

Information About the HVTN 048 Vaccine Trial

(updated 5/15/03)

WHAT IS THE HVTN 048 TRIAL?

HVTN 048 is a trial to look at the safety and immune response of an experimental HIV vaccine. The vaccine candidate is called EP HIV-1090, and it is known as a DNA plasmid type of vaccine. Scientists designed this vaccine candidate to teach the human body how to fight off HIV infection. The hope is that a vaccine can eventually keep people from becoming infected with HIV.

This vaccine is NOT produced from live virus or from infected human cell lines, so there is NO possibility that it contains live or killed HIV virus. Therefore, it is NOT possible that you can get HIV infection or AIDS by receiving this vaccine.

WHY IS THE TRIAL BEING DONE?

Scientists want to know more about this candidate vaccine because it seems to have the ability to make the immune system respond in ways that could help the body fight HIV. Once these responses have been found in studies in the lab, scientists have to find out if the candidate vaccine works the same way in people. This trial is called a Phase I trial, which means that it will test to see that the vaccine candidate is safe and that it has an effect on the human immune system.

WHAT KIND OF VACCINE CANDIDATE IS BEING TESTED IN HVTN 048?

The Epimmune EP HIV-1090 DNA plasmid vaccine.

WHAT DOES THE VACCINE CANDIDATE CONTAIN?

The vector, or carrying device, for this vaccine candidate is DNA plasmid, a small molecule of DNA that can easily be made to carry the working part of the vaccine. The working part of the vaccine is made from small, harmless pieces of HIV known as epitopes. These pieces cannot cause HIV infection. The hope is that they will teach the body's immune system how to recognize and fight HIV if it is exposed to the real virus. There is also another particular epitope, which should help the immune system have a stronger and longer-lasting response. All of this is mixed with a liquid, called an adjuvant, which helps the body absorb the rest of the vaccine into skin and muscle cells.

HOW DOES THE HVTN 048 VACCINE CANDIDATE WORK?

The vaccine candidate has been made using substances like ones in your body. These parts are put together in the lab in a new combination. The first part, DNA plasmid, is used because it works just like other substances that can be absorbed into your body. In the lab, scientists use machines to insert tiny pieces of DNA into the plasmid. The DNA pieces make proteins that are like ones in HIV. The DNA pieces are modified and cannot cause HIV no matter what happens. But they should be enough to teach your body how to fight off real HIV, in case you are ever exposed to it. Scientists have tried to make the

candidate vaccine so that it is strange enough that your body learns how to fight it, but enough like what is in your body already that it does not harm you.

HOW COULD THIS VACCINE CANDIDATE HELP PREVENT HIV/AIDS?

After the vaccine candidate is injected and is absorbed into the cells of the body, the immune system is meant to recognize that this vaccine candidate is a foreign invader. The immune system should learn to recognize and fight off the parts of the vaccine candidate that look like real HIV. Then, if the body is ever exposed to real HIV, it should have learned how to fight it off.

HAS THIS VACCINE CANDIDATE BEEN STUDIED BEFORE?

The vaccine candidate EP HIV-1090 has been given to a small number of HIV infected people in tests for the therapeutic value of this vaccine candidate. There have been no observed safety issues in these trials. The vaccine candidate has never been given to people who are not infected with HIV. There are several parts to this vaccine candidate. Some of the parts have been studied in humans, and some of them have so far only been studied in the lab and in animals. Scientists have looked carefully at the information from these studies and believe that the vaccine candidate looks safe and that it seems to help the immune system respond to HIV.

IS THIS VACCINE CANDIDATE SAFE?

Many studies have been done with animals and in the lab that show that humans should be able to safely be given this vaccine candidate. Some of the parts of the vaccine candidate have been used in people before. While some parts have been used in other drugs, however, this is a new vaccine candidate. There is always the possibility that there could be problems that no one expected. This is why this candidate vaccine needs to be tested in a few volunteers for the first time.

WHAT IS KNOWN SO FAR ABOUT HOW PEOPLE RESPOND TO THIS VACCINE CANDIDATE?

The vaccine candidate has never been given to people who are not infected with HIV. Phase I trials are currently being conducted with persons who are already HIV-infected.

CAN THIS VACCINE CANDIDATE CAUSE HIV INFECTION?

No. This vaccine is not produced from live virus, so there is NO possibility that it can contain live or killed HIV virus. In addition, the vaccine uses only a piece of the virus protein. THERE IS NO WAY TO DEVELOP AIDS FROM THIS VACCINE CANDIDATE.

HOW IS THE SAFETY OF THE VACCINE CANDIDATE MONITORED?

Many people, from scientists and doctors to community members, looked carefully at the candidate 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.

WHO REVIEWED AND APPROVED THE TRIAL?

The vaccine is considered investigational and that means that the U.S. Food and Drug Administration (FDA) and the Botswana Health Research Unit/Health Research Development Committee will allow the use of this experimental vaccine only in research with a small number of participants. The vaccines are made according to the guidelines reviewed by the FDA and the Botswana Health Research Unit. The United Nations AIDS (UNAIDS) Vaccine Committee of the World Health Organization provided an ethics review of the study.

WHO IS SPONSORING THE 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 Epimmune, Inc. The HIV Vaccine Trials Network will conduct the trial.

WHEN AND WHERE IS THE TRIAL BEING CONDUCTED?

The study will begin May, 2003. The trial is being conducted through the Harvard Medical School in Boston, Massachusetts, St. Louis University in St. Louis, Missouri, and the Botswana-Harvard Partnership for HIV Research and Education in Gaborone, Botswana.

WHAT IS THE DESIGN OF THIS TRIAL?

Forty-two people will be enrolled in the trial, with 36 of those receiving candidate vaccine and six people getting a placebo. Volunteers will be assigned randomly to receive one of three different dosage amounts. The trial will last 18 months, with the injections received over a six-month course, followed by a year of observation. There will be 12 clinic visits, 4 injection dates, and 12 blood draws.

This is a multi-center, randomized, adjuvant-controlled, double-blinded study. It is multi-center because there are several 'centers,' or sites, where people are being given the candidate vaccine. It is called 'randomized' because the trial participants are assigned to get either one of the three dosages of the candidate vaccine or the placebo randomly. 'Adjuvant-controlled' means that the bit of the vaccine candidate that helps the body absorb the vaccine is also given to the control group. This is like saying that everyone gets the same basic liquid in his or her shot, whether or not the working part of the vaccine candidate is there. Neither the participants nor the doctors and scientists know who gets the vaccine candidate and who gets the placebo, and that makes the trial 'double-blinded'.

WHEN WILL THIS VACCINE CANDIDATE MOVE ON TO A BIGGER TRIAL?

This study is an important step in understanding many of the questions about the safety of the vaccine candidate, what the best dose is, and how much the immune system responds. Depending on the results of this trial, this vaccine candidate might be considered for a larger Phase II trial. If the vaccine candidate moves into a Phase II trial scientists will be looking to find out more about how to use this drug safely and in a way

that helps people's bodies fight off HIV. Participants in this trial will not be eligible for participation in a Phase II trial of this product.

WHY IS THIS VACCINE BEING TESTED IN BOTH THE U.S. AND AFRICA? DOES THIS MEAN THAT A VACCINE THAT WORKS IN THE U.S. COULD ALSO WORK IN AFRICA OR ASIA?

HIV treatment drugs work against all strains of HIV. The goal is to discover a vaccine that also works for everyone. HIV vaccine scientists are committed to provide an HIV vaccine that will help everyone, in all countries.

WHO IS ELIGIBLE TO PARTICIPATE IN THE TRIAL?

Generally healthy, HIV-1 uninfected adults (male and female) between the ages of 18 and 40.

HOW WILL THE VOLUNTEERS BE PROTECTED?

Before deciding to enter the trial, potential volunteers 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 unknown risks. These may include side effects due to injection into a muscle, and issues of social harm associated with taking part in HIV studies. Volunteers will be reminded frequently that being part of this trial does not mean that they are less likely to become infected with HIV. Volunteers are provided with counseling at each visit, explaining current ways to avoid HIV infection.

Volunteers 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. Volunteers will be given plenty of time to consider whether or not they want to participate. Volunteers do not have to join the study. Volunteers can leave the study at any time without losing the benefits of their standard medical care.

ARE THERE NON-MEDICAL RISKS?

Yes. Some vaccines may cause you to appear HIV positive. Volunteers will be counseled to only get HIV testing at the trial site because the site will have specific tests which can differentiate between appearing HIV positive and true HIV infection. If a person appears HIV positive according to standard tests but does not truly have infection, there is NO possibility of medical side effects or HIV infection from the vaccine candidate. However, others may treat volunteers unfairly if the candidate vaccine causes them to appear HIV positive. Participants will not be able to donate blood and they may also have difficulties with: getting insurance, hospitalization, traveling to other countries, employment, Military/Peace Corps service, or relationships with friends and family.

Some people have experienced discrimination when they told others that they were participating in clinical research for an HIV vaccine.

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

All volunteers must be HIV negative when they enroll in the trial. The vaccine candidate cannot cause infection with HIV. If the volunteer becomes HIV infected during the study due to sexual behavior or drug use, he or she will not receive any additional injections. The participant will be referred to an appropriate doctor for medical care, but the study staff will want to continue to monitor his or her health. If there are any other studies for which the 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 A PERSON BECOME QUALIFIED TO BE IN THE TRIAL?

To see if one qualifies to take part in this trial, a potential participant will be asked about his/her medical history and have a physical examination. A participant will have blood drawn for routine tests and to check on the person's immune system. A urine sample will also be collected for routine urine analysis. There will be a series of personal questions asked about one's sexual activity and drug use. Pregnancy tests will be administered to women who are able to become pregnant. Women who are pregnant will not be allowed to participate in this trial. All potential trial volunteers are screened to ensure that they are HIV negative upon entering the trial.

HOW CAN I GET 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) or by visiting their website at www.clinicaltrials.gov. More information about the HIV Vaccine Trials Network (HVTN) can be found on their website at www.hvtn.org.