



HIV VACCINE  
TRIALS NETWORK

## Questions and answers: HVTN 204 vaccine trial

Last updated October 10, 2005

### 1. What is the HVTN 204 trial?

HVTN 204 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 study vaccines are safe and well tolerated, and whether they cause an immune response.

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?

Vaccines are given to prevent infection or fight disease. Currently there is no vaccine that prevents HIV-negative people from becoming infected with HIV, or that fights disease in people who are infected. Part of the process of finding HIV vaccines that will work 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 experimental vaccines can cause HIV infection.***

### 5. What kind of vaccines are being tested?

This study is testing 2 experimental HIV vaccines: *VRC-HIVDNA016-00-VP* (“DNA vaccine”) and *VRC-HIVADV014-00-VP* (“adenoviral vector vaccine”).

The DNA vaccine, *VRC-HIVDNA016-00-VP*, is composed of six plasmids. Plasmids are biological structures made up of DNA. They are easy to work with, and scientists can put small segments of

genes from the DNA of other organisms into them. Plasmids then “carry” this new material. It is what they are carrying, though, that does the real work. In the DNA vaccine, each of the six plasmids contains a man-made HIV gene: Clade B *gag*, *pol*, and *nef*, and Clade A, Clade B, and Clade C *env* (A *clade* is a subtype of HIV).

The adenoviral vector vaccine, *VRC-HIVADV014-00-VP*, is composed of four adenovirus vectors, each with an HIV gene insert. A *vector* is a packaging system that can help deliver the vaccine more effectively into the right part of the body or into the right cell, to create an immune response to the vaccine. Adenovirus is a virus that causes illnesses such as colds and respiratory infections. In this study vaccine, the four vectors are forms of adenovirus type 5 (Ad5) with key genetic sequences removed, so that virus cannot replicate and will not cause infection in humans. An *insert* consists of some extra genes added into the vector. In this study vaccine, the genes added are Clade B HIV-1 *gag/pol* and Clade A, Clade B, and Clade C HIV-1 *env*.

Nothing in either of these study vaccines can cause HIV or AIDS.

## 6. Why is this trial being done?

This is a Phase II trial, meaning its main purposes are to test if the study vaccines are *safe* to give to people, and to test for an *immune response* to the vaccines. The trial is being coordinated with other studies of the same products by the US Military HIV Research Program (USMHRP) and the International AIDS Vaccine Initiative (IAVI).

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 some people, researchers are interested in finding out more about the vaccines’ potential. If the results of HVTN 204 and the USMHRP and IAVI studies show that this combination of vaccines is safe, well tolerated and causes an immune response, there will be a much larger trial to test whether the vaccines can prevent HIV infection.

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

The idea behind both of the study vaccines is to train the immune system to prevent HIV from infecting cells or eliminate cells that show signs of HIV infection, thus potentially reducing the damage that HIV can do to the body. If a person later becomes infected with HIV, hopefully the immune system would be prepared to respond.

The DNA vaccine contains pieces of man-made *gag*, *pol*, *nef*, and *env*, genes found in HIV. These genes instruct the body to make the corresponding HIV proteins Gag, Pol, Nef, and Env.

The adenoviral vector vaccine is designed to make the HIV proteins Gag, Pol, and Env. These proteins may cause the immune system to produce antibodies and cellular (lymphocyte) responses that may recognize and attack HIV.

Although the study vaccines are designed to train the immune system to recognize HIV, they cannot cause HIV infection themselves, because pieces of HIV that are necessary for infection have been left out.

## 8. What do the study vaccines contain?

The DNA vaccine, *VRC-HIVDNA016-00-VP*, contains the following:

- six plasmids;
- the HIV genes Clade B *gag*, *pol*, and *nef*, and Clade A, Clade B, and Clade C *env*; and

- a salt water solution.

The adenoviral vector vaccine, VRC-HIVADV014-00-VP, contains the following:

- four vectors consisting of a weakened, noninfectious form of adenovirus type 5;
- the HIV genes Clade B *gag/pol* and Clade A, Clade B, and Clade C *env*; and
- a salt water solution.

**9. Have these vaccines been studied before?**

The DNA vaccine and the adenoviral vector vaccine have been tested in animals with no serious side effects, although animal testing does not necessarily predict results in humans.

Both study vaccines are currently being tested in humans in other trials. For details, see Question 15.

**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 allowed to join. Women planning to become pregnant during the first 9 months of the study period are also not allowed to join.

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 204 is an international trial, and research sites are located in six countries. The trial began enrolling participants on September 22, 2005. It will be conducted in six US cities: Baltimore, MD; Boston, MA; Providence, RI; Birmingham, AL; Nashville, TN; and Rochester, NY. It will also be conducted in Port-au-Prince, Haiti; Kingston, Jamaica; Rio de Janeiro and São Paulo, Brazil; and Cape Town, Soweto, and KOSH (Klerksdorp, Orkney, Stilfontein, and Hartbeesfontein), South Africa.

**13. What is the design of this trial?**

HVTN 204 is a multicenter, randomized, placebo-controlled, double-blind trial. ‘Multicenter’ means the trial is being conducted in more than one research site. ‘Randomized’ means that participants are randomly assigned to get either the study vaccines or placebo at all their injection visits. ‘Placebo-controlled’ means that some people are given placebo, so the researchers can tell if the study vaccines make a difference. ‘Double-blind’ means that neither the participants nor the scientists know who is getting the study vaccines and who is getting placebo until after the trial is over.

The trial will enroll about 480 people, 240 in the Americas (Haiti, Jamaica, Brazil, USA) and 240 in southern Africa (Botswana and South Africa). The geographic diversity of participants allows researchers to evaluate the immune responses of people with different levels of previous exposure to adenovirus, a key component of one of the study vaccines.

