



## **Questions and Answers: HVTN 044 HIV Vaccine Trial**

### **WHAT IS THE HVTN 044 VACCINE TRIAL?**

HVTN 044 is a trial to look at the safety and immune response of an experimental HIV vaccine. The term 'HVTN 044' is the name that the HIV Vaccine Trials Network (HVTN) uses to refer to this particular trial. The experimental vaccine is called VRC-HIVDNA-009-00-VP, and it is a DNA plasmid vaccine. In addition, there is an adjuvant, or 'helper,' that is also made of DNA plasmid. This adjuvant is called VRC-ADJDNA004-IL2-VP.

This vaccine is NOT produced from live virus or from HIV-infected human cells, so there is NO possibility that it contains live or killed HIV virus. Therefore, there is NO WAY to get HIV infection or AIDS by receiving this vaccine.

### **WHY IS THE TRIAL BEING DONE?**

Scientists want to know more about this experimental vaccine in order to find out if it can make the immune system respond in ways that could help the body fight HIV. Laboratory research has shown that this experimental vaccine might be able to cause an immune response, and scientists have to find out if the vaccine works the same way in people. This trial is called a Phase I trial, which means that it will primarily test to see if the experimental vaccine is safe in varying dose amounts, and will also note if it has an effect on the human immune response.

This trial is specifically being done to determine the safety and immune response of this experimental vaccine used in combination with an adjuvant, or helper. The adjuvant is intended to help the body respond to the vaccine. The experimental vaccine used in this trial is currently being tested by itself in another trial (referred to as protocol VRC 004) conducted by the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID).

### **WHAT KIND OF EXPERIMENTAL VACCINE IS BEING TESTED IN HVTN 044?**

The experimental vaccine is a DNA plasmid vaccine that encodes the proteins Gag, Pol, and Nef from Clade B HIV-1, and the Env protein from Clades A, B, and C HIV-1. This vaccine will be combined with a DNA plasmid cytokine adjuvant, which produces the protein IL-2/Ig (See below for further explanation).

### **HOW COULD THIS EXPERIMENTAL VACCINE HELP PREVENT HIV/AIDS?**

The base of this vaccine is a DNA plasmid. Plasmids are biological structures made up of DNA. Plasmids are easy to work with, and scientists can put small pieces of genes from other organisms into them. Plasmids then carry this new material inside their structure. It is what they are carrying, though, that does the real work.

In this experimental vaccine, scientists use synthetic (man-made) HIV genes. Genes hold instructions for making proteins. These synthetic genes are put into the DNA plasmid, which carries the genes into the body. Once there, the genes are expected to produce proteins that are very similar to the ones that the HIV virus makes. Scientists think these proteins will teach the body how to defend itself against HIV. The body will hopefully learn to recognize these proteins, and then if the body is exposed to HIV in the future it might remember how to fight it.

### **WHAT DOES THE HVTN 044 VACCINE CONTAIN?**

In this experimental vaccine, the plasmid contains several synthetic genes. These genes are all made based on subtype B HIV-1. Subtypes, which are also called clades, are slight variations of HIV. Scientists do not yet know if these subtypes will matter in developing a vaccine. The genes that are carried by the plasmid are expected to produce four different proteins normally made by HIV: Gag, Pol, and Nef. There are also three genes that will make the Env protein, one each from subtype A, B and C. These man-made genes are a tiny part of the information in HIV.

This trial is studying the experimental vaccine along with another substance, which is called an adjuvant. A vaccine adjuvant is any substance given along with a vaccine that helps the body respond to the vaccine. The adjuvant used in this experimental vaccine is another man-made plasmid DNA. This DNA will tell the body to make a small amount of an artificial protein called IL-2/Ig. The IL-2/Ig protein has two parts: One part is called Interleukin-2, or IL-2, which is a type of protein, normally produced by the body that has been used by doctors to treat some diseases. The other part of IL-2/Ig is called immunoglobulin, or Ig, which is another type of protein also produced by the body normally. Scientists believe that the IL-2 protein attached to the Ig protein, called IL-2/Ig, will stay in the body longer than IL-2 protein by itself. They believe that if the IL-2/Ig protein stays in the body longer, it will help people develop an immune response to the DNA vaccine.

