



HIV VACCINE
TRIALS NETWORK

Questions and answers: HVTN 071 vaccine trial

Last updated June 19, 2007

1. What is the HVTN 071 trial?

HVTN 071 is the name of a clinical trial designed to test the safety and immune response of an experimental HIV vaccine. The trial will be run by the HIV Vaccine Trials Network (HVTN). The experimental vaccine used in this trial is described in Question 4 below.

The purpose of the trial is to further characterize the immune response to the experimental vaccine, or “study vaccine,” and to investigate which lab tests tell us the most about how the immune system responds to the study vaccine. It will also test whether the study vaccine is safe and well tolerated.

The products used in this trial are not produced from live HIV or from HIV-infected human cells. ***There is no possible way that the product in this trial can cause HIV infection.***

2. What is a vaccine trial?

A vaccine is given to prevent infection or fight disease. Currently there is no licensed vaccine against HIV. Part of the process of finding an effective HIV vaccine is testing the experimental vaccines that seem most likely to help the body fight HIV. A vaccine trial is a way to test specific experimental vaccines to see if they are safe to give to people and to evaluate how they might work to prevent or fight HIV. The people who participate in vaccine trials play an important part in the scientific research that may lead to an HIV vaccine.

3. Who are the people who participate in HIV vaccine trials?

There are many types of people who participate in HIV vaccine trials. All participants must be generally healthy and HIV negative (free of HIV infection). Before deciding to enter the trial, potential participants are provided with information about HIV and AIDS, the purposes of the trial, possible risks and benefits of participation, and trial procedures.

People have many reasons for joining HIV vaccine trials, including a desire to help others. People of many races and ethnicities have joined vaccine trials in the past and are needed in all types of vaccine research.

4. What kind of vaccine is being tested?

HVTN 071 tests an experimental vaccine named MRK Adenovirus serotype 5 HIV-1 *gag/pol/nef*. None of the products used in this study can cause HIV or AIDS.

This vaccine consists of a *viral vector* containing selected HIV gene *inserts*. A *vector* is a packaging system that can help deliver the vaccine more effectively into the part of the body or cells that create an immune response. In this study vaccine, the vector is a weakened form of adenovirus serotype 5 (Ad5) that has had key pieces removed so that the adenovirus cannot replicate in humans. If adenovirus *replicates*, it causes illnesses such as colds and respiratory infections.

A synthetic *insert* contains some extra genes added into the vector. In this case, the genes added are HIV genes (*gag*, *pol*, and *nef*).

5. Can this study vaccine cause HIV infection?

It is *impossible* to get HIV infection or AIDS from this study vaccine. It is not made from live HIV, killed HIV, or HIV-infected cells.

There is no possible way that this study vaccine can cause HIV infection.

6. Why is this trial being done?

This is a phase 1b trial, which means that the study vaccine has been tested in humans before.

Based on the research that has been done so far, the study vaccine has shown promising characteristics, but this does not mean researchers yet know if the vaccine will protect people. After testing the study vaccine in the laboratory, in animals, and in other clinical trials in humans, researchers are interested in finding out more about its potential.

7. How could the study vaccine help prevent HIV/AIDS?

The study vaccine is designed to work by mimicking some of the shapes and structures of HIV. It allows the body to make HIV proteins that may cause a response from the immune system. During this response, the immune system may produce antibodies and cellular (in white blood cells called lymphocytes) responses that recognize HIV as foreign without ever actually being exposed to real live HIV.

This process is meant to train the immune system to recognize HIV or the cells that are infected with HIV. If a person who has received the study vaccine is later exposed to HIV, hopefully the immune system would be prepared to respond quickly. This immune system preparation may potentially reduce the damage that HIV can do to the body. However, it is not known if the vaccine actually works to prevent HIV/AIDS. More clinical trials need to be done to learn if the vaccine works.

8. Has this vaccine been studied before?

As of May 2007, the study vaccine has been tested in more than 3190 people, all of whom have received at least one injection of the vaccine. Some people who received the study vaccine experienced pain, redness, tenderness, and/or swelling at the injection site. Some also experienced fever, nausea, headache, chills, tiredness, and sore throat. These are common reactions to vaccinations in general.

