allow for questions and discussion.



Group Discussion

Clinical research approaches can be medical, behavioral, or management.

1. Can you give an example of a medical approach?
2. Can you give me an example of a behavioral approach?
3. Can you give me an example of a management approach?

Understanding the Clinical Research Process and Principles of Clinical Research 17

There is no Participant Guide page for this slide.


See the instructions in the Instructor's Guide for leading whole group discussions.

Read the first question on the slide. Allow time for participants to think about some examples.

Because this is the first discussion in the workshop, participants may be reluctant to speak up for fear of saying the wrong thing. Be prepared to provide an answer to the first question yourself.

Possible answers for these questions:

1. Medical approach: vaccine
2. Behavioral approach: education program with adolescents to use condoms during intercourse
3. Management approach: population-based surveillance of HIV-related risk behaviors



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.

Understanding the Clinical Research Process and Principles of Clinical Research 18

Participant Guide, page 7

Be sure to discuss the Good Clinical Practice (GCP) stand and the good clinical laboratory practice standards. Emphasize the importance of the same, thorough requirements throughout the world. These standards and guidelines protect people.

Allow for questions and discussion.



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

- 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

Participant Guide, page 8

Allow for questions and discussion.

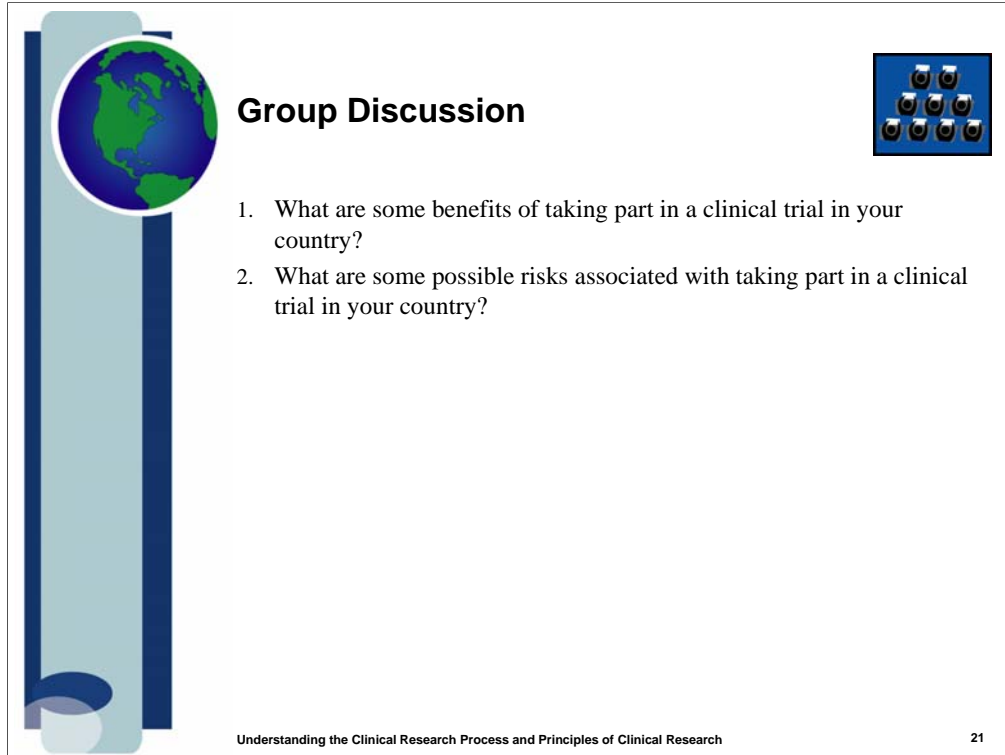


What Are Some of the Possible Risks Associated with Taking Part in a Clinical Trial?

- 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

Participant Guide, page 8

Allow for questions and discussion.



Group Discussion

1. What are some benefits of taking part in a clinical trial in your country?
2. What are some possible risks associated with taking part in a clinical trial in your country?

Understanding the Clinical Research Process and Principles of Clinical Research 21

There is no Participant Guide page for this slide.

Please review the section of the Instructor's Guide about leading "Small Group Activities."


Answers to these questions will vary considerably among different locations. For these questions, look for location-specific answers.

If possible, research the activities in the location where this workshop is being delivered to have some answers available.


Provide an example, if necessary, to get participants started. Examples for the questions are:

1. A 25-year-old University of Botswana student, is participating with BOTUSA in the TDF2 Trial. Benefits for him are free medications, a free check-up, health advice from a doctor once a month, and free transportation to his appointments.

2. Possible side effects of experimental vaccines could include fever, chills, rash, aches and pains, nausea, headache, dizziness, and fatigue. Injections can cause pain, soreness, redness, and swelling on the part of the body where the vaccine shot is given.



Clinical Research Activity



With your group:

- Review the case study you are given
- Read the two questions
- Review the benefits and risks of taking part in a clinical trial page in your Participant Guide
- Brainstorm some possible benefits for the person in the case study
- Brainstorm some possible risks for the person in the case study
- Share your group's ideas with the class (be sure to describe the person in your case study)

Understanding the Clinical Research Process and Principles of Clinical Research 22

There is no Participant Guide page for this slide.

Please review the section of the Instructor's Guide about leading "Small Group Activities."

