



## HIV VACCINE TRIALS NETWORK

### Questions and answers: HVTN 503 vaccine trial

Last updated November 8, 2006

#### 1. What is the HVTN 503 trial?

HVTN 503, also known as Phambili, is a clinical trial to test the efficacy and safety of an experimental HIV vaccine. The trial will be run by the HIV Vaccine Trials Network (HVTN) in conjunction with the South African AIDS Vaccine Initiative (SAAVI) and the US National Institutes of Health (NIH) National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS), and with pharmaceutical support provided by Merck Research Laboratories (MRL). The study will be conducted in the Republic of South Africa and is supported by the South African AIDS Vaccine Initiative. A companion study (known as the Step Study or HVTN 502/Merck 023) is currently underway in the Americas and Australia. The experimental vaccine, or “study vaccine,” is described in Question 5 below.

The main purposes of this trial are to obtain more information about the safety of the experimental vaccine (or “study vaccine”) in humans and to learn if the study vaccine has the potential to prevent HIV infection or lower the level of HIV in the blood if someone becomes infected. Specifically, the trial will investigate whether a vaccine designed to target Clade B HIV virus could potentially be effective in regions where Clade C is predominant.

The product in this trial is not produced from live virus or from HIV-infected human cells. There is no possibility that it contains live (or killed) HIV virus. ***There is no possible way that the product 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 a successful 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 a specific experimental vaccine to see if it is safe to give to people and eventually to find out if it might work to prevent or fight HIV infection. The people who participate in vaccine trials play an important role in the scientific research that may lead to an HIV vaccine.

#### 3. Who are the people who participate in HIV vaccine trials?

Many types of people participate in HIV vaccine trials. In this trial, all participants must meet certain criteria, as described in Question 10 below.

People have many reasons for joining HIV vaccine trials, including a desire to help others and a desire to advance scientific knowledge. 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 this study vaccine. The study vaccine is not made from live HIV, killed HIV, or HIV-infected cells.

*There is no possible way that this study vaccine can cause HIV infection.*

**5. What kind of vaccine is being tested?**

The investigational vaccine is called MRKAd5 HIV-1 gag/pol/nef. It is composed of 3 adenovirus vectors, each with an HIV gene insert.

A *vector* is a packaging system that can help deliver the vaccine more effectively into the part of the body or cells to create an immune response. In this study vaccine, the vector is a weakened form of adenovirus type 5 (Ad5), with key pieces removed so that the adenovirus cannot replicate in humans. (If adenovirus *replicates*, it causes illnesses such as colds and respiratory infections.)

A synthetic *insert* consists of some extra genes added into the vector. In this case, the genes added are HIV genes (*gag*, *pol*, and *nef*).

**6. Why is this trial being done?**

Based on the research that has been done so far, this study vaccine has shown promising characteristics. After testing the study vaccine in the laboratory, in animals, and in some people (to see if it is safe and if it provokes an immune response), researchers are interested in finding out more. Specifically, they want to know if the vaccine has the potential to prevent HIV infection completely, or if it can at least lower the level of HIV in the blood if a person becomes infected after getting the vaccine.

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

The study vaccine is designed to work by mimicking the shapes and structures of HIV. The study vaccine allows 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 without ever actually being exposed to HIV.

This process is meant to train the immune system to recognize HIV or the 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. This preparation may prevent HIV infection or could 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, including this one, need to be done to learn if the vaccine works.

**8. What do the study vaccines contain?**

The study vaccine contains the following components:

- A weakened form of adenovirus type 5
- The HIV genes *gag*, *pol*, and *nef*
- Inactive ingredients

**9. Have these vaccines been studied before?**

As of November 1, the study vaccine has been tested in more than 1300 people, all of whom have received at least 1 injection of the vaccine. Some people who received the study vaccine experienced

pain, redness, tenderness, and/or swelling at the injection site. Some also experienced fever, nausea, headache, chills, tiredness, and sore throat. These are common reactions to vaccinations in general.

In trials of study vaccines, people have frequent laboratory testing of blood and urine samples. In the blood and urine samples collected from previous trial participants who received this vaccine, some changes in test results were seen. These changes did not cause symptoms, and test results generally returned to their usual values without treatment. It is not known if the temporary changes in lab test results were related to the study vaccine or if they happened for other reasons.

**10. Who is eligible to participate in this trial?**

Participants must be healthy adults between 18 and 35 years old who have been sexually active in the last 6 months and are 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.

Pregnant or breastfeeding women are not allowed to join the trial. Women who join the trial must agree to use an effective family planning method starting at least 21 days before they get their first injection and continuing until 1 month after their last study injection, which is 6 months after joining the study.

**11. How can people find out if they are qualified to join this trial?**

People who are interested in joining HVTN 503 should contact their local study site or visit <http://www.hvtn.org> to find appropriate contact information. Potential participants will be asked about their medical history and will be given a physical examination. They then will have blood and urine samples taken for routine analysis and will be 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. All volunteers are tested to ensure they are HIV-negative (free of HIV infection).

**12. When and where is this trial being conducted?**

HVTN 503 is expected to begin enrolling participants in November 2006. When all regulatory approvals are received, it will be conducted at multiple sites in the Republic of South Africa.

**13. What is the design of this trial?**

The trial will enroll about 3000 people. Half of these people will be given 3 doses of the study vaccine over the course of 6 months, and the other half will be given 3 doses of a placebo (an injection without any active vaccine).

