



HIV VACCINE
TRIALS NETWORK

Questions and answers: HVTN 084 vaccine trial

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1. What is the HVTN 084 trial?

HVTN 084 is the name of a clinical trial to test the safety of 2 experimental HIV vaccines. We will also look to see how people’s immune systems react to the vaccine. The study vaccines used in this trial are described in Question 4 below.

The products used in this trial are not produced from anything containing the virus (either live or killed HIV) or from HIV-infected human cells. *These study vaccines cannot cause HIV infection.*

2. Who is conducting this trial?

The Division of AIDS (DAIDS), within the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH), sponsors this study. The NIH is part of the United States government.

The HIV Vaccine Trials Network (HVTN) will run the trial. The HVTN is an international collaboration of scientists, educators, and community members searching for an effective and safe HIV vaccine. The HVTN is supported through a cooperative agreement with NIAID.

3. What is a vaccine trial?

A vaccine study is a way to test the safety of a vaccine, and can also be used to find out if a vaccine might help prevent or fight HIV. Currently there is no licensed vaccine against HIV. In order to develop an HIV vaccine, researchers need to test the study vaccines in humans.

4. What kind of study vaccines are being tested in HVTN 084?

HVTN 084 tests 2 study vaccines called recombinant adenoviral vector VRC-HIVADV014-00-VP (clade B Gag-Pol; clades A, B, C Env) and recombinant adenoviral vector VRC-HIVADV054-00-VP (clade B Gag-Pol). From here on, we will call these the “study vaccines.” They are experimental preventive HIV vaccines supplied by the Dale and Betty Bumpers Vaccine Research Center (VRC), which is part of the US National Institutes of Health. None of the products used in this study can cause HIV or AIDS.

The two study vaccines are “adenoviral vector” vaccines. They are made out of a certain kind of adenovirus called Adenovirus Type 5 (Ad5). Adenoviruses cause colds, coughs, and diarrhea. A vector is a packaging system that can help deliver the vaccine into the correct part of the body or into the correct cell to create an immune response. The vaccines used in this study have been changed in two ways; their Ad5 vector cannot cause the infections usually caused by natural adenoviruses. In addition, they contain pieces of manufactured DNA that look like pieces from HIV. When the study vaccines are injected, the DNA tells the body to make proteins that look like HIV proteins. There is

no actual HIV in the vaccines. In responding to these proteins, a person's immune system may learn to recognize HIV without being exposed to actual HIV.

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

Both vaccines have been given to people before, mostly without any serious health concerns. In one group of men, however, vaccines using the Ad5 vector seemed to *increase* the risk of HIV infection if they were exposed to the virus. That higher risk of HIV seemed to be in a group of men who had some things in common. In addition to getting the vaccine, they either had antibodies to Ad5, or they were uncircumcised, or both.

To be in the HVTN 084 study, you must have no detectable antibodies to Ad5. If you have a penis, you must also be circumcised.

5. Are these study vaccines safe?

Based on the data from previous studies, scientists believe that the study vaccines are suitable for use in this study. However, there is always the possibility that there could be problems no one expected. That is why these study vaccines, like any new drug or vaccine, need to be tested in people in a clinic setting. Each participant's health and safety will be watched closely throughout the trial.

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

6. 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.

These study vaccines cannot cause HIV infection.

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

As described in Question 4, the study vaccines contain pieces of manufactured DNA that look like pieces from HIV. There is no actual HIV in the vaccines. When the study vaccines are injected, the DNA tells the body to make proteins that look like HIV proteins. In responding to these proteins, a person's immune system may learn to recognize HIV without being exposed to actual HIV. An immune system that can recognize HIV if it comes along later may be more able to fight the virus and to decrease the damage that HIV can do to the body. However, it is not known if the vaccines will prevent HIV/AIDS. More clinical trials need to be done to learn if the vaccines work.

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

8. Why is this trial being done?

We are doing this study to answer several questions:

- Are the study vaccines safe to give to people?

- Are people able to take the study vaccines without becoming too uncomfortable?
- Does one study vaccine create a different immune response than the other?

