



HIV VACCINE
TRIALS NETWORK

Questions and answers: HVTN 060 vaccine trial

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1. What is the HVTN 060 trial?

HVTN 060 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 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?

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 a specific experimental vaccine to see if it is safe to give to people, and eventually to find out about whether it 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 any products used in this trial. They are not made from live HIV, killed HIV, or HIV-infected cells.

There is no possible way that the products used in this trial can cause HIV infection.

5. What kinds of vaccine are being tested?

This study tests several different products. None of the products used in this study can cause HIV or AIDS.

Main study products: gag DNA vaccine and IL-12 adjuvant

HVTN 060 is mainly testing a DNA-based vaccine. This study vaccine contains a modified gene of HIV-1 known as *gag*.

In addition to the *gag* DNA vaccine, researchers are also testing an *adjuvant* — a substance added to a vaccine to increase the immune response. The adjuvant being tested in this study is also DNA-based, containing a modified human gene known as *IL-12*. This gene is expected to express the protein interleukin 12, which can stimulate the production of disease-fighting white blood cells.

Other study products: MEP vaccine and two adjuvants

About 30 participants (out of 156) will also be given an injection of an additional study vaccine, for researchers to see if a combination of vaccines is well tolerated and causes an immune response. The different vaccine, a *multi-epitope peptide vaccine* (MEP), is the study vaccine being tested in a related trial, HVTN 056. MEP is composed of four peptides (bits of protein) that the body uses to get the attention of the immune system and train it to attack HIV. The peptides were designed in a laboratory to resemble certain parts of HIV.

MEP is given with two adjuvants, named RC529-SE and GM-CSF. RC529 consists of man-made fat molecules designed to mimic a bacterial compound known to stimulate certain cells of the immune system. GM-CSF is a protein made by the immune system that boosts the white blood cell population; it is often given to cancer patients on chemotherapy to help restore their blood cells.

6. Why is this trial being done?

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 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 and in animals, researchers are interested in finding out more about their potential. HVTN 060 is one of a set of related trials designed to test if a combination of study vaccines (*gag* DNA and MEP, as well as the adjuvants) are well tolerated, and whether they cause an immune response. Other trials in this set include HVTN 056 (mainly testing MEP) and HVTN 063 (mainly testing *gag* DNA, with an adjuvant containing a modified human gene known as *IL-15*). Another trial, HVTN 061, continues the MEP testing by testing “boosts” of *gag* DNA or of extra MEP injections in people who got MEP in HVTN 056.

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

The DNA in the study vaccine (*gag*, a gene found in HIV) instructs the body to make part of the Gag protein. The body may then react to the presence of this protein. The idea is to train the immune system to eliminate cells that show signs of HIV infection, thereby reducing the damage that HIV can do to the body. If a person later becomes exposed to HIV, hopefully the immune system could be prepared. The study vaccines used in this trial (*gag* DNA and MEP) cannot cause HIV infection themselves.

The DNA in the adjuvant (*IL-12*) instructs the body to make the protein interleukin 12, a normal protein in the body that can stimulate the production of disease-fighting white blood cells. Using an adjuvant may increase the strength of an immune response against HIV.

The key to the MEP vaccine (given to some participants; see Question 5 above) is a group of four peptides—bits of protein that the body uses to get the attention of the immune system and train it to attack HIV. The peptides were designed in a laboratory to resemble certain parts of HIV. The peptides can move into cells of the body. Once there, they are taken to the surface of the cell, where

they act like flags to catch the attention of the immune system. The immune system responds by sending infection-fighting blood cells, called cytotoxic T lymphocytes (CTLs, also called “killer T cells”), to kill the “infected” cells.

8. What do the study vaccines contain?

The *gag* DNA vaccine contains a modified HIV-1 *gag* gene and, in some doses, the *IL-12* DNA adjuvant. It also contains a small amount of bupivacaine, a local anesthetic, to help the cells take up the DNA.

The MEP vaccine contains four artificial HIV peptides (bits of protein), the RC529-SE adjuvant, and the GM-CSF adjuvant.

9. Have these vaccines been studied before?

Main study products: gag DNA vaccine and IL-12 adjuvant

The *gag* DNA vaccine and *IL-12* adjuvant have been tested in animals with no serious side effects. Animal testing, however, does not always show what will happen in people. HVTN 060 is one of two trials (the other is HVTN 063) testing these products in people for the first time.

Other study products: MEP vaccine and 2 adjuvants

The MEP vaccine (given to some participants; see Question 5 above) is being tested in people in another trial, HVTN 056. In that trial, in the first few days after injection, most participants have experienced mild to moderate pain or tenderness (or both) at the injection site. About half of the participants have experienced fatigue or have felt unwell. In a few cases, the side effects, such as fatigue, injection site pain or tenderness, were severe enough to interfere with normal daily activities. Some participants have missed work for a day. In most people these side effects gradually went away within a few days. In a few people the symptoms lasted a few days longer. No one has experienced serious side effects from the vaccine.

The adjuvant RC529-SE is being tested as part of the MEP vaccine, but otherwise has not been tested in people. GM-CSF is licensed for use in the treatment of cancer patients. Its use as an HIV vaccine adjuvant is experimental; it has been used as an adjuvant in other vaccine trials (hundreds of people) with no serious side effects.

