



Questions and Answers: HVTN 042 HIV Vaccine Trial

WHAT ARE THE NAMES OF THE EXPERIMENTAL VACCINES USED IN THIS TRIAL?

Researchers call these experimental vaccines the LIPO-5 vaccine and the ALVAC-HIV (vCP1452) vaccine. The HIV Vaccine Trials Network (HVTN) is conducting the trial, which is referred to as HVTN 042.

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 so that researchers can prove that the experimental vaccine is safe, and eventually to find out more 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.

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 the following: information about HIV and AIDS; the reasons for the trial; possible risks and benefits of participation; and trial procedures.

CAN AN EXPERIMENTAL HIV VACCINE CAUSE AIDS OR HIV INFECTION?

It is impossible to get HIV infection or AIDS from these experimental vaccines. These experimental vaccines are made in a laboratory. They are not made from live HIV or from HIV-infected cells. They do not contain live or killed HIV.

THERE IS NO POSSIBLE WAY THAT THESE HIV EXPERIMENTAL VACCINES CAN CAUSE HIV INFECTION.

WHAT KIND OF EXPERIMENTAL VACCINES ARE BEING TESTED IN THIS TRIAL?

The LIPO-5 vaccine is called a lipopeptide vaccine. Peptides are small pieces of proteins that the body uses to get the attention of the immune system and prepare it to attack. The ALVAC-HIV vaccine is a live vector vaccine made from a virus unrelated to HIV. The live vectors used in vaccines are chosen or engineered not to cause disease themselves. Live vectors can carry information about HIV into the body to help teach the immune system how to fight against HIV.

WHY ARE THESE EXPERIMENTAL VACCINES BEING TESTED?

Based on the research that has been done so far, these experimental vaccines have shown some promising characteristics. After testing the experimental vaccines in the laboratory and in animals, researchers are interested in finding out more about their potential. In this trial, researchers are making sure that the vaccines are safe and do not cause health problems at various dose amounts. They will also see if the experimental vaccines cause an immune response. The two vaccines are being tested together because researchers believe that pairing these vaccines in what is called a prime-boost regimen may create a better immune response than either vaccine approach alone.

WHAT IS THE EXPERIMENTAL VACCINE LIPO-5 SUPPOSED TO DO?

The first experimental vaccine, LIPO-5, is a lipopeptide vaccine. The body uses peptides, which are tiny pieces of proteins, to 'communicate' with the immune system. In a peptide vaccine such as LIPO-5, particular peptides from HIV genes are chosen because they contain information that researchers think will be important to teach the immune system how to recognize and fight HIV. Lipids, a type of fat cell, are used to help the body absorb the peptides. Joining the lipids and the peptides makes a lipopeptide, which may produce a better response than peptides alone.

In a lipopeptide vaccine, the lipopeptides are able to move into the cells of the body. Once inside the cells, the peptides are taken to the surface of the cells, where they serve like tiny flags to catch the attention of the immune system. A part of the immune system that fights infection (killer T-cells) is then able to 'read' the peptides. Hopefully, the information that killer T-cells get from the peptides will help the body learn how to fight HIV if the body is ever exposed to the virus in the future due to natural infection.

WHAT IS THE OTHER EXPERIMENTAL VACCINE, ALVAC, SUPPOSED TO DO?

In the ALVAC vaccine, canarypox is the live vector that is used to carry information about HIV. Canarypox is a disease that affects birds but does not cause disease in humans. The canarypox can do two things: it can carry a large amount of information about HIV, and it can stimulate an immune response. This response is a way to get the attention of the immune system, and the HIV information that the canarypox carries may give the immune system the specific tools it needs to recognize and fight HIV.

HAVE THESE EXPERIMENTAL VACCINES BEEN STUDIED BEFORE?

The LIPO-5 experimental vaccine has been tested in 14 people, with no serious side effects. A very similar vaccine has been tested in over 100 people with no serious side effects.

The ALVAC experimental vaccine has been tested in over 800 people with no serious side effects. A very similar experimental vaccine has been tested in over 2,000 people with no serious side effects.

This is the first human trial to test the LIPO5 and ALVAC experimental vaccines in combination.

WHO IS ELIGIBLE TO PARTICIPATE IN THIS TRIAL?

Healthy, HIV-uninfected men and women between the ages of 18 and 50 who meet certain criteria are eligible for the study.

WHAT INFORMATION IS GIVEN TO POTENTIAL TRIAL PARTICIPANTS?

Interested volunteers are given a full range of information about the potential risks and benefits of their participation. Each potential participant is taken through an informed consent process in which the details of the trial plan and the risks and benefits are discussed and questions are answered. If new information about the safety of the vaccines is learned in the course of the trial, participants will be informed in a timely fashion. Trial information is conveyed in a manner understandable to each of the communities in which there is a trial.

HOW CAN A PERSON FIND OUT IF HE OR SHE IS QUALIFIED TO BE IN THE TRIAL?