9. How many people are in this trial?

The trial will involve 100 participants: 50 participants will receive the recombinant adenoviral vector VRC-HIVADV014-00-VP (clade B Gag-Pol; clades A, B, C Env) vaccine and 50 participants will receive the recombinant adenoviral vector VRC-HIVADV054-00-VP (clade B Gag-Pol) vaccine.

10. Who is eligible to participate in HVTN 084?

All participants must meet certain criteria to be eligible for the trial.

Participants must be healthy adults who are between 18 and 50 years old and HIV negative (free of HIV infection). They must have no detectable antibodies to the Ad5 virus and be at low risk for HIV infection. Male participants must be circumcised.

Potential participants are asked about their medical history and are given a physical examination. They then have blood and urine samples taken for routine testing. They are also asked about their sexual activity and drug use. Those who are pregnant or breastfeeding are not eligible to participate in this trial.

11. When and where is this trial being conducted?

HVTN 084 is an international trial and will be done in 3 countries. The trial is expected to begin enrolling participants around December 2010 / January 2011. If all regulatory approvals are received, it will be conducted in 4 cities: São Paulo, Brazil; Barranco and Iquitos, Peru; and Lausanne, Switzerland.

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

The HVTN works hard to protect the safety and rights of the participants. Before they join the trial, volunteers are given information about HIV and AIDS, about the reasons for the trial, about possible risks and benefits, and about trial procedures. The clinic staff allows plenty of time to talk with volunteers, answer their questions, and give information in writing.

After the trial has been fully explained, volunteers are asked to sign an informed consent form. They sign this form before being screened for eligibility and before enrolling. The informed consent form helps confirm that participants have made an informed decision about joining the trial. Volunteers will have plenty of time to think about whether they want to join the trial. They may decide not to enroll. 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 vaccines are not causing them problems. Participants will be given any new information that could affect whether they want to stay in the study.

Participants are reminded often that being in a vaccine trial does not mean they are protected from HIV. They are counseled at every clinic visit on ways to avoid HIV. (This counseling might include,

for example, talking about correct condom use.) It is important for participants to understand that any new study vaccine may have both medical and nonmedical risks.

13. Could the study vaccines cause a positive result on an HIV test?

Some study vaccines may make a trial participant test positive on an HIV antibody test, even if the participant is not infected with HIV.

One way vaccines can create an immune response is by causing the body to make antibodies. Antibodies are made by the body to fight infection. Common HIV tests look for antibodies against HIV. This means that after a participant gets a study HIV vaccine, a standard HIV test may say the person has HIV, even if that isn't the case. This result is called a "vaccine-induced positivity."

This clinic has special HIV tests that look for the virus itself instead of looking for antibodies. These tests can be used to determine if a positive test result is due to the vaccines or a true infection.

No health problems are associated with a positive HIV test result that is caused by a vaccine. But someone who gets that type of test result may be 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 problems 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 can help with any such problems. Services exist to help any study participant with a vaccine-induced positive HIV test result.

14. 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 study vaccines would need to be investigated in other clinical trials—phase 2 and phase 3 studies, for example—to test safety in more people, to get a better idea of whether the immune system responds to the vaccines, and to see if the study vaccines help prevent HIV infection. The results of HVTN 084 will help researchers determine whether they should proceed with other trials. Participants who received study vaccines in HVTN 084 in general will not be eligible for any future trial of these products, unless it is specifically required for that future trial.

15. Who reviewed and approved this trial?

The study vaccines are considered investigational, meaning the US FDA only allows them to be used 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 084 are monitored by Institutional Review Boards (IRBs) or Independent Ethics Committees (IECs) at each participating clinical research center. The safety of the trial is also monitored by local Institutional Biosafety Committees (IBCs). Community members are involved throughout the trial to ensure that the rights of participants are being protected and that their needs are being met.

16. For more information

About AIDS vaccine clinical trials: AIDS Clinical Trials Information Service, www.clinicaltrials.gov

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

If you have additional questions that were not answered by this document, please ask us.

You can contact: