



HIV VACCINE  
TRIALS NETWORK

## Questions and answers: HVTN 055 vaccine trial

Last updated: September 2, 2005

### 1. What is the HVTN 055 trial?

HVTN 055 is the name of a clinical trial to test the safety of a group of experimental HIV vaccines. The study vaccines are described in Question 5 below. A secondary purpose of the trial is to see if the vaccines cause an immune response—that is, a response from the body that might help protect against HIV.

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 vaccine against HIV. Part of the process of finding an HIV vaccine 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 so that researchers can prove that the experimental vaccines are safe, and eventually to find out more about whether 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. 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 a study vaccine cause HIV infection?

It is *impossible* to get HIV infection or AIDS from experimental vaccines. They are made in laboratories—not from live HIV, killed HIV, or HIV-infected cells.

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

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

Four study vaccines are being tested in HVTN 055. Each vaccine is a poxvirus vector with an HIV gene insert. A *vector*, such as a weakened non-HIV virus, is used to carry a few HIV genes into the body to create an immune response. An *insert* is some extra genes, in this case a few of the genes in HIV, added into the vector. Neither the virus vector nor the HIV genes can cause HIV or AIDS. The virus vectors have been changed so they are unlikely to spread in your body or be contagious to people around you.

Two poxvirus vectors and two inserts are being tested. One vector, modified vaccinia Ankara (MVA), was originally developed to protect against smallpox. The other vector is made from fowlpox virus (FPV) vaccine, which protects chickens from poxvirus infections.

The two HIV gene inserts are *env/gag* and *tat/rev/nef-RT*. The designations *env*, *gag*, *tat*, *ref*, *nef*, and *RT* refer to some of the genes found in HIV.

Each of the two vectors is combined with each of the two inserts. This makes a total of four vaccine products. Their names are:

- MVA *env/gag*
- MVA *tat/rev/nef-RT*
- FPV *env/gag*
- FPV *tat/rev/nef-RT*

Depending on which study group the study participants are assigned to, they will receive different combinations of these vaccine products or controls over several clinic visits (see Question 13 below).

**6. Why is this trial being done?**

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

This is a Phase I trial, meaning its main purpose is to test if the study vaccines are *safe* to give to people. A secondary purpose is to test for an immune response.

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

The key to these vaccines is the HIV gene inserts (*env/gag* or *tat/rev/nef-RT*). Researchers expect that, when someone is given this kind of vaccine, the HIV genes will stimulate the cells in the body to make certain HIV proteins. The body may then react to the presence of these proteins. The idea is to train the immune system to eliminate cells that show signs of HIV infection, thus reducing the damage that HIV can do to the body. If a person later becomes exposed to HIV, the immune system could be prepared to respond.

**8. What do the study vaccines contain?**

Each of the four study vaccines contains the following:

- a poxvirus, either modified vaccinia Ankara (MVA) or fowlpox virus (FPV),
- an HIV gene insert, either *env/gag* or *tat/rev/nef-RT*, and
- saline solution (salt water).

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

HVTN 055 is the first time these experimental study vaccines will be tested in humans. However, over 100,000 people have received similar MVA vaccines, with no serious side effects. Also, similar FPV vaccines have been given in research studies to over 300 people with cancer, with no serious side effects.

The study vaccines have been tested in animals. The MVA used in this study has been given to mice, rabbits, and monkeys with no serious side effects; all four study vaccines have been given to rabbits

with no serious side effects. Animal testing, however, does not always show what will happen in people.

HVTN 055 began on October 14, 2004. Since then, about 50 people have received the study vaccines. No serious side effects have been reported.

**10. Who is eligible to participate in this trial?**

Participants must be healthy, HIV-negative adults between 18 and 50 years old. 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 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.

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

Volunteers who have received smallpox vaccine cannot enroll in the trial, because the smallpox vaccine might interfere with the way the body responds to the study vaccines. (Most people born in the US before 1972 were vaccinated with smallpox vaccine, and many people have received it in recent years as a precaution against bioterrorism.)

Volunteers who have heart problems, or who are at high risk for heart problems, cannot enroll in the trial. This is because of the similarity between the MVA vector and the smallpox vaccine, which on very rare occasions has caused heart problems (myocarditis or pericarditis). The experimental MVA vaccine in this study contains a much weaker virus than the smallpox vaccine and is not expected to cause heart problems; so far, around 200 people have received experimental MVA vaccines and no heart problems related to vaccine have been reported. During the trial, participants will be given electrocardiogram (ECG) and other assessments to check for any heart problems.

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 055 enrolled its first participant on October 14, 2004 in Rochester, New York. It is being conducted in four US cities: Birmingham, AL; Rochester, NY; St. Louis, MO; and Seattle, WA. It will also be conducted in two Brazilian cities, Rio de Janeiro and São Paulo.

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

HVTN 055 will enroll about 150 people. It has two parts, Part A (5 groups of 12 people) and Part B (3 groups of 30 people). The groups are given different combinations of the four study vaccines, and the results of the groups will be compared.