To see if they qualify to take part in this trial, potential participants will be asked about their medical history and have a physical examination. Potential participants will have blood drawn for routine analysis. A urine sample will also be collected for routine urine analysis. A series of personal questions will be asked about sexual activity and drug use. Pregnancy tests will be administered to women who want to join the trial. Women who are pregnant or breast-feeding will not be allowed to participate in this trial. All potential trial participants are screened to make sure that they are HIV negative upon entering the trial. Information about participants will be kept confidential and will be used only for trial purposes.

WHEN AND WHERE IS THE TRIAL BEING CONDUCTED?

The trial will take place in ten continental U.S. cities: Boston, Massachusetts; Providence, Rhode Island; Rochester, New York; New York, New York; Baltimore, Maryland; Birmingham, Alabama; Nashville, Tennessee; St. Louis, Missouri; San Francisco, CA; and Seattle, Washington.

WHAT IS THE DESIGN OF THIS TRIAL?

This trial is planned to enroll 174 people, with approximately 17 people per site. Participants will be divided into five groups. One group will receive the LIPO-5 vaccine alone, one group will receive the ALVAC vaccine alone, and three groups will receive the two vaccines together. Each of the three combination groups will receive a different amount of LIPO-5 in combination with a fixed amount of the ALVAC vaccine. Participants will be randomly assigned to these treatment groups.

Each participant will be involved for 30 months (two-and-a-half years), and the whole trial will take place over approximately 3 years. There will be approximately eleven planned clinic visits. Injections will be given at four of these visits. Two of the groups will be receiving one injection per visit. Three of the groups will have two visits with one injection per visit, and two visits during which there will be two injections. Each participant will receive his or her injections within a six-month period. All clinic visits will occur in the first 18 months. During the final year of study participation, participants will be contacted every six months via phone, mail, or email with follow-up questions.

This trial is randomized, which means that the trial participants are randomly assigned to a treatment group. Some of the participants will get one or both of the experimental vaccines, and some will get a placebo, depending on which group they are randomly assigned to. A placebo is an inactive substance that allows scientists to study if there is a difference between those who get the experimental vaccine and those who do not. Since the trial evaluates the experimental vaccines in relation to the placebo, the trial is called 'placebo-controlled.' This study has two different placebos. Neither the participants nor the doctors, clinic staff or scientists know who gets the experimental vaccines and who gets the placebo, and that means the trial is 'double-blinded'. Thus, scientists refer to this trial as a randomized, placebo-controlled, double-blinded trial.

HOW WILL THE SAFETY AND RIGHTS OF THE 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 deciding to enter the trial, potential participants are provided with the following: information about HIV and AIDS; the reasons for the trial; possible risks and benefits of participation; and trial procedures. Written information will be provided, and clinic staff will devote time to discussion with participants in order to make sure that all of their questions are answered.

During the trial, the clinic staff will monitor the participants to make sure that the experimental vaccines are not causing problems. If researchers learn any new information about the safety of the trial, this information will be provided to study participants. Participants will be able to decide whether or not to stay in the study based on any new information they learn.

Participants will be reminded frequently that being part of this trial does not mean that they are less likely to become infected with HIV. Participants are provided with counseling at each visit that includes an explanation of current proven ways to avoid HIV infection (including, for instance, correct and consistent condom use).

Clinic staff will take time to answer all of a potential volunteer's questions. People who are eligible and willing to participate after the study has been fully explained to them will be asked to sign an informed consent form before they enroll in the study. This form will help ensure that participants have been given all the information they need. Participants will be given plenty of time to consider whether or not they want to join the trial. Participants do not have to join the study. Participants can leave the study at any time without losing the benefits of their standard medical care.

ARE THESE EXPERIMENTAL VACCINES SAFE?

These experimental vaccines seem to be well-tolerated by the body. These experimental vaccines are still new, however, and scientists do not know everything about them yet. The ALVAC experimental vaccine has been tested in over 800 people, and the LIPO-5 experimental vaccine has been tested in 14 people, and neither experimental vaccine

has caused any serious side effects. Some vaccines can cause a reaction at the site of injection, such as swelling or soreness, or mild flu-like symptoms such as headache, aches, and fever. Such reactions tend to be mild and usually resolve (end) within a few days. Two participants in past trials of a different LIPO experimental vaccine have had an inflammation of the eye, which scientists do not think is related to the experimental vaccine. They are not yet sure, however, so clinic staff will watch carefully for this possible side effect.

While scientists believe that there are no serious safety risks with these experimental vaccines, there is always the possibility that there could be problems that no one expected. This is why this experimental vaccine, like any new drug or vaccine, needs to be tested in participants in a controlled clinical setting. Participants' health and safety will be closely monitored throughout the trial.

The experimental vaccine does not contain live HIV virus, and therefore there is no way for the experimental vaccine to cause HIV infection.

HOW IS THE SAFETY OF THESE EXPERIMENTAL 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 U.S. Food and Drug Administration (FDA); the U.S. National Institute of Allergy and Infectious Diseases (NIAID), and the HIV Vaccine Trials Network (HVTN).