Distribute the case study handouts for this activity: Clinical Research Activity. Each person in a group should receive a copy. Remember that there are four different case studies.


Note: Most small groups will have similar answers for this activity. The main purpose of the activity is to build confidence to work together and share experiences. Be prepared to offer specific examples and ask open questions to encourage independent thinking.

Before going to the next section of this workshop, stop to:

-Review what was learned in this section (there is no PowerPoint slide for this review)

-Ask for questions and allow for questions

-Write any "parking lot" issues or information you need to come back to on a blank flip chart (a parking lot is where we capture all questions we may not necessarily have an answer during the workshop. Write these questions on a flip chart and follow up with the participants. Parking lot items are also good reminders for instructors to consider including in future workshops.



CLINICAL RESEARCH PROCESS

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

Understanding the Clinical Research Process and Principles of Clinical Research 23

Participant Guide, page 9

This module will last approximately 65 minutes.



What Is the Clinical Research Process?

- 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?

Pre-clinical testing is required before testing humans. 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

If a vaccine, microbicide, or other strategy has a potential benefit, it is prepared for human testing. Pre-clinical testing takes approximately three to four years.

Participant Guide, page 9

Allow for questions and discussion.



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.

Participant Guide, page 10

Allow for questions and discussion.



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.

Participant Guide, page 10

Allow for questions and discussion.



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

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.

Participant Guide, page 11

Allow for questions and discussion.



What Is Phase III (Large-Scale Testing)?


This large-scale testing (1,000-3,000 participants/volunteers) 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. After a phase III study is successfully completed, a company can request marketing approval from the FDA.

Participant Guide, page 11

Allow for questions and discussion.



Group Discussion



1. During Phase I of a clinical trials, why do you think only HIV-negative volunteers can participate in the trial?
2. What are the potential risks of taking part in a Phase I clinical trial?
3. What are the potential risks of taking part in a Phase II trial?

Understanding the Clinical Research Process and Principles of Clinical Research

30

There is no Participant Guide page for this slide.

Possible answers for these questions:

1. HIV-negative participants provide a more-accurate picture of how safe the vaccine, microbicide, or other strategy is and what side effects occur at specific dosage levels.
2. Some risks might be: 1) the severity of the side effects that might occur; 2) the potential for a participant to become HIV-positive during the trial (not as a result of the trial/treatment), which may impact responses to the dosage/treatment.
3. One important risk might be that the control group receiving the placebo may delay treatment options, if needed.



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.

Participant Guide, page 11

Allow for questions and discussion.



What Is Approval (Available for Prescription)?

Health care providers are able to prescribe. Even after approval, reviews continue to ensure safety over time. For example, all cases of adverse events must be reported, and quality control standards must be met (sometimes studies to evaluate long-term effects are also required).

The accelerated approval process for serious diseases is designed to:

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

Accelerated approval can occur if a treatment will have an impact on survival, day-to-day functioning, and likelihood that a disease, if left untreated, will progress from a less severe condition to a more serious one.

Accelerated approval does not compromise the standards for the safety and effectiveness of the treatments that become available through this process.

Participant Guide, page 12

Note: Be sure to mention Kaletra during the discussion of this slide because a discussion question at the end of this section refers to Kaletra. Kaletra for the treatment of HIV/AIDS was reviewed and approved in 3.5 months (a very quick approval) in September 2000.

Allow for questions and discussion.



What Are Post-Marketing Studies?

Post-marketing studies (special studies and long-term effectiveness/use) are also called phase IV studies. 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.

Participant Guide, page 12

Allow for questions and discussion.

Group Discussion


1. A New Drug Applications/Biologics License Application is filed with the Food and Drug Administration (FDA). The FDA is an organization in the United States. Why do you think FDA approval is important for licensing in other countries?
2. Kaletra was reviewed and approved in 3.5 months (a very quick approval) in September 2000. How much do you know about the impact of early approval of Kaletra?

Understanding the Clinical Research Process and Principles of Clinical Research 34


There is no Participant Guide page for this slide.

Possible answers for these questions:

1. THE FDA maintains high standards for safety and effectiveness. The FDA evaluates products developed outside the United States and assures that the quality of non-U.S. products meets the same standards as U.S. products. Products not approved by the FDA may be substandard. Substandard products might not be effective and might worsen the situation by stimulating the development of drug-resistant strains of the virus that causes HIV/AIDS.
2. Early approval of Kaletra provided treatment to more people much more quickly. Some features of Kaletra make it important for a variety of reasons: 1) Kaletra can be taken with or without food; 2) refrigeration is not necessary, which is important in some countries; 3) children between ages 6 months and 12 years can take it and a liquid formulation is available for babies and children who can't swallow pills; 4) Kaletra is listed as a recommended treatment in the federal guidelines on treating HIV-positive pregnant women.



