



HIV VACCINE TRIALS NETWORK

Questions and answers: HVTN 069 vaccine trial

1. What is the HVTN 069 trial?

HVTN 069 is the name of a clinical trial to test the safety and immune response of two experimental HIV vaccines. The trial will be run by the HIV Vaccine Trials Network (HVTN). The study vaccines are described in Question 5 below.

The trial will test whether the experimental vaccines, or “study vaccines,” are safe and well tolerated. For one of the study vaccines, the trial will also compare the effects that different administration routes have on the immune response. A *route* is the way in which a study vaccine is given.

The products in this trial are not produced from live virus or from HIV-infected human cells. There is no possibility that they contain live (or killed) HIV virus. ***There is no possible way that the products 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 eventually to find out if 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). People have many reasons for joining HIV vaccine trials, including altruism (a desire to help others). Before deciding to enter the trial, potential participants are provided with information about HIV and AIDS, about the reasons for the trial, about possible risks and benefits of participation, and about trial procedures.

4. Can these study vaccines cause HIV infection?

It is ***impossible*** to get HIV infection or AIDS from these study vaccines. They are not made from live HIV, killed HIV, or HIV-infected cells.

There is no possible way that these study vaccines can cause HIV infection.

5. What kinds of vaccines are being tested?

HVTN 069 tests two experimental vaccines, named *VRC-HIVDNA009-00-VP* (DNA vaccine) and *VRC-HIVADV014-00-VP* (adenoviral vector vaccine). None of the products used in this study can cause HIV or AIDS.

DNA vaccine: The DNA vaccine is composed of four DNA *plasmids* (small, circular DNA molecules). One plasmid is designed to produce the Gag/Pol/Nef proteins from HIV subtype B. The other three plasmids are designed to produce the Env protein from HIV subtypes A, B, and C.

Adenoviral vector vaccine: The adenoviral vector vaccine is composed of four adenoviral vectors, each with an HIV gene insert.

A *vector* is a packaging system that can help deliver the vaccine more effectively into the correct part of the body or into the correct cell to create an immune response. In this study vaccine, the four vectors are weakened forms of adenovirus type 5 (Ad5), with key pieces removed so that the virus cannot replicate in humans. (If adenovirus *replicates*, it causes illnesses such as colds and respiratory infections.)

An *insert* consists of some extra genes added into the vector. In this study vaccine, the genes added are subtype B HIV-1 *gag/pol* and the *env* gene from HIV subtypes A, B, and C.

6. Why is this trial being done?

This is a Phase IB trial, which means that the study vaccines have already been tested to make sure they are safe for people. The main purpose of this study is to test whether the study vaccines are well tolerated and safe to give to people by different routes: intramuscular (IM), intradermal (ID), and subcutaneous (SC). Vaccines administered *intramuscularly* are injected into a muscle, vaccines administered *intradermally* are injected between layers of the skin, and vaccines administered *subcutaneously* are injected under the skin. Investigators want to determine how the route of administration affects a person's immune response to the vaccines.

Based on the research that has been done so far, the study vaccines have shown promising characteristics. After testing the study vaccines in the laboratory, in animals, and in other early clinical trials, researchers are interested in finding out more about their potential.

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

The study vaccines are designed to work by mimicking the shapes and structures of HIV. Both the DNA vaccine and the adenoviral vector vaccine allow 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 (lymphocyte) responses that recognize HIV without ever actually being exposed to 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. This preparation may potentially reduce the damage that HIV can do to the body. However, it is not known if the vaccines actually work to prevent HIV/AIDS. More clinical trials need to be done to learn if the vaccines work.

8. What do the study vaccines contain?

The DNA vaccine contains the HIV genes subtype B *gag/pol/nef*; the *env* gene from subtypes A, B, and C; and a salt water solution.

The adenoviral vector vaccine contains four vectors consisting of a weakened, noninfectious form of adenovirus type 5 (Ad5); the HIV genes subtype B *gag/pol*; the *env* gene from subtypes A, B, and C; and a salt water solution.