The team that designed the protocol (trial plan) will monitor the trial throughout its duration. This team includes a range of people, from scientists and doctors to community members. In addition to the protocol team, the HVTN has a Protocol Safety Review Team and a Safety Monitoring Board. Both of these groups will carefully monitor the safety of the participants. If there seem to be any problems, the trial will be put on hold. After additional review by those independent of the study, the trial can be stopped, if necessary.

ARE THERE NON-MEDICAL RISKS TO PARTICIPATING IN AN HIV VACCINE TRIAL?

Potential trial participants should consider the ways in which becoming a trial volunteer could affect their lives. 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 instance, spouses, friends, and family members may become upset when they learn about a participant's involvement in a trial. 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. People have experienced discrimination when they told others that they were participating in clinical research for an HIV vaccine. Participants are asked to carefully consider all the risks, physical and personal, before they decide to participate in a trial.

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 your immune system) 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 experimental vaccines cause a participant to get this result, it does not mean that he or

she 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 will be counseled to only get HIV testing done at their trial site because the site will have 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 experimental vaccines. No medical side effects or health problems are associated with appearing HIV infected on certain tests. However, others may treat participants unfairly if the experimental vaccines cause them to receive a false positive test result. Participants will not be able to donate blood and they may also have difficulties with the following: getting insurance, medical/dental care, traveling to other countries, employment, Military/Peace Corps service, or relationships with friends and family. Clinic staff are available to help with any difficulty, and services exist to help participants if they receive a false-positive HIV result.

It is important to remember that being given the experimental vaccines does not mean the participant is protected from HIV infection that is due to sexual contact, sharing of injection drug equipment, or any other transfer of blood or bodily fluids. Trial participants will also not know whether they have received the experimental vaccines or the placebo, which is an inactive substance 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 help or information. Study staff will be able to talk to insurance companies, employers, and others to explain a participant's participation in the study.

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 will have only a participant ID number, not a name. Samples used for tests are only identified by number, not by name. Any test results are confidential, and will not be made part of your medical records. We cannot guarantee absolute privacy. Most groups that review the safety of and conduct the trials will be able to review the records. All the members of these groups are obligated to keep any information confidential. Additionally, certain information about trial participants may be released if required by law.

In the United States, the U.S. 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 participants at the trial sites.

WHAT WILL HAPPEN TO PARTICIPANTS IF THEY BECOME HIV-INFECTED FROM THEIR BEHAVIOR DURING THE COURSE OF THE TRIAL?

If a participant gets the experimental vaccines, it does not mean that he or she is protected from HIV infection. Since this is a Phase I trial testing for safety and immune response, it is not intended to test whether the experimental vaccines can protect against HIV infection. All participants must be HIV negative when they enroll in the trial. The experimental vaccines cannot cause infection with HIV. 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 experimental vaccines. *Participants will be counseled to avoid behavior that would put them at risk for HIV infection.*

If a participant becomes HIV infected during the study, he or she will not receive any additional injections. 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.

HOW LONG WILL IT TAKE TO FIND OUT IF THESE EXPERIMENTAL VACCINES WORK?

This study is an important step in understanding how these experimental vaccines work. Researchers will gather data about the safety of the experimental vaccines, and will start to answer questions about how they make the immune system respond. This kind of trial is called a Phase I trial. If the experimental vaccines look promising, they can move into a Phase II trial. Phase II trials involve more people and answer more questions about safety and immune response. The most promising experimental vaccines can then be tested in Phase III trials, in which researchers can find out if the vaccine works effectively. It will be many years until researchers have a vaccine that will be effective, but this trial is an important way to move the world closer to an HIV vaccine.

WHO IS SPONSORING THE 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 U.S. Department of Health and Human Services (DHHS), in collaboration with the French Agence Nationale de Recherche sur le SIDA (the National Agency of AIDS Research). The product was created by Aventis-Pasteur, Inc.

WHO IS CONDUCTING THE TRIAL?

The HIV Vaccine Trials Network (HVTN) will run 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).

WHO REVIEWED AND APPROVED THE TRIAL DESIGN?

The experimental vaccines are made according to the guidelines established by the U.S. Food and Drug Administration (FDA), and have been reviewed by them. The experimental vaccines are considered investigational, meaning that the FDA will allow the use of these experimental vaccines only in research with a small number of participants. The protocol team (the people who designed the trial) also carefully reviewed the information about the experimental vaccines before deciding to begin the trial.

Additionally, the trial and the participants' safety and rights are monitored by local Institutional Bio-Safety Committees and Institutional Review Boards (IRB) or Ethics Committees. All of these committees are local to the sites at which the trial is conducted. Community members are involved throughout the process in order to help ensure that participants' rights are protected and that their needs are being met.

HOW CAN I OBTAIN MORE INFORMATION ABOUT THE TRIAL?

For more information about AIDS vaccine clinical trials, please visit the *AIDSinfo* website at www.aidsinfo.nih.gov or call (1-800-448-0440) from within the United States. For more information about the HIV Vaccine Trials Network (HVTN), visit our website at www.hvtn.org.