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.

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 060 is an international trial, with research sites located in three countries. The trial is expected to begin enrolling participants around August 2005. It will be conducted in three US cities: Baltimore, MD; Birmingham, AL; and Nashville, TN. It will also be conducted in Kingston, Jamaica; and Chiang Mai, Thailand.

13. What is the design of this trial?

The trial will enroll about 156 people. It has two parts, Part A (48 people) and Part B (108 people). In both parts, most people will be given injections of study vaccines. For further comparison, a few people are given a placebo (an injection without any active vaccine or adjuvant) consisting of sterile salt water.

Part A is evenly divided into four groups. Over the course of three months, each group receives three injections of study vaccine. In particular, all groups receive the same amount of *gag* DNA vaccine (1500 micrograms), while receiving a different dose of *IL-12* adjuvant (0, 100, 500, or 1500 micrograms). An individual participant will be given the same adjuvant dose in each of the three injections; the dose is escalated for groups, not individuals. The researchers will determine whether a dose is safe and well tolerated before escalating to a higher dose.

DESIGN OF PART A

(Note: two of the 12 people in each group will be given placebo instead of the study vaccines listed here.)

Group	# of people	First day	+1 month	+3 months
1	12	<i>gag</i> DNA only	<i>gag</i> DNA only	<i>gag</i> DNA only
2	12	<i>gag</i> DNA + 100 mcg <i>IL-12</i>	<i>gag</i> DNA + 100 mcg <i>IL-12</i>	<i>gag</i> DNA + 100 mcg <i>IL-12</i>
3	12	<i>gag</i> DNA + 500 mcg <i>IL-12</i>	<i>gag</i> DNA + 500 mcg <i>IL-12</i>	<i>gag</i> DNA + 500 mcg <i>IL-12</i>
4	12	<i>gag</i> DNA + 1500 mcg <i>IL-12</i>	<i>gag</i> DNA + 1500 mcg <i>IL-12</i>	<i>gag</i> DNA + 1500 mcg <i>IL-12</i>

Part B, which begins only after Part A is complete, is evenly divided into three groups. Again, over the course of three months each group receives three injections of *gag* DNA vaccine (1500 micrograms). One of these groups will receive no *IL-12* adjuvant, and the other two groups will receive it at the highest dose from Part A that the researchers have determined is safe enough to give to more people. Then, over the course of six more months, the groups in Part B will receive two more injections: either of *gag* DNA alone, or of *gag* DNA with the *IL-12* adjuvant, or of the MEP vaccine and its adjuvants RC529-SE and GM-CSF. The course of injections for groups in Part B runs nine months altogether.

DESIGN OF PART B

(Note: six of the 36 people in each group will be given placebo instead of the study vaccines listed here.)

Group	# of people	First day	+1 month	+3 months	+6 months	+9 months
5	36	<i>gag</i> DNA only	<i>gag</i> DNA only	<i>gag</i> DNA only	<i>gag</i> DNA only	<i>gag</i> DNA only
6	36	<i>gag</i> DNA + <i>IL-12</i>	<i>gag</i> DNA + <i>IL-12</i>	<i>gag</i> DNA + <i>IL-12</i>	<i>gag</i> DNA + <i>IL-12</i>	<i>gag</i> DNA + <i>IL-12</i>
7	36	<i>gag</i> DNA + <i>IL-12</i>	<i>gag</i> DNA + <i>IL-12</i>	<i>gag</i> DNA + <i>IL-12</i>	1000 mcg MEP	1000 mcg MEP

HVTN 060 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 a study vaccine or placebo at all their injection visits. ‘Placebo-controlled’ means that some people are given placebo, so the researchers can tell if the study vaccine makes a difference. ‘Double-blind’ means that neither the participants nor the scientists know who is getting the study vaccine and who is getting the placebo until after the trial is over.

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 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 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 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 the study vaccines is the main purpose of HVTN 060. The *gag* DNA vaccine and the *IL-12* adjuvant 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 safe enough to use in human trials. The MEP vaccine is being tested in people in another trial, HVTN 056. No one in that trial has experienced serious side effects from the MEP vaccine or its adjuvants, RC529-SE and GM-CSF.

There have been earlier studies of DNA vaccines for such diseases as malaria and hepatitis B, as well as HIV. Such vaccines have been generally well tolerated, with no serious side effects.

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 the study vaccines 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 060 will monitor the safety of the trial. This team carefully considered the available information to decide if the study vaccine was safe enough to begin a human trial. The HVTN also has a Safety Monitoring Board that is independent of this particular trial. 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 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 vaccine may 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 vaccine does not mean the participant is protected from HIV infection. Trial participants will also not know whether they have received the study vaccine or the 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 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 information or for help to resolve problems.

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 may cause the body to produce these antibodies. In this case, the standard HIV test could show a positive result. If a study vaccine 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 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.

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 receiving injections, but clinic staff will ask to continue monitoring their health for the rest of their scheduled time in the trial, and the researchers will test to see how the body controls HIV infection.

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?

Depending on the results of HVTN 060 and other trials, these experimental vaccines might be tested further in a larger Phase II 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 vaccines help prevent HIV infection. Participants in HVTN 060 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 were developed by Wyeth Vaccines Research.

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, pharmaceutical companies, 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 060 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

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