Clinical Research Process Activity



With your group:

- Review the additional information about your case study
- Review your Participant Guide and the Glossary in your Participant Guide to find definitions to the words assigned to you
- Select one of the assigned words
- Practice explaining the word to the person in your case study
- Demonstrate to the class how you would explain the word (be sure any new information about the person in your case study)

Understanding the Clinical Research Process and Principles of Clinical Research 35

There is no Participant Guide page for this slide. See the instructions for conducting small group activities in the Instructor's Guide. Distribute the case study handouts for this activity: Clinical Research Process Activity. Each person in a group should receive a copy, and each group should get the same person's case study. Allow each table group to select the person who will pretend to be the case study person(s) and doctor. Before asking participants to demonstrate (role play) the person and doctor, provide an example. If possible, ask one of the non-participants in the room to help you. Select a glossary item (for example, "HIV" or "AIDS"). Take the role of doctor/clinic person, and explain (in simple terms) what the word is that you selected. Practice the role play with the non-participant while the table groups are working. At the end of the role play, be sure to say "Do you have any question?" to model the correct role play techniques for the participant role plays. Encourage thoughtful questions and responses. Debrief notes after a group has role played the situation in front of the class:

1. Encourage the workshop participants to ask questions about the word and definition after seeing the role play
2. Encourage participants to ask for examples (be prepared to provide examples, if needed)
3. Summarize the activity by reminding participants how:
 - a. Difficult it is to describe difficult subjects and words in simple terms
 - b. Important it is to make sure people understand what is explained to them
 - c. Difficult it is for some people to communicate they might not understand what is being said

Before going to the next section of this workshop, stop to:

-Review what was learned in this section (there is no PowerPoint slide for this review)

-Ask for questions and allow for questions

-Write any "parking lot" issues or information you need to come back to on a blank flip chart

Break for lunch.




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

Participant Guide, page 13

This module will last approximately 130 minutes.



What Are the Elements and Principles of Clinical Research?

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

Understanding the Clinical Research Process and Principles of Clinical Research

37

Participant Guide, page 13

Briefly review the items in the list. Each of the items will be covered in depth shortly.



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.

Participant Guide, page 14

Allow for questions and discussion.



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 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.

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.

Participant Guide, page 14

Allow for questions and discussion.



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 hospitals, universities, doctors' offices, or community clinics.

Participant Guide, page 15

Allow for questions and discussion.



What Are Eligibility Criteria?

Eligibility criteria are guidelines that describe characteristics that must be minimally shared by all participants. The criteria differ from study to study. Criteria include:

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

Eligibility criteria 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.

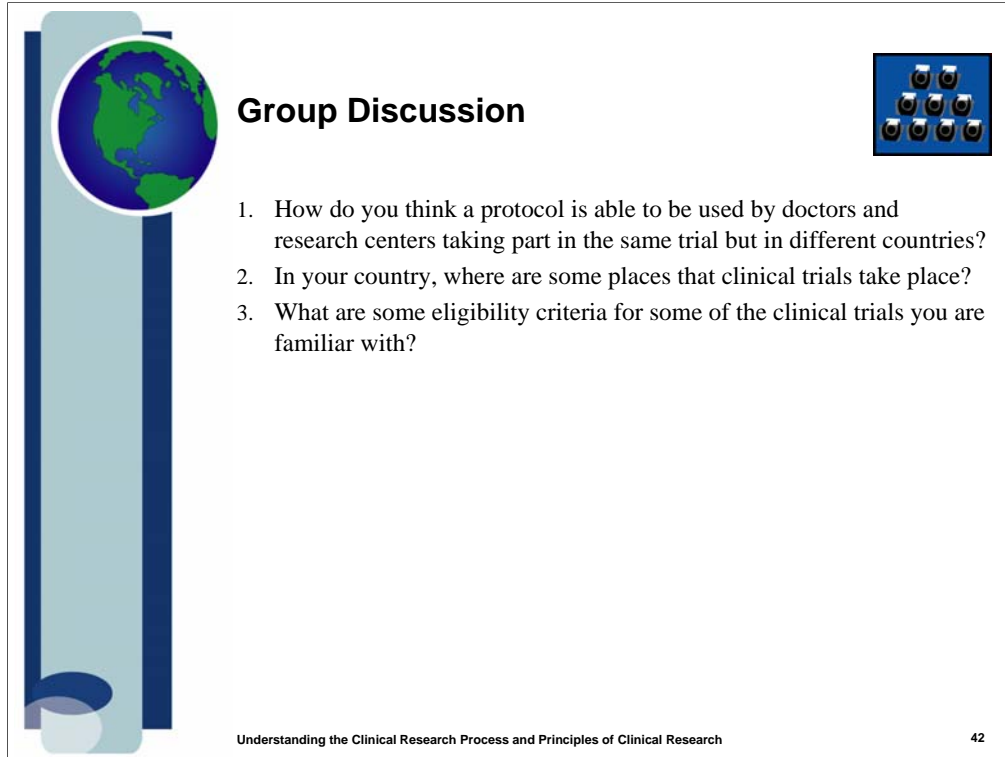
Enrolling participants with similar characteristics helps to ensure that the results of the trial will be a result of what is under study and not other factors. In this way, eligibility criteria help researchers achieve accurate and meaningful results. These criteria also minimize the risk of a person's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

Understanding the Clinical Research Process and Principles of Clinical Research

41

Participant Guide, page 16

Allow for questions and discussion.



Group Discussion

1. How do you think a protocol is able to be used by doctors and research centers taking part in the same trial but in different countries?
2. In your country, where are some places that clinical trials take place?
3. What are some eligibility criteria for some of the clinical trials you are familiar with?

Understanding the Clinical Research Process and Principles of Clinical Research 42

There is no Participant Guide page for this slide.