Some groups within the trial will receive placebo, or inactive substance. The placebo used in this trial is saline solution (sterile salt water).

### **CAN THIS EXPERIMENTAL VACCINE CAUSE HIV INFECTION?**

*It is impossible to get HIV infection or AIDS from this experimental vaccine.* This experimental vaccine is made in a laboratory. It is not made from live HIV or from HIV-infected cells. It does not contain live or killed HIV.

**THERE IS NO POSSIBLE WAY THAT THIS HIV EXPERIMENTAL VACCINE CAN CAUSE HIV INFECTION.**

### **HAS THIS EXPERIMENTAL VACCINE BEEN STUDIED BEFORE?**

This experimental vaccine has been given to about 50 people in one trial that is currently ongoing. There have been no serious side effects observed so far. A similar experimental vaccine has also been given to a small number of people in a trial that is currently running, and there have been no observed significant problems related to the vaccine in this trial either. The experimental vaccine was tested in monkeys, mice and rabbits, with no evidence of harmful side effects or toxicity. Lab tests also show that the

experimental vaccine produced potentially promising immune system responses in mice and monkeys. Based on this information, scientists believe that the experimental vaccine looks safe, and that it causes enough of an immune response in animals that it is worth studying in humans.

### **IS THIS EXPERIMENTAL VACCINE SAFE?**

DNA plasmid vaccines seem to be well-tolerated by the body. Other kinds of HIV-1 DNA vaccines have been given to over one hundred participants with no serious side effects from the vaccine. This experimental vaccine is new, however, and scientists do not yet know everything about the safety risks of this candidate. Possible risks include autoimmune problems (where the body reacts against its own tissues) and incorporation of vaccine DNA into the body's DNA, which could cause cancer or other unknown results. Scientists have not seen any evidence of this happening in the laboratory, animals or people, but the possibility exists. If researchers learn of any new risks during the course of the trial, the participants will be informed.

While scientists believe that there are no serious safety risks, 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 THE EXPERIMENTAL 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 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. The protocol team looked carefully at the information about the experimental vaccine to make sure that they thought it was safe enough to begin the trial. In addition to the protocol team, the HVTN has a Safety Monitoring Board, which will carefully watch to make sure nothing goes wrong. 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.

### **WHEN AND WHERE IS THE STUDY BEING CONDUCTED?**

The trial began in December, 2003 at three sites in the continental United States: Columbia University, New York, NY; the University of Maryland, Baltimore, MD; and the Harvard Medical School, Boston, MA.

**WHAT IS THE DESIGN OF THIS TRIAL?**

This trial will enroll approximately 70 people, with approximately 23 people per site. Participants will be divided into five groups, each of which will be divided into four treatment sections: DNA plasmid experimental vaccine and adjuvant; DNA plasmid experimental vaccine and placebo; placebo and adjuvant; and placebo alone. Participants will be randomly assigned to these treatment sections. Neither participants nor clinic staff will know who is in which treatment section until the end of the study.

Each participant will be involved for 18 months, and the whole trial will take place over approximately 2 years. There will be sixteen planned clinic visits for 54 participants. At four of these visits two injections will be given, one into each arm, for a total of eight injections given on four different days. For 16 participants there will be a total of 20 planned clinic visits, with eight visit days on which injections will be given. These participants will receive a total of 16 injections given on eight different days. Each participant will receive his or her injections within a six-month period.

This is a three-site, randomized, placebo-controlled, double-blinded study. It is called 'randomized' because the trial participants are randomly assigned to get either one of the dose schedules of the experimental vaccine, adjuvant, and/or the placebo. 'Placebo-controlled' means that some participants are given an inactive substance so that scientists can tell if there is a difference between those who get the experimental vaccine and those who do not. Neither the participants nor the doctors and scientists know who gets the experimental vaccine and who gets the placebo, and that makes the trial 'double-blinded'.

**WHEN WILL THIS EXPERIMENTAL VACCINE MOVE ON TO A BIGGER TRIAL?**

This study is an important step in understanding many of the questions about the safety of the experimental vaccine, how the experimental vaccine and the adjuvant work together, and how much the immune system responds. Depending on the results of this and other trials, this experimental vaccine might be considered for a larger Phase II trial. If the experimental vaccine moves into a Phase II trial, scientists will be looking to find out more about how to use this experimental vaccine safely and in a way that helps people's bodies fight off HIV. Participants in this Phase I trial will not be eligible for participation in any future trial of this product.