9. Have these vaccines been studied before?

Both of the experimental vaccines in this trial have been studied before, in other trials. We do not know if this trial will have similar results.

The DNA vaccine in this study has been given to more than 200 people in the arm muscle. A few people experienced small temporary changes in laboratory and urine tests while in the study. These changes did not cause symptoms, and test results returned to the usual values without treatment. It is

not known if the temporary changes in lab test results were related to the study vaccine or happened for other reasons. In this study participants will have laboratory testing of blood and urine to check for changes. One person had hives that started 4 days after vaccination. It is not known if the hives were related to the vaccine, but it is possible. Sometimes a small bump or scab that heals well without treatment may occur at the injection site.

The adenoviral vector vaccine in this study has been given to more than 200 people in the arm muscle. Some people experienced headache, nausea, fever, chills, tiredness, pain, and/or redness at the injection site. These are common reactions to vaccinations in general, especially those with an adenovirus type 5 (Ad5) vector. A few people experienced small temporary changes in laboratory and urine tests, but it is not known if these reactions were caused by the study vaccine or happened for other reasons. Giving the adenoviral vector vaccine between skin layers or under the skin may cause itchiness or a small scab at the injection site. There may be other side effects that we do not know about.

10. Who is eligible to participate in this trial?

Participants must be healthy adults between 18 and 50 years old and HIV-negative (free of HIV infection). All participants must meet certain medical and non-medical criteria for eligibility. Volunteers are carefully screened to make sure they meet the eligibility requirements.

11. How can people find out if they are qualified 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 sexual activity and drug use.

Women who want to join the trial will be given a pregnancy test. Pregnant or breastfeeding women are not eligible to join. Women who join the trial must agree to use effective birth control starting at least 21 days before they get their first injection and continuing until their last clinic visit.

All volunteers are tested to ensure they are HIV-negative (free of HIV infection). A volunteer who is HIV positive at screening cannot enroll in the trial.

Information about participants will be kept confidential and will be used only for trial purposes.

12. When and where is this trial being conducted?

HVTN 069 is an international trial and its research sites are located in two countries. The trial is expected to begin enrolling participants around November 2006. If all regulatory approvals are received, it will be conducted in five cities: Birmingham, AL; Boston, MA; New York, NY; Providence, RI; Seattle, WA; and Iquitos, Peru.

13. What is the design of this trial?

The trial will enroll about 90 people, divided into three groups. People in all three groups are given three DNA injections during the trial: an intramuscular (IM) injection at the beginning of the trial, a second IM injection one month after the trial begins, and a third IM injection two months after the trial begins. People in Group 1 are given an injection of the adenoviral vector vaccine IM six months after the beginning of the trial. People in Group 2 are given an injection of the adenoviral vector vaccine intradermally (ID) six months after the beginning of the trial. People in Group 3 are given an injection of the adenoviral vector vaccine subcutaneously (SC) six months after the beginning of the trial.

In addition to the injections, trial participants make other clinic visits for blood draws and evaluations. An individual participant will visit the study clinic about 12 times over the course of a year.

Group	# of people	STUDY DESIGN			
		Prime			Boost
		First day	+1 months	+2 months	+6 months
1	30	4 mg DNA vaccine (IM)	4 mg DNA vaccine (IM)	4 mg DNA vaccine (IM)	10 ¹⁰ PU Ad5 vaccine (IM)
2	30	4 mg DNA vaccine (IM)	4 mg DNA vaccine (IM)	4 mg DNA vaccine (IM)	10 ¹⁰ PU Ad5 vaccine (ID)
3	30	4 mg DNA vaccine (IM)	4 mg DNA vaccine (IM)	4 mg DNA vaccine (IM)	10 ¹⁰ PU Ad5 vaccine (SC)

HVTN 069 is a multicenter, open label, randomized 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 which study vaccine they are getting (in this case, all participants receive the same doses of the same vaccines). *Randomized* means that each participant is randomly assigned to one of the groups.