Possible answers for these questions:

1. A protocol defined the process for systematic collection, description, analysis and interpretation of data. Key attributes of good research are proper planning, accuracy in data collection, and proper unbiased interpretation. A principal investigator works with the members of the research team to make sure the study is administered consistently in all its locations.
2. Possible answers may include: doctor's office, clinic, and hospitals. There may be others, depending on the location of the workshop.
3. Answers should include age, gender, medical history, current health status, and lab values. There may be others.



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. 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 (translation or interpretive assistance can be provided)
- At an appropriate educational level

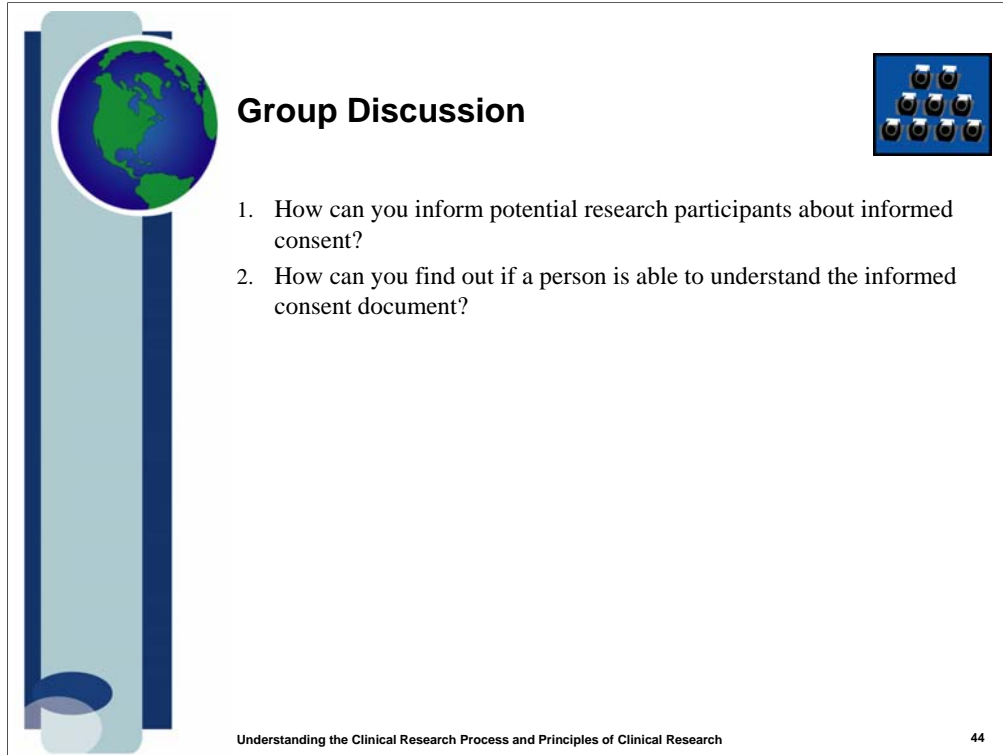
An informed consent document includes details about the study, including its purpose, duration, required procedures, who to contact for more information, and an explanation of risks and potential benefits. The participant then decides whether to sign the document.

Participant Guide, page 17

Instructor note: 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).

Allow for questions and discussion.



Group Discussion


1. How can you inform potential research participants about informed consent?
2. How can you find out if a person is able to understand the informed consent document?

Understanding the Clinical Research Process and Principles of Clinical Research 44

There is no Participant Guide page for this slide.

Possible answers might include:

1. Answers will vary based on the workshop participant's experience. Encourage discussion about making sure that potential research participants actually have an opportunity to hear about what their rights are.
2. Answers will vary, but should include: ability to read; ability to see; ability to speak; ability to hear; ability to read the consent document before signing; ability to answer questions with more than a "yes" or "no."
3. There is an optional third question for this discussion. Use your discretion about asking this question, depending on the makeup of the workshop participants, other observers who might be in the room, and available time for what might turn out to be a lengthy discussion. The optional third question is: "What would you do if you found that informed consent was not practiced in your community?"



What Are Some Types of Clinical Trials?

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.

Understanding the Clinical Research Process and Principles of Clinical Research 45

Participant Guide, page 18

Review the examples in the Participant Guide:

- 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.

Allow for questions and discussion.



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. Important terms used in clinical trials are:

- Placebo
- Randomization
- Single- and double-blind studies

Participant Guide, page 19

Note: There is a lot of very important content in the Participant Guide that does not appear on the slide. Be sure to direct participants to this page of the Participant Guide and review the page with them.

Allow for questions and discussion.



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.

Participant Guide, page 20

Note: There is a lot of very important content in the Participant Guide that does not appear on the slide. Be sure to direct participants to this page of the Participant Guide and review the following information with them:

- Definition of patient volunteer
- Definition of control
- The last paragraph about consent

Allow for questions and discussion.



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


Participant Guide, page 21

Note: Be sure to review the last paragraph and bullet points in the Participant Guide.

Allow for questions and discussion.



Group Discussion



Earlier in this workshop, you practiced explaining some common research terms. Some other important terms are important for you to understand and explain to others. How would you explain these terms to other less-experienced people?

- Single-blind study
- Double-blind study
- Control
- Patient volunteer
- Inclusion and exclusion criteria


Understanding the Clinical Research Process and Principles of Clinical Research 49

There is no Participant Guide page for this slide.