**WHO IS SPONSORING THIS TRIAL?**

This trial is sponsored by the Division of AIDS (DAIDS), a subset of the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH), all of which are departments within the U.S. Department of Health and Human Services (DHHS). The product was created by the Vaccine Research Center (VRC), which is also part of NIAID.

**WHO IS CONDUCTING THE TRIAL?**

The trial will be run by the HIV Vaccine Trials Network (HVTN), a global partnership dedicated to conducting international clinical HIV vaccine trials. The HVTN is funded by the National Institutes of Health (NIH).

**WHO REVIEWED AND APPROVED THE TRIAL?**

The experimental vaccine is considered investigational, meaning that the U.S. Food and Drug Administration (FDA) will allow the use of this experimental vaccine only in research with a small number of participants. The experimental vaccine is made according to the guidelines established by the FDA, and has been reviewed by them.

Additionally, the trial and the participants' safety and rights are monitored by the local Institutional Bio-Safety Committees and the 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 and needs are being met.

**WHO IS ELIGIBLE TO PARTICIPATE IN THIS STUDY?**

Healthy, HIV-1-uninfected adults of either gender between the ages of 18 and 40 who meet certain criteria are eligible for the study.

**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 ensure that they are HIV negative upon entering the trial.

**HOW WILL THE PARTICIPANTS BE PROTECTED?**

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. Any new, experimental vaccine may have both medical and non-medical risks.

During the trial, the clinic staff will monitor the participants to make sure that the experimental vaccine is 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, explaining current proven ways to avoid HIV infection (including, for instance, correct and consistent condom use).

Participants who are eligible and willing to participate after the study has been fully explained to them will be asked to sign an informed consent before they enroll in the study. Participants will be given plenty of time to consider whether or not they want to

participate. 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 THERE NON-MEDICAL RISKS?**

There are ways in which being a vaccine participant can cause personal problems. Spouses, friends, and family members may become upset when they learn about a participant's participation. Participating in a trial also restricts a participant's behavior. For instance, some 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 you to appear HIV positive. Standard HIV tests look for antibodies (parts of your immune system) that recognize HIV. The experimental vaccine may cause the body to produce these antibodies. In this case, the standard HIV test could show a positive result. If the experimental vaccine causes a participant to get this result, it does not mean that he or she is infected with HIV. Further tests can be given to clarify whether the participant has what is called a *false positive*. A false positive means that some tests make a person look infected, while other tests show that there is actually no infection.

It is important to remember that being given the experimental vaccine does not mean the participant is protected from HIV infection that is due to sexual contact or the transfer of blood or bodily fluids. Participants are therefore counseled to avoid behavior that will put them at risk of HIV infection.

Participants will be counseled to only get HIV testing at their trial site because the site will have access to specific tests, which can differentiate between appearing HIV positive and true HIV infection. 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 vaccine causes them to appear HIV positive. 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. Services exist to help participants if they receive a vaccine-induced positive-HIV result.

To help avoid these problems, 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 HAPPEN TO PARTICIPANTS IF THEY BECOME HIV-INFECTED FROM THEIR BEHAVIOR DURING THE COURSE OF THE TRIAL?**

Since this is a Phase I trial testing for safety and immune response, it is not intended to test whether the experimental vaccine can protect against HIV infection. All participants must be HIV negative when they enroll in the trial. The experimental vaccine cannot cause infection with HIV. Being given the experimental vaccine does not mean that the participant is protected from HIV infection. 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 participants will be referred to an appropriate doctor for medical care, but the study staff will want to continue to monitor their 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 CAN I OBTAIN MORE INFORMATION ABOUT THE TRIAL?**

More information about AIDS vaccine clinical trials can be obtained by calling the AIDS Clinical Trials Information Service (1-800-TRIALS-A) from within the United States or by visiting their website at [www.clinicaltrials.gov](http://www.clinicaltrials.gov). More information about the HIV Vaccine Trials Network (HVTN) can be found on their website at [www.hvtn.org](http://www.hvtn.org).