



HIV VACCINE TRIALS NETWORK

Questions and answers: HVTN 067 vaccine trial

1. What is the HVTN 067 trial?

HVTN 067 is the name of a clinical trial to test the safety and immune response of 2 experimental HIV vaccines. The trial will be run by the HIV Vaccine Trials Network (HVTN). The experimental vaccines used in this trial are described in Question 4 below.

The trial will test whether the experimental vaccines, or “study vaccines,” are 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 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, the reasons for the trial, possible risks and benefits of participation, and trial procedures.

People of many races and ethnicities have joined vaccine trials in the past and are needed in all types of vaccine research.

4. What kinds of vaccines are being tested?

HVTN 067 tests 2 experimental vaccines, named *EP-1233* (DNA vaccine) and *MVA-mBN32* (MVA vaccine). None of the products used in this study can cause HIV or AIDS.

DNA vaccine: The DNA vaccine is made of DNA, a natural substance that tells the body to produce certain proteins. It contains modified genes of HIV-1 and an adjuvant. An *adjuvant* is a substance added to a vaccine to increase the immune response. The adjuvant being used in this study vaccine is a man-made substance called polyvinylpyrrolidone (PVP).

MVA vaccine: The MVA vaccine is made from a virus called modified vaccinia Ankara (MVA). The MVA virus in the vaccine has been changed so that it cannot grow in humans or spread to other people. Like the DNA vaccine, the MVA vaccine also contains modified genes of HIV-1.

5. 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.

6. Why is this trial being done?

This is a Phase 1 trial, which means that its main purpose is to test whether the study vaccines are safe to give to people. Another purpose of the trial is to find out if the 2 study vaccines work well in a prime-boost regimen. In a *prime-boost regimen*, an initial vaccination (the “prime”) is given first to create an immune response in the body, and a later vaccination (the “boost”) serves to increase the body’s immune response.

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, clinical 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 MVA 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 as foreign without ever actually having been exposed to real live HIV.

This process is meant to train the immune system to recognize HIV or 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 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. Have these vaccines been studied before?

Vaccines that are similar to the DNA vaccine and the MVA vaccine used in this trial have been studied before in other trials. We do not know if this trial will have similar results.

A DNA vaccine similar to the DNA vaccine in this study has been given to more than 80 people in previous trials. MVA vaccines similar to the MVA vaccine in this study have been given to more than 850 people in previous trials. Some of the participants in these previous trial experienced headache, nausea, fever, chills, tiredness, diarrhea, and pain and/or redness at the injection site. These are common reactions to vaccinations in general. 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 if they happened for other reasons. In this study, participants will have regular testing of blood and urine to check for changes that might be caused by the study vaccine.

9. Who is eligible to participate in this trial?

Participants must be healthy adults who are between 18 and 40 years old and HIV-negative (free of HIV infection). 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 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 their sexual activity and drug use.

People who want to join the trial and are capable of becoming pregnant will be given a pregnancy test. Those who are pregnant or breastfeeding are not eligible to join. Anyone who joins the trial and is capable of becoming pregnant 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 (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 clinical trial purposes.

11. When and where is this trial being conducted?

HVTN 067 is being conducted at 3 research sites in the US only. The trial is expected to begin enrolling participants around April 2007. If all regulatory approvals are received, it will be conducted in Baltimore, MD; Nashville, TN; and Rochester, NY. The Chairperson for the Protocol Team is located at St. Louis University Medical Center.

12. What is the design of this trial?

The trial will enroll about 108 people, divided into 3 groups.

Most of the people in Group 1 will receive 2 injections of the DNA vaccine (the “prime”) intramuscularly (IM) in the deltoid muscle (upper arm) at the beginning of the trial and again 1 month later. Members of this group will then receive an injection of the MVA vaccine (the “boost”) subcutaneously (SC) in the upper arm 3 months after the trial begins and again 6 months after the trial begins.