Definitions for these words can be found on Participant Guide pages 19, 20, and 21 and in the glossary.

Ask participants to provide examples from their own experience, if possible. Provide your own location-specific examples, if possible.

Note: Be careful this discussion does not drift into real-life negative examples where the study activities were inappropriate and/or personal.



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

Understanding the Clinical Research Process and Principles of Clinical Research 50

Participant Guide, page 22

Note: Be sure to review all sections on this page.

This is a good point to show a 9-minute video about the Belmont Report, depending on the location and experience of the participants. The video is in English. This video was developed for the 25th anniversary of the Belmont Report. The video provides the context for the original report for those who are not familiar with the report's principles and uses. Instructions for locating and downloading the video are provided in the Instructor's Guide.

Before showing the video, tell participants you are showing a 9-minute video. They should just watch and listen. After the video they will have an opportunity to ask questions and talk about what they just saw.

Show the video.

Debrief the video by asking anyone if they have questions about what they heard and saw. One common question may be how the Belmont Report affects research ethics outside the United States. Remind participants that research ethics applies to everyone, and everyone is responsible.

Allow for questions and discussion.




What Is Respect for Persons, Beneficence, and Justice?

Respect for Persons	Beneficence	Justice
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)		

Participant Guide, page 23

Allow for questions and discussion.



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

Understanding the Clinical Research Process and Principles of Clinical Research 52

Participant Guide, page 24

Note: Be sure to review all sections on this page.

Note: Before showing the next slide, introduce the slide with this statement: “In an earlier discussion, we talked about how trials can be conducted in a variety of locations. We discussed how important it is for researchers to define protocols so they can be used in the same way, no matter where they are conducted. The Ethics Committee or Institutional Review Board is responsible for making sure the research is conducted correctly, accurately, and ethically. On the next slide, there are two questions about the Ethics Committee and Institutional Review Board in your community.”

Allow for questions and discussion.

Group Discussion

1. What does an Ethics Committee (EC) or Institutional Review Board (IRB) do in your location?
2. Describe the different kinds of people who are members of the EC/IRB in your area?

Understanding the Clinical Research Process and Principles of Clinical Research 53

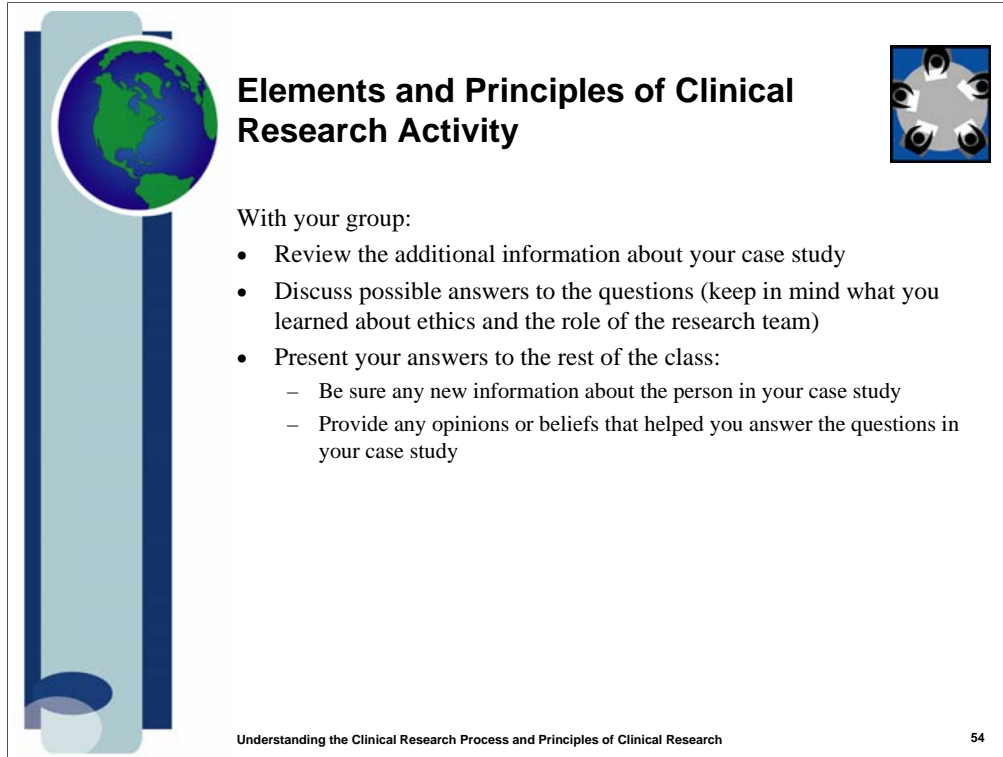
There is no Participant Guide page for this slide.

Be sure to introduce this group discussion by saying: “In an earlier discussion, we talked about how trials can be conducted in a variety of locations. We discussed how important it is for researchers to define protocols so they can be used in the same way, no matter where they are conducted. The Ethics Committee or Institutional Review Board is responsible for making sure the research is conducted correctly, accurately, and ethically.”

Then ask the questions on the slide.

Answers will vary considerably for this discussion, depending on the location. If participants are unable to answer these questions, lead a group discussion about the items on page 24 of the Participant Guide. As you review the bullet points on the page, ask open questions such as “Why do you think this is important?.”