14. 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 make sure that the safety and rights of the participants are given the highest priority. There are several ways that the HVTN tries to make its trials as safe and convenient as possible, but it is important for participants to realize that any new, experimental vaccine may have both medical and non-medical 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. 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 enrolling. This form helps ensure that participants have all the information they need. 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, clinic staff monitors participants to make sure the study vaccines are 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).

15. Are these study vaccines safe?

Evaluating the safety of the study vaccines is one of the main purposes of HVTN 069. The study vaccines have 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 vaccines are suitable for use in human trials.

There have been earlier studies with these vaccines. See Question 9 above for a description of the results of these studies.

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

The study vaccines do not contain live HIV virus, and therefore there is no way for them to cause HIV infection.

16. How is the safety of the study vaccines monitored?

Several groups monitor 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 team that designed HVTN 069 will monitor the trial throughout its duration. This team 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 vaccines were safe enough to begin this trial.

In addition to the protocol team, the HVTN also has a Safety Monitoring Board. Both of these groups 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.

17. Are there non-medical 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 non-medical, 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 spouses, friends, or family members.

Participating in a trial also restricts the volunteer's behavior. For instance, participants are asked not to donate blood and women should avoid pregnancy 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 can (at a participant's request and with their permission) talk to insurance companies, employers, and others to explain a participant's involvement in a trial.

The study vaccines may cause a positive result on a standard HIV test even though the participant may not be infected with HIV (see Question 18), and such a result may lead to being treated unfairly by others.

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.

18. Could the study vaccines 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 test result that is positive, even if the participant is not infected with HIV. Standard 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. If the study vaccines cause this result, it does not necessarily mean the study participant is infected with HIV. A vaccine-

induced positive result means that some tests make a person *appear* infected; other HIV tests look for the presence of the virus instead of the presence of antibodies.

Participants are counseled to get HIV testing done only at their trial site because the site has access to specific tests that can differentiate between vaccine-induced positives and true HIV infection. These tests will be available for as long as the participant needs them, even after the study ends.

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 result.

19. 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. Any information collected about participants will be kept as private as possible. Most records have only a participant ID number, not a 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 in the case of government audit. These exceptions will be explained to volunteers at US trial sites.

20. 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 they *prevent* HIV infection. Participants may be able to get infected with HIV through sexual contact, sharing injection drug equipment, or any other exchange of blood or bodily fluids—even if they are receiving the study vaccine.

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 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.

There are many drugs that can be used to treat HIV infection, but none of these drugs can cure 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.

21. How long will it take to find out if the study vaccines work?

It could take several years to find out if the study vaccines work. These experimental vaccines are currently being investigated in other Phase I and Phase II studies to test safety in more people and to get a better idea of whether the immune system responds to the vaccines. If results are promising,

more trials will be conducted to see if the study vaccines help prevent HIV infection. The results of HVTN 069 will help researchers determine whether they should proceed with trials using administration routes other than intramuscular. Participants in HVTN 069 will not be eligible for any future trial of these products.

22. 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 National Institutes of Health (NIH), an agency of the US Department of Health and Human Services (DHHS).

The study vaccines, VRC-HIVDNA009-00-VP and VRC-HIVADV014-00-VP, were developed by the Dale and Betty Bumpers Vaccine Research Center (VRC), NIAID, NIH, DHHS (Bethesda, Maryland, USA).

23. Who is conducting this trial?

The HIV Vaccine Trials Network (HVTN) will run the trial. The HVTN is in a global partnership with researchers, 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 the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH), an agency of the US Department of Health and Human Services (DHHS).

24. Who reviewed and approved this trial?

The study vaccines are considered investigational, meaning the US Food and Drug Administration (FDA) allows their use only in research. They have been made according to FDA guidelines and were 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 safety and rights of participants in HVTN 069 are monitored by Institutional Review Boards (IRB)/Independent Ethics Committees (IEC) local to each research center, and the safety of the trial is monitored by local Institutional Biosafety Committees. Community members are involved throughout the trial to ensure that the rights and needs of participants are being met.

25. 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