For the rest of the time in the trial (about 4 years), participants will be tested for HIV infection every 6 months. All trial participants will be given counseling to reduce risk behavior. Because the trial enrolls people whose behavior puts them at high risk for HIV infection, it is expected that some people will become infected despite the counseling they receive to reduce risk behaviors. Some of these people will have received placebo, but others may have received the investigational vaccine. These HIV-infected placebo and vaccine recipients will be tested to see if the study vaccine lowers the level of HIV in the blood. People who become infected with HIV will be followed for an additional 18 months after their diagnosis.

HVTN 503 is a multicenter, randomized, placebo-controlled, double-blinded trial. *Multicenter* means the trial is being conducted in more than one research site. *Randomized* means that participants are

randomly assigned to get either the study vaccine or the 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-blinded* 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?**

This trial adheres to international standards for the ethical conduct of research as established by the Helsinki Declaration of the World Medical Assembly and Council for International Organizations of Medical Sciences (CIOMS) guidelines.

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, the reasons for the trial, possible risks and benefits, and trial procedures. Clinic staff allow time for participants to talk with volunteers and ask 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 consent process will help ensure that participants have been given all the information they need. Volunteers will be given 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 will monitor participants to make sure the study vaccine is not causing problems. Throughout the trial, any pertinent 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 these study vaccines safe?**

Based on the data from animal studies and earlier trials in people, scientists believe that the study vaccine is safe enough to use in this trial. One purpose of HVTN 503 is to get more information about the safety of the study vaccine.

There have been earlier studies with these vaccines. See Question 9 above for a description of the results of these studies.

While scientists believe that there are no serious safety risks with the study vaccine, there is always the possibility that there could be problems that no one expected. This is why the study 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 study vaccine does not contain live HIV virus, so there is no way for it to cause HIV infection.

**16. How is the safety of this trial 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 scientists, doctors, community members, and

organizations such as the Medicines Control Council of South Africa (MCC); the US Food and Drug Administration (FDA); the South Africa Department of Agriculture's Genetically modified Organisms (GMO) Committee; the US National Institutes of Health (NIH); the HIV Vaccine Trials Network (HVTN); and Merck & Co., Inc. In addition, each institution conducting the trial has the study plan and consent documents reviewed by an ethics committee. For this trial, there is also an additional review by a biosafety committee for each institution.

The team that designed HVTN 503 will monitor the trial throughout its duration. This team includes a range of people, from scientists and doctors to South African 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.

There will also be an independent Data and Safety Monitoring Board (DSMB), a group of experts (not affiliated with Merck and Co., Inc.; the HVTN; or the clinical trial investigators) who will carefully monitor the safety of the trial participants. If there are safety concerns, the DSMB can recommend that the trial be modified or stopped.

**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 risks that could affect a participant's social life. Trial participation could lead to conflicts 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.

By participating in a trial, a participant also risks experiencing restrictions or limitations on normal behavior and activities. For instance, participants are asked not to donate blood, and women should avoid pregnancy until 1 month after their last study injection.

Participants may experience problems if they tell people they are taking part in clinical research for an HIV vaccine. In the case of any problems, 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. Participants could also have problems if they miss work to go to study appointments or due to feeling unwell after vaccination.

The study vaccine will likely 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. The study site can provide free testing for as long as participants need it to tell the difference between HIV infection and a positive result caused by the study vaccine.

It is important to remember that being given a study vaccine does not mean the participant is protected from HIV infection. Trial participants will also not know whether they have received a study vaccine or a 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 information or for help to resolve problems.

**18. Could the study vaccine 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 test result that is positive, even if the participant is not infected with HIV. Standard HIV tests look for antibodies (part of the immune system) that recognize HIV. The study vaccine may cause the body to produce these

antibodies. If this happens, the standard HIV test could show a positive result. If the study vaccine causes this result, it does not necessarily mean the study participant is infected with HIV. A vaccine-induced positive result means that some tests make a person *appear* infected.

There are other types of HIV tests that 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 that can differentiate between vaccine-induced positives and true HIV infection. These tests will be available for as long as the participant needs them, even after the study ends.

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 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 result.

**19. What will be done with a participant's trial records?**

Information about trial participants will be used only for research related to HIV vaccines or vaccine trials. 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.

**20. What will happen to participants if they become HIV-infected from their behavior during this trial?**

The study vaccine cannot *cause* HIV infection, but we do not know if it *prevents* HIV infection. Trial participants may 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, participants 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 vaccine works?**

Depending on the results of HVTN 503 and other trials, this study vaccine might be tested further in larger trials to see if it helps prevent HIV infection or lowers the level of HIV in the blood if someone becomes infected. Participants in HVTN 503 may not be eligible for any future trial of these products.

The results of the ongoing HVTN 502/Step Study could affect the course of HVTN 503. Because HVTN 502 is testing the same product as HVTN 503, HVTN 502 might generate new information that could change the way scientists want to study the product.

**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 are provided by Merck Research Laboratories.

**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 vaccine is considered investigational, meaning the Medicines Control Council of South Africa (MCC) and the US Food and Drug Administration (FDA) allow its use only in research. The study vaccine has been made according to MCC and FDA guidelines and was reviewed by the MCC and 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 503 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](http://www.clinicaltrials.gov)

About the HIV Vaccine Trials Network: [www.hvtn.org](http://www.hvtn.org)