The key point to take away from this discussion is that EVERYONE is responsible for protecting human rights in research activities.



Elements and Principles of Clinical Research Activity

With your group:

- Review the additional information about your case study
- Discuss possible answers to the questions (keep in mind what you learned about ethics and the role of the research team)
- Present your answers to the rest of the class:
 - Be sure any new information about the person in your case study
 - Provide any opinions or beliefs that helped you answer the questions in your case study

Understanding the Clinical Research Process and Principles of Clinical Research 54

There is no Participant Guide page for this slide.

Distribute the case study handouts for this activity: Elements and Principles of Clinical Research Activity. Each person in a group should receive a copy, and each group should get the same person's case study.

Note: Walk around and listen to the table groups as they discuss the questions in their case study. Depending on the experience level, they should be able discuss specifics about what is and is not allowed by the research team during a first appointment with a potential research participants. Important, too, is to seek examples of workshop participant empathy toward the case study person. For less-experienced groups, "human" issues will probably become more important and focus on how people are treated during the first appointment. While working with individual table groups, ask open questions like, "Have you thought about how the research team feels?" and "Have you thought about why interviewees might not want to share information they think might make them ineligible?," etc.

Prior to delivering the workshop, try to get a clear understanding of how participants are selected and treated in that location. Also seek to include a local member of a research team or EC/IRB member to offer specific insights.

Before going to the next section of this workshop, stop to:

- Review what was learned in this section (there is no PowerPoint slide for this review)
 - Ask for questions and allow for questions
 - Write any "parking lot" issues or information you need to come back to on a blank flip chart
- Break for 15 minutes.



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

Participant Guide, page 25

This module will last approximately 90 minutes.

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

- Global Community
- National Community
- Larger Community
- Surrounding Community
- Participant's Family and Close Friends

Understanding the Clinical Research Process and Principles of Clinical Research 56

Participant Guide, page 25

Note: In the graphic, note that these are external influences. The graphic is not meant to imply that each of these “communities” is aware of an individual’s clinical trial.

Allow for questions and discussion.



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.

Participant Guide, page 26

Allow for questions and discussion.

Group Brainstorm and Discussion

1. Who is in YOUR community?
2. Why is it important to have different kinds of people in a community?

Understanding the Clinical Research Process and Principles of Clinical Research 58

There is no Participant Guide page for this slide.

Note: At this point in the workshop, participants are probably ready for a break and something different more energetic. Consider asking everyone to stand up for this discussion (they are also free to move around). That will get people out of their seats, which will likely also spark some new brain activities. The instructor's responsibility is to write what participants share on a flip chart or whiteboard.

Introduce this activity by saying, "We're now going to do some brainstorming. Brainstorming is a fun way to collect new ideas...no idea is a bad idea in brainstorming. In fact, in brainstorming, these new ideas can be silly and even wrong! But there are a few rules for brainstorming:

- Think of as many ideas as possible
- Say each idea as it comes to you
- Build on other people's ideas
- Think of absurd, humorous, crazy ideas
- Keep up a rapid pace
- Be positive
- Do *not* question, criticize, or challenge other people's ideas

Brainstorm the first question on the slide. Allow approximately 5 minutes for participant ideas. Encourage creativity and spontaneity. Write the brainstorm ideas on a flip chart or board.

Then lead a discussion about the importance of having different people in a community. Answers might include: variety, experience, empathy, understanding, skills, comfort, etc. If time permits, ask how community members are important to HIV/AIDS research. Answers should include all of the same answers.



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.

Now most CABs are comprised of individuals representing various parts of the community, such as religious groups, schools or universities, media and non-government organizations/community-based organizations.

Participant Guide, page 26

Note: Review all paragraphs in the Participant Guide.

Note: The Uganda effort was not U.S. based.

Allow for questions and discussion.



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).

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

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

Participant Guide, page 27

Note: review the bullets on this page: they have not been included in the PPT.

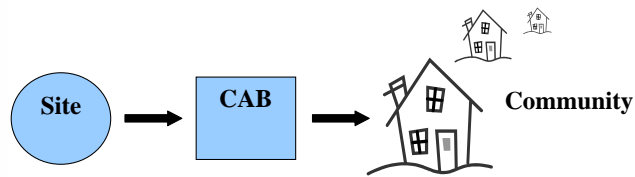
Allow for questions and discussion.



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.

CAB members take on active roles in planning for and implementing AIDS prevention and therapeutic trials.



Participant Guide, page 28

Note: Review the bullets in the Participant Guide.

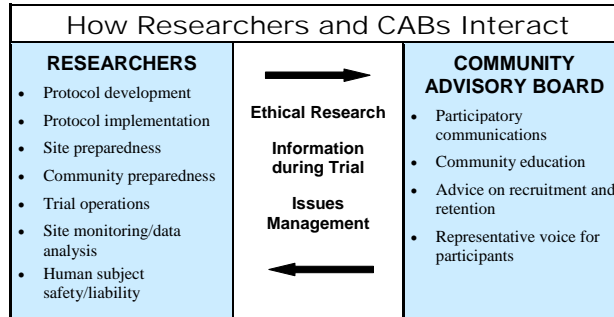
Note: In some locations, other sites and groups may be involved with a CAB to link the site with the community.