Most of the people in Group 2 will receive an injection of the DNA vaccine IM in the deltoid at the beginning of the trial and again at 1 month, 3 months, and 6 months after the trial begins.

Most of the people in Group 3 will receive an injection of the MVA vaccine SC in the upper arm at the beginning of the trial and again at 1 month, 3 months, and 6 months after the trial begins.

Vaccines administered *intramuscularly* are injected into a muscle, while vaccines administered *subcutaneously* are injected under the skin.

A few people in each group will receive a control instead of either of the vaccines. A *control* is an inactive substance that does not contain vaccine. Researchers will compare the results from people who got the study vaccines with the results from people who got a control. This process helps researchers to measure the effects of the study vaccines. This study includes 2 different controls: the control for the MVA vaccine is Tris-buffered saline (TBS), which contains sterile salt water, and the control for the DNA vaccine contains PVP in a sterile salt water solution.

In addition to the injections, trial participants will have other clinic visits for blood draws and evaluations. An individual participant will visit the study clinic about 11 times over the course of a year.

STUDY DESIGN

Group	Number of people	First day	+1 month	+3 months	+6 months
1	30	1 mL DNA + 1 mL DNA (IM)	1 mL DNA + 1 mL DNA (IM)	0.5 mL MVA (SC)	0.5 mL MVA (SC)
	6	PVP + PVP (IM)	PVP + PVP (IM)	TBS (IM)	TBS (IM)
2	30	1 mL DNA + 1 mL DNA (IM)	1 mL DNA + 1 mL DNA (IM)	1 mL DNA + 1 mL DNA (IM)	1 mL DNA + 1 mL DNA (IM)
	6	PVP + PVP (IM)	PVP + PVP (IM)	PVP + PVP (IM)	PVP + PVP (IM)
3	30	0.5 mL MVA (SC)	0.5 mL MVA (SC)	0.5 mL MVA (SC)	0.5 mL MVA (SC)
	6	TBS (SC)	TBS (SC)	TBS (SC)	TBS (SC)

HVTN 067 is a multicenter, randomized, placebo-controlled, double-blind (within group) trial. *Multicenter* means the trial is being conducted in more than 1 research site. *Randomized* means that each participant is randomly assigned to 1 of the groups. *Placebo-controlled* means that some people are given placebo or control so that the researchers can determine the effect of the study vaccines. *Double-blind (within group)* means that while the participants and scientist will know who is in each of the 3 groups, neither the participants nor the scientists know who within each group is getting the study vaccine and who is getting the control until after the trial is over.

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. 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 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 vaccines are not causing them problems. Any new information researchers learn about the safety of the trial will be provided to all 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. Are these study vaccines safe?

Evaluating the safety of these study vaccines is one of the main purposes of HVTN 067. 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 human trials using vaccines similar to the ones used in this trial. 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 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.

15. How is the safety of the study vaccines 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 067 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.

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 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 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 vaccines 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 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 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. 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 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. 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 they *prevent* HIV infection. Participants who are receiving the study vaccine may still be able to 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 vaccines work?

It could take several years to find out if the study vaccines work. These experimental vaccines 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 see if the study vaccines help prevent HIV infection. The results of HVTN 067 will help researchers determine whether they should proceed with other trials. Participants who received the study vaccines in HVTN 067 will not be eligible for any future trial of these study vaccines.

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 DNA vaccine, *EP-1233*, was developed by Pharmexa-Epimmune (San Diego, CA, USA). The MVA vaccine, *MVA-mBN32*, was developed by Bavarian Nordic A/S (Kvistgaard, Denmark).

22. Who is conducting this trial?

The HVTN will run the trial. The HVTN is a global partnership of 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 NIAID at NIH, an agency of DHHS.

23. Who reviewed and approved this trial?

The study vaccines are considered investigational, meaning the US 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 067 are monitored by Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs) local to each clinical research center, and the safety of the trial is monitored by local Institutional Biosafety Committees (IBCs). 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