Participants will be divided into two groups. Over the course of six months, participants in each group will be given four injections:

- Group 1: three injections of DNA vaccine (day of enrollment, one month after enrollment, and two months after enrollment) and one of the adenoviral vector vaccine (six months after enrollment).
- Group 2: four injections of a placebo consisting of sterile salt water (at the same times as people in Group 1).

For six months after the last injection (i.e., one year after enrollment), all participants will be followed to see if the study vaccines are safe and well tolerated and if they cause an immune response.

#### **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 works to make its trials as safe and convenient as possible, but it is important for participants to realize that any new, experimental vaccines 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 allow ample time to talk with volunteers and answer their questions, and information is also provided in writing.

After the trial has been fully explained, volunteers are asked to sign an *informed consent* form before enrolling. This form will help ensure that participants have been given all the information they need. Volunteers will be given 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 monitor participants to make sure the study vaccines are not causing problems. Any 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 the study vaccines safe?**

Evaluating the safety of this combination of study vaccines is one of the main purposes of HVTN 204. 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 DNA vaccine is being tested in people in two other studies, VRC 007 and VRC 008. In VRC 007, in the first few days after injection, some participants experienced mild superficial skin lesions,

which gradually went away within two weeks. No one has experienced serious side effects from the vaccine, with the possible exception of one participant with chronic hives. It is not known whether this reaction is due to the study vaccine or to a pre-existing allergy in the participant.

The adenoviral vector vaccine is also being tested in people in other trials, VRC 006, VRC 009, VRC 010, HVTN 054, and HVTN 057. In those trials, in the first few days after injection, some participants have experienced mild to moderate pain or tenderness (or both) at the injection site. In addition, some participants have experienced mild to moderate symptoms such as fatigue, headache and muscle ache. Two people reported severe malaise. One person also had a high temperature. These side effects gradually went away within a few days. The adenoviral vector will also be tested in VRC 008, as a “boost” to the DNA vaccine.

The study vaccines do not contain live HIV virus, and therefore there is no way for the study vaccines 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.

Physicians and nurses on the team that designed HVTN 204 will monitor the safety of the trial. This team carefully considered the available information to decide if the study vaccines were suitable for use in a human trial. 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, or who do not have enough information about HIV vaccines. For example, some people have reported that being in a trial has upset their spouse, 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 first 9 months that they are participating in 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 will likely cause a false positive result on a standard HIV test (see Question 18), and such a result may lead to being treated unfairly by others.

It is important to remember that being given the study vaccines does not mean the participant is protected from HIV infection. Trial participants will also not know whether they have received the study vaccines or placebo, which is an inactive substance (sterile salt water) with no protective properties. Participants are therefore counseled to avoid behavior that will put them at risk of HIV infection.

To help avoid problems that could come from participating in a trial, participants will be given a number to call for information or help to resolve problems. At some sites, participants will be offered an identification card that shows they joined an HIV vaccine study.

**18. Could the study vaccines cause a “false positive” result on an HIV antibody test?**

Some experimental vaccines may cause a trial participant to have an HIV test that appears HIV positive. Standard HIV tests look for antibodies (a part of the immune system) that recognize HIV. The study vaccines will likely cause the body to produce these antibodies. In this case, the standard HIV test could show a positive result. If the study vaccines causes this result, it does not necessarily mean the study participant is infected with HIV. A false positive 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 which can differentiate between false positives and true HIV infection. These tests will be available even after the study ends.

No medical side effects or health problems are associated with a false positive HIV test result. But such a result may lead to being treated unfairly by others. People with a positive HIV test, even a false 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. Clinic staff are available to help with any difficulty, and services exist to help any study participant with a false positive HIV result.

**19. What will be done with a participant’s trial records?**

Information about 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. Samples used for tests are identified by number only, not by name. Any test results are confidential, and will not be made part of participants’ 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 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.

For study participants in the US, a Certificate of Confidentiality from the US Food and Drug Administration (FDA) helps protect participant confidentiality. This certificate means that researchers and clinicians cannot be forced to give identifiable information to anyone 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 the trial sites.

**20. What will happen to participants if they become HIV-infected from their behavior during this trial?**

The study vaccines cannot *cause* HIV infection, but there is no guarantee that they *prevent* HIV infection. Participants can still get infected with HIV through sexual contact, sharing of 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 will stop participating in the trial. These individuals will be referred for medical treatment, management, and counseling. These individuals will also be referred to appropriate ongoing clinical trials or observational studies.

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.

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

Depending on the results of HVTN 204 and other trials, these experimental vaccines might be tested further in a much larger Phase III (“efficacy”) trial. Such a trial would continue to test safety and immune response in more people, but also give an idea of whether the vaccines can prevent HIV infection. Participants in HVTN 204 will not be eligible for an efficacy trial.

**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-HIVDNA016-00-VP (“DNA vaccine”) and VRC-HIVADV014-00-VP (“adenoviral vector vaccine”), are provided by the Dale and Betty Bumpers Vaccine Research Center (VRC), a part of NIAID.

**23. Who is conducting this trial?**

The HIV Vaccine Trials Network (HVTN) will run the trial. The HVTN is a global partnership of researchers, government, industry, academic institutions, and community members. The HVTN is dedicated to conducting international clinical HIV vaccine trials in the safest, most efficient, and scientifically most 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 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 vaccines before deciding to begin the trial.

The safety and rights of participants in HVTN 204 are monitored by Institutional Biosafety Committees (IBC) and Institutional Review Boards (IRB)/Independent Ethics Committees (IEC) local to each research center. 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](http://www.clinicaltrials.gov)

About the HIV Vaccine Trials Network: [www.hvtn.org](http://www.hvtn.org)