Allow for questions and discussion.



How Do Researchers and CABs Interact?

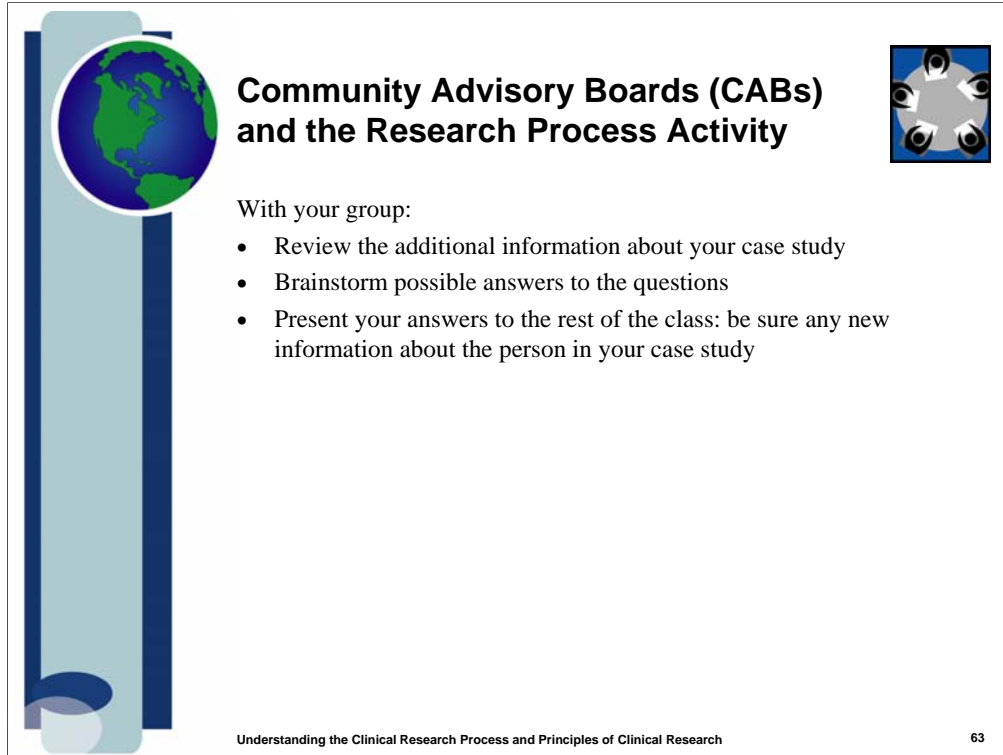
Researchers and CAB members cooperate to ensure ethical research, share scientific and community information during a trial, and manage their activities collaboratively. Researchers know it is important to have general support from the communities that will be involved in the research for a trial to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



Participant Guide, page 29

Note: Review the additional material in the Participant Guide.

Allow for questions and discussion.



Community Advisory Boards (CABs) and the Research Process Activity

With your group:

- Review the additional information about your case study
- Brainstorm possible answers to the questions
- Present your answers to the rest of the class: be sure any new information about the person in your case study

Understanding the Clinical Research Process and Principles of Clinical Research 63

There is no Participant Guide page for this slide.

This is the final activity of the workshop. Allow extra time for this activity because the topics covered here are important and meaningful. By the time this activity is conducted, the workshop participants will likely be working well together and willing to share ideas. This interaction is an important conclusion to tie together the focus of the workshop.

Distribute the case study handouts for this activity: Community Advisory Boards (CABs) and the Research Process Activity. Each person in a group should receive a copy, and each group should get the same person's case study.

Refer participants to the graphic on page 25 of the Participant Guide to understand how large a community can be.

Note: Walk around and listen to the table groups as they discuss the questions in their case study. While working with individual table groups, ask open questions like, "Have you thought about how a person's community might affect his/her health options and accessibility to research opportunities?" and "Have you thought about how CAB members can help within the bounds of confidentiality?," etc.

After all the presentations are complete, lead a whole group discussion about:

- The definition of confidentiality
- The importance of confidentiality
- What might happen if confidentiality is breached to the people in the case studies
- How clinical research is affected if there is a breach of confidentiality by the research team or CAB members

Before going to the next section of this workshop, stop to:

- Review what was learned in this section (there is no PowerPoint slide for this review)
- Ask for questions and allow for questions
- Write any "parking lot" issues or information you need to come back to on a blank flip chart

KEY PARTNERSHIPS

In this section, we will describe and discuss:


- The clinical trials network
- The Community Partners organization

Understanding the Clinical Research Process and Principles of Clinical Research 64

Participant Guide, page 30


Note: Carefully review the content in the paragraph above the graphic in the Participant Guide. Emphasis the six clinical trials networks. Tell participants you will explain what the colored circles mean in a minute. The important point for this slide is that the networks supported by Community Partners are found throughout the world.

This module will last approximately 15 minutes. There are no activities or discussions for this module, so be sure to allow participants to ask questions. At this point in the workshop, participants will be ready to finish.



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.