The study vaccines are given at five clinic visits over the course of seven months. They are given in pairs — at a given vaccination visit, a participant will receive the two MVA products *or* the two FPV products. Depending on which group the study participants are assigned to, they will be given either the same study vaccines every time (all MVA or all FPV), or different study vaccines at different

clinic visits (MVA at some visits, FPV at others). For further comparison, a few people in each group are given a *control*, consisting of the vector (MVA or FPV) without any HIV genes inserted.

HVTN 055 is a multicenter, controlled, randomized, double-blind trial. ‘Multicenter’ means that the study is conducted in more than one research clinic. ‘Controlled’ means that some people are given MVA or FPV alone (without HIV genes), so the researchers can tell if the HIV genes make a difference. ‘Randomized’ means that participants are randomly assigned to get some combination of study vaccines (or the control). ‘Double-blind’ means that neither the participants nor the scientists know who is getting study vaccine and who is getting control.

**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 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 devote time to talk to 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 vaccine is 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 clinic visits on ways to avoid HIV infection (including, for example, correct and consistent condom use).

**15. Are these study vaccines safe?**

Evaluating the safety of these study vaccines is the main purpose of HVTN 055. Since the study began on October 14, 2004, about 50 people have received the study vaccines. No serious side effects have been reported.

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 of similar vaccines. Over 100,000 people have received similar MVA vaccines, with no serious side effects. Also, similar FPV vaccines have been given in clinical trials to over 300 people with cancer, with no serious side effects.

While scientists believe that there are no serious safety risks with these study vaccines, there is always the possibility that there could be problems that no one expected. This is why the 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 vaccine 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 055 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. Clinical professionals at the HVTN and NIH receive weekly reports of safety-related information. If a problem occurs, they will be alerted immediately. The HVTN also has a Safety Monitoring Board not affiliated with this particular trial. These groups will carefully monitor the safety of the participants. If there appear to be problems involving participant safety, the trial will be temporarily stopped. After additional review by independent monitors, the trial can be modified, or stopped for good if the vaccines are considered unsafe.

In addition, the HVTN has a Science Committee and a Safety Monitoring Board. Both of these groups review 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 stopped if necessary.

**17. Are there non-medical risks?**

Participants are asked to carefully consider all risks, medical and non-medical, before joining a trial. 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 trial.

Others have experienced discrimination when they told people they were participating 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.

It is important to remember that being given a study vaccine does not mean the participant is protected from HIV infection. HIV infection can be contracted by sexual contact, sharing of injection drug needles and syringes, or any other transfer of blood or bodily fluids. Trial participants will also not know whether they have received a study vaccine or a control, which consists of only the vector (MVA or FPV) with no HIV gene inserts. 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 offered an identification card that shows that they joined an HIV vaccine study. A number will be listed on the card that may be called for help or information.

**18. Could the study vaccine cause a "false positive" result on an HIV antibody test?**

Some experimental vaccines may cause a trial participant to have an HIV test result that appears HIV positive. Standard HIV tests look for antibodies (proteins in the blood) that recognize HIV. The experimental vaccines may cause the body to produce these antibodies. In this case, the standard HIV

test could show a positive result. If the study vaccines cause this result, it does not mean the study participant is infected with HIV. Further tests can be done to clarify whether the participant has what is called a *false positive* HIV test. A false positive means that some tests make a person appear infected, while other tests can prove that there is actually no infection.

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. The trial site will offer periodic free retesting as long as the positive HIV test is due to the study vaccines.

No medical side effects or health problems are associated with appearing HIV-infected on certain tests. But a false positive test 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 with getting insurance, medical/dental care, traveling to other countries, employment, service in the military or Peace Corps, or 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 for HIV vaccine or vaccine trial–related research only. 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.

In the United States, the US government has given the HVTN a Certificate of Confidentiality to help 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 indication that they *prevent* HIV infection. Since this is a Phase I trial testing for safety and immune response, it is not intended to test whether the study vaccines can protect against 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. Participants are counseled to avoid behavior that would put them at risk of HIV infection. If a participant becomes HIV infected during the study, his or her participation in the study will be terminated. The participant will be referred to an appropriate doctor for medical care and counseling, but the study staff will want to continue to monitor his or her health. If there are any other studies for which a participant is qualified and wants to join, he or she will be asked to provide an additional blood specimen and sign a new consent form that will explain the details of that study.

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

Depending on the results of HVTN 055 and other trials, this experimental vaccine might be tested further in a larger trial. Such a trial would test safety in more people, and give a better idea of whether the immune system responds to a vaccine. If results remain promising, more trials would be planned to see if the study vaccine helps prevent HIV infection. Participants in HVTN 055 will not be eligible for any future trials 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 are made by Therion Biologics Corporation.

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

The HIV Vaccine Trials Network (HVTN) is running the trial. The HVTN is a global partnership of researchers, governments, pharmaceutical industries, academic institutions, and community members. The HVTN is dedicated to conducting international clinical HIV vaccine trials in the safest, most efficient way possible. The HVTN is funded by the National Institute of Allergy and Infectious Diseases (NIAID).

**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. The FDA has reviewed the vaccines' manufacturing information, animal studies information, and the current clinical trial protocol. 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 055 are monitored by Institutional Biosafety Committees (IBC) and Institutional Review Boards (IRB) 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)