9. Who is eligible to participate in this trial?

Participants must be healthy adults who are between 18 and 50 years old and HIV negative. All participants must meet certain medical and nonmedical criteria for eligibility. Volunteers who are considering participation are carefully screened to make sure they meet the eligibility requirements.

10. How can people find out if they are eligible to join this trial?

Potential participants are asked about their medical history and given a physical examination. They then have blood and urine samples taken for routine analysis and are asked a series of personal questions about their sexual activity and drug use.

People who want to join the trial and were born female will be given a pregnancy test. Those who are pregnant or breastfeeding are not eligible to join. Anyone who joins the trial and was born female must agree to use effective birth control starting at least 21 days before the first injection and continuing until the last clinic visit.

All volunteers are tested to ensure they are HIV negative. A volunteer who is HIV positive at screening cannot enroll in the trial.

Information about participants will be kept confidential.

11. When and where is this trial being conducted?

HVTN 071 is being conducted at sites in the US only. The trial is expected to begin enrolling participants around July 2007. If all regulatory approvals are received, it will be conducted in 4 cities: Birmingham, AL; Nashville, TN; Rochester, NY; and Seattle, WA.

12. What is the design of this trial?

HVTN 071 is a multicenter, open-label trial. *Multicenter* means the trial is being conducted in more than one research site. *Open-label* means that both the participants and the scientists know what treatment each participant is receiving. Thus, in this trial, participants and scientists know that all participants are receiving the study vaccine.

This trial will enroll about 60 participants. All of these people will be given 3 doses of the study vaccine over the course of 6 months. All study vaccine injections will be given *intramuscularly* (IM), which means they are injected into a muscle.

STUDY DESIGN

Number of people	First day	+1 month	+6 months
60	1 mL MRKAd5 HIV-1 <i>gag/pol/nef</i> (IM)	1 mL MRKAd5 HIV-1 <i>gag/pol/nef</i> (IM)	1 mL MRKAd5 HIV-1 <i>gag/pol/nef</i> (IM)

In addition to the injections, trial participants will attend other clinic visits for blood draws and evaluations. Individual participants at the Birmingham, Nashville, and Rochester sites will visit the study clinic about 8 to 10 times over the course of a year. Participants at the Seattle site will have at least 19 scheduled visits. The number of visits differs depending on the city in which the participant enrolls in the trial.

At the Birmingham, Nashville, and Rochester sites, we will take a large blood sample from each participant twice, at 30 and 52 weeks after the first injection. The amount of blood taken during these draws is about the same amount taken when someone donates blood. This amount of blood will allow researchers to use a variety of tests to study the immune response to the vaccine. Researchers will also evaluate which tests may tell us the most about how the immune system responds to the study vaccine.

At the Seattle site, each participant will undergo a procedure called leukapheresis, which enables us to collect a large sample of white blood cells only. During leukapheresis, the participant is connected to a machine that draws blood from one arm, removes the white blood cells, and returns the remaining blood to the participant through the other arm. Leukapheresis will be conducted in each participant 2 times during the study, at 30 and 52 weeks after the first injection. The leukapheresis procedure will yield enough white blood cells to characterize the immune response to the study vaccine, and will also allow researchers to save specimens for future tests related to HIV and HIV vaccines.

Before large blood draws or leukapheresis, we will monitor each participant’s health to see if the procedures are safe for them.

Also at the Seattle site only, we will take extra blood samples after each injection and collect semen or cervical fluids. These samples will enable the researchers to investigate the immune responses produced by the vaccine. These procedures—leukapheresis, extra blood draws, and collection of

genital secretion samples—are being done only in Seattle participants because their samples can be delivered fresh to the processing lab, which is located in Seattle.

13. How will the safety and rights of participants be protected?

Trial participants play a very important role in the search for an HIV vaccine, and the HVTN works hard to protect the safety and rights of the participants. The HVTN makes its trials as safe and convenient as possible, but it is important for participants to realize that any experimental vaccine may have both medical and nonmedical risks.

Before they join the trial, volunteers are provided with information about HIV and AIDS, about the reasons for the trial, about possible risks and benefits, and about trial procedures. The clinic staff allows ample time to talk with volunteers, answer their questions, and provide information in writing.

After the trial has been fully explained, volunteers are asked to sign an informed consent form before being screened for eligibility and before enrolling. This form helps confirm that participants have made an informed decision about joining the trial. Volunteers will have plenty of time to consider whether or not they want to join the trial. They may decide not to enroll as participants. If they do enroll, they may still leave the trial at any time without losing the benefits of their standard medical care.

During the trial, the clinic staff monitors participants to make sure the study vaccine is not causing them problems. Any new information researchers learn about the safety of the trial will be provided to participants. Participants will be able to decide whether or not to stay in the study based on any new information they learn.

Participants are reminded frequently that being part of a vaccine trial does not mean they are protected from HIV infection. They are counseled at each clinic visit on ways to avoid HIV infection (including, for example, correct and consistent condom use).

14. Is this study vaccine safe?

Evaluating the safety of the study vaccine is one of the purposes of HVTN 071. The study vaccine has been tested in animals with no serious side effects, although animal testing does not necessarily predict results in humans. Based on the data from animal studies, scientists believe that the study vaccine is suitable for use in human trials.

There have also been several studies in humans using this vaccine. See Question 8 above for a description of the results of these studies.

While scientists believe that there are no serious safety risks with the study vaccine, there is always the possibility that there could be problems that no one expected. This is why this study vaccine, like any new drug or vaccine, needs to be tested in participants in a controlled clinical setting. Participants' health and safety will be closely monitored throughout the trial.

The study vaccine does not contain live HIV virus, and therefore there is no way for it to cause HIV infection.

15. How is the safety of the study vaccine monitored?

Several groups are monitoring this trial for safety and to make sure it is being done according to appropriate scientific and ethical standards. These groups include the US Food and Drug Administration (FDA), the US National Institutes of Health (NIH), and the HVTN itself.

The Protocol Team that designed HVTN 071 includes a range of people, from scientists and doctors to community members. Physicians and nurses on the team monitor the safety of the trial. This team carefully considered the available information to decide if the study vaccine was safe enough to begin

this trial. The HVTN also has a Safety Monitoring Board that will carefully monitor the safety of the participants. If there seem to be problems, the trial will be put on hold. After additional review by independent monitors, the trial can be modified or stopped if necessary.

16. Are there nonmedical risks?

Participants are asked to carefully consider all risks before joining a trial. Some risks are medical (related to health and safety), but there are also nonmedical, or social, risks. Trial participation takes time and commitment. It can also lead to complications with others who do not agree with the participant's choice to join the trial, or who do not have enough information about HIV vaccines. For example, some people have reported that being in a trial has upset their partners, friends, or family members.

Participating in a trial can also restrict a volunteer's behavior. For instance, participants are asked not to donate blood and should avoid becoming pregnant during the trial.

Participants may experience discrimination when they tell people they are taking part in clinical research for an HIV vaccine. In the case of discrimination, study staff members can (only if a participant requests and the staff has the participant's permission) talk to other parties to help resolve problems. For example, staff members can talk to insurance companies, employers, and others to explain a participant's involvement in a trial.

The study vaccine may cause a positive result on a standard HIV test, even if the participant is not infected with HIV. A positive HIV test result may lead to being treated unfairly by others (see Question 17 for more information on this risk).

It is important to remember that being given a study vaccine does not mean a participant is protected from HIV infection. Participants are therefore counseled to avoid behavior that will put them at risk of HIV infection.

17. Could the study vaccine cause a "false-positive," or vaccine-induced positive result on an HIV antibody test?

Some experimental vaccines may cause a trial participant to have an HIV antibody test result that is positive, even if the participant is not infected with HIV. Standard serological HIV tests look for antibodies (a part of the immune system) that recognize HIV. The study vaccines may cause the body to produce these antibodies. If this happens, the standard HIV test could show a positive result.

The study vaccine used in HVTN 071 is likely to cause a vaccine-induced positive HIV test result. However, if the study vaccine does cause this result, it does not mean the study participant is infected with HIV. A vaccine-induced positive result means that some test results interpret the body's immunity as if it is due to *actual* HIV infection, when in fact it is induced by a vaccine.

However, there are other HIV tests that look for the presence of the virus itself instead of the presence of antibodies. These tests can be used by the research team or others to clear up uncertainty about the true basis for a "positive" HIV test result. Because of the risk of vaccine-induced positive HIV antibody tests, participants are counseled to get HIV testing done only at their trial site. The site has access to the tests that can differentiate between vaccine-induced positives and true HIV infection.

No medical side effects or health problems are associated with a vaccine-induced positive HIV test result. But such a result may lead to being treated unfairly by others. People with a positive HIV test, even a vaccine-induced positive, are not allowed to donate blood. They may also have difficulties getting insurance or medical/dental care, traveling to other countries, obtaining employment, serving in the military or Peace Corps, or with their relationships with friends and family. The clinic staff is available to help with any such difficulty, and services exist to help any study participant with a vaccine-induced positive HIV test result.

18. What will be done with a participant's clinical trial records?

Information about clinical trial participants will be used only for research related to HIV vaccines or vaccine trials or HIV immunity. Any information collected about participants will be kept as private as possible. Most study records have only a participant ID number, not the participant's name. All test results are confidential and will not be made part of a participant's medical records.

We cannot guarantee absolute privacy. For example, certain information about trial participants may be released if required by law. In addition, most groups that review the safety of the trials and conduct the trials will be able to review the records—but all the members of these groups are obligated to keep any information confidential.

At all US sites, a Certificate of Confidentiality helps protect participant confidentiality. This certificate means that researchers and clinicians cannot be forced to give identifiable information to anyone who is not connected to the study, even in court proceedings. There are some exceptions to the Certificate of Confidentiality, such as government audit. These exceptions will be explained to volunteers at US trial sites.

19. What will happen to participants if they become HIV infected as a result of their behavior during this trial?

The study vaccines cannot *cause* HIV infection, but there is no guarantee that it *prevents* HIV infection. Participants who are receiving the study vaccine may still become infected with HIV through sexual contact, sharing injection drug equipment, or any other exchange of blood or bodily fluids.

All participants must be HIV negative when they enroll in the trial. Once in the trial, they are counseled to avoid behavior that would put them at risk of HIV infection. Those who become infected during the trial are terminated from the vaccine study, referred for medical treatment and management of the HIV infection, and told about other appropriate clinical or observational studies in which they can participate.

Although no drugs can cure HIV infection, there are many drugs that can be used to treat HIV infection. These drugs are not provided as part of this trial. Participants who become infected during the trial will be referred to an appropriate doctor for medical care and counseling.

20. How long will it take to find out if the study vaccine works?

It could take several years to find out if the study vaccine works. This study vaccine is being studied in other clinical trials to see if it helps prevent HIV infection or ameliorates disease. If the vaccine works, the results of HVTN 071 will help researchers evaluate which immune responses may be important in protecting against HIV. Participants who receive the study vaccine in HVTN 071 will not be eligible for any future trial of this product.

21. Who is sponsoring this trial?

This trial is sponsored by the Division of AIDS (DAIDS), within the National Institute of Allergy and Infectious Diseases (NIAID) at the NIH, an agency of the US Department of Health and Human Services (DHHS).

The study vaccine, MRK Adenovirus serotype 5 HIV-1 gag/pol/nef, was developed by Merck and Co., Inc. (Whitehouse Station, NJ, USA).

22. Who is conducting this trial?

The HIV Vaccine Trials Network (HVTN) will run the trial. The HVTN is a global network of researchers and community members that collaborates with government agencies, pharmaceutical

companies, academic institutions, and community members. The HVTN is dedicated to conducting international clinical HIV vaccine trials in the safest, most efficient, and most scientifically rigorous way possible. The HVTN is funded and supported by NIAID at NIH, an agency of DHHS.

23. Who reviewed and approved this trial?

The study vaccine is considered investigational, meaning the US FDA allows its use only in research. It has been made according to FDA guidelines and was reviewed by the FDA. The Protocol Team (the people who designed the trial) also carefully reviewed the information about the study vaccine before deciding to begin the trial. The trial has been reviewed and approved by the HVTN and by the Division of AIDS (DAIDS) at NIH.

The safety and rights of participants in HVTN 071 are monitored by Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs) local to each clinical research center. Community members are involved throughout the trial to ensure that the rights and needs of participants are being met.

24. For more information

About AIDS vaccine clinical trials: AIDS Clinical Trials Information Service, 1-800-TRIALS-A (USA only); www.clinicaltrials.gov

About the HIV Vaccine Trials Network: www.hvtn.org