Understanding the Clinical Research Process and Principles of Clinical Research 65

Participant Guide, page 31

Note: Review the information in the table in the Participant Guide. The graphic shows the six network locations:

Red circles: AIDS Clinical Trials Group (ACTG)

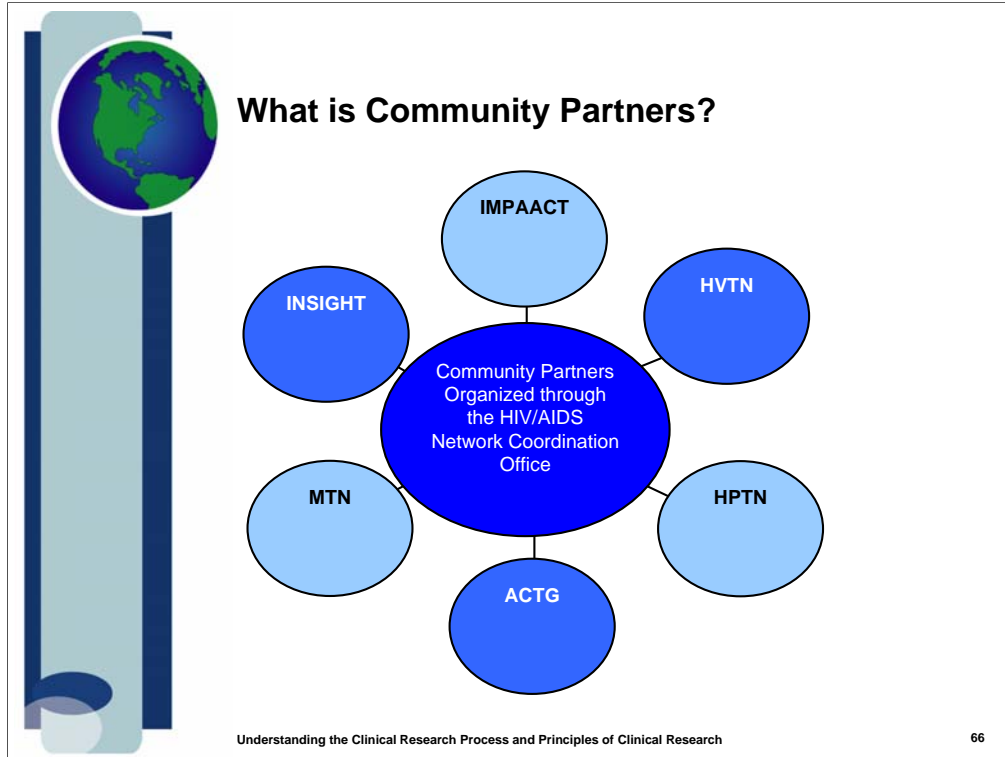
Orange circles: HIV Prevention Trials Network (HPTN)

Yellow circles: HIV Vaccine Trials Network (HVTN)

Green circles: International Maternal, Pediatric, Adolescent AIDS Clinical Trials (IMPAACT)

Blue circles: International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)

Purple circles: Microbicide Trials Network (MTN)



Participant Guide, page 32

Note: Read the introductory paragraph before discussing the graphic. Tell participants this graphic shows how the networks come together and work through Community Partners.

Allow for questions and discussion.



What Are Some Cross-Network Activities?

- Cross-network activities include:
- Community involvement
- Data management
- Evaluation metrics
- Training development and distribution
- Scientific leadership
- Laboratory processing
- Research site management and clinical trials logistics and issues identification and resolution
- Behavioral science integration

Participant Guide, page 33

Note: be sure to review the specifics of each bullet in the Participant Guide.



Which Organizations Support the Six 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
- Statistical and operations centers
- Central laboratories
- Contract Research Organizations (CROs)

Participant Guide, page 34


Allow for questions and discussion.



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. 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)



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
- The International AIDS Vaccine Initiative (IAVI)
- The Center for HIV-AIDS Vaccine Immunology (CHAVI)
- William J. Clinton Foundation
- The Global Fund to Fight AIDS, Tuberculosis and Malaria
- UNAIDS, the Joint United Nations Programme on HIV/AIDS

Understanding the Clinical Research Process and Principles of Clinical Research 70

Participant Guide, page 35

Review the details of the bulleted items in the Participant Guide. Also review the last paragraph on the page to emphasize the importance of collaboration and the efforts of all.

Allow for questions and discussion.

Summarize the module before going to the conclusion.



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

Participant Guide, page 36

This module will last approximately 20 minutes.

What Do You Know?

Answer 10 questions about clinical research.

Understanding the Clinical Research Process and Principles of Clinical Research

72

There is no Participant Guide page for this slide.

This activity functions as a post-test to find out how much participants learned about the information presented in this workshop. Avoid mentioning the word “test” so participants do not become stressed.

See the Instructor Guide for various options to deliver this activity. It can be delivered by using a handout or reading aloud the questions and asking for participant’s to provide the answers.

Answers to the questions are:

1a, 2a, 3c, 4b, 5g, 6a, 7a, 8a, 9e, 10c

If possible, ask participants to see if they received more correct answers now that they have attended the workshop:

- Congratulate participants who improved their scores
- Ask any non-improving participants if they learned new information after taking the workshop and emphasize that learning new information is most important.

After reviewing the answers:

- Review any items on the parking lot
- Allow for any final questions and discussions
- Ask participants to complete the Workshop Evaluation form at the end of their Participant Guides and turn it in to you before leaving
- THANK PARTICIPANTS for their contributions, energy, and attendance