

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Merck & Co., Inc. V526, 001-00, dated January 3, 2005

A Phase I Dose Ranging Study of the Safety, Tolerability, and Immunogenicity of a 3 Dose Regimen of the MRKAd5 HIV-1 Trigene and the MRKAd6 HIV-1 Trigene Vaccines Alone and In Combination in Healthy Adults

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

If you are seen at the Hospital of the University of Pennsylvania[HUP], your contacts are:

Principal Investigator:	Ian Frank, MD	(215) 662-7419
Investigators:	Pablo Tebas, MD	(215) 615-4321
	David Metzger, PhD	(215) 746-7346
Coordinators:	Joseph Quinn, RN	(215) 349-8092
	Randee Silverman, RN	(215) 349-8092

24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

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INTRODUCTION

You are being invited to take part in a research study because you are a healthy volunteer between the ages of 18 and 50. This consent form has information to help you decide if you want to participate. Take your time, read this form carefully, and ask the study doctor or staff any questions you may have.

The study doctor will be paid by the Sponsor, Merck & Co., Inc., for conducting this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to:

Test the safety of the research study vaccines (MRKAd5 HIV-1 Trigene and MRKAd6 HIV-1 Trigene) alone and in combination (to make it easy to remember, we will call it the *study vaccine*)

This is a research study to test a new vaccine that has not yet been approved for sale.

There may be reasons why you are not allowed to take part in this study. Some of these reasons include:

- You are not 18 to 50 years of age.
- You have a known history of anaphylaxis (a severe allergy that can be deadly) from or are allergic to any part of the study vaccine.
- You have received a live virus vaccine within 30 days prior to injection, an inactivated vaccine within 5 days prior to injection, or blood transfusion or blood products within 3 months prior to injection with the first dose of Study Vaccine/placebo.
- You are scheduled to receive a live virus vaccine, an inactivated vaccine, or blood transfusion or blood products within 14 days following the first dose of Study Vaccine/placebo.

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- You know or suspect that you have a problem with the way your immune system works.
- You weigh less than 105 lbs.
- You are pregnant, breast-feeding, plan to get pregnant or donate eggs, plan to get someone pregnant or plan to donate sperm during the first year of the study.
- You have a history of malignancy, with the exception of basal cell or squamous cell skin cancer.
- You have had an injection of DEPO-PROVERA™ at the planned injection site within the past year, or plan to during the first 30 weeks of the study
- You have had a recent (within 2 years) history of chronic alcohol abuse.
- You have certain medical problems. Some minor medical problems may be allowed. The study team will discuss these with you.
- You have a psychiatric problem that could affect your safety and compliance.
- You have previously received an investigational HIV vaccine.
- You are at high risk to get HIV. The study team will discuss how to calculate your risk with you.
- You are not in good health. The study team will discuss how this will be determined.
- You are unwilling or unlikely to adhere to lower risk sex practices during the course of the study in the opinion of the study doctor.

The study doctor or staff will discuss these and any other reasons why you may not be allowed to enter the study.

#### HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 146 people will be in the study; about 5-7 people will be in the study at PENN. People will enter the study in three Stages. You will be in the study about 60 weeks.

#### WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?

If you take part in the study, you will need to do the following:

- Come to the clinic for all study visits and procedures. There are about 15 study visits. If necessary, you may be asked to return to the clinic for more visits and/or lab tests. The length of the study visits will vary.
- Receive study vaccine or placebo at your 2<sup>nd</sup>, 6<sup>th</sup> and 10<sup>th</sup> clinic visit. Not everyone in this study will get the study vaccine. Some people will get a placebo, an inactive substance that does not contain vaccine. We will compare the results from the people who got the study vaccine with the results from the placebo group. This helps us to measure the effects of the study vaccine. You will be assigned by chance (like the toss of a coin) to get all shots of study vaccine or all shots of placebo. In all Stages of the study, you have about a 4 in 5 chance of receiving the study vaccine and about a 1 in 5 chance of receiving the placebo. Neither you nor the study doctor will know which of these you are getting. In case of an emergency, the study doctor can get this information.

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- Fill out a Vaccination Report Card and bring it with you to the clinic when told by the study nurse. This vaccination report card will help you keep track of how you are feeling for a while after getting each shot. We will ask you to record injection-site reactions for 5 days and record your temperature for 14 days, as well as any bad effects, medications taken, or procedures you've had. We will show you how to fill out this card.
- Agree to use birth control if you are a woman who could get pregnant. You must agree to use effective birth control for about 52 weeks (1 year) of the study. The types of birth control that we would want you to use are hormonal contraceptives (birth control pills, patches or shots), intrauterine device (IUD) diaphragm with spermicide, condoms or abstinence. If you are a man and have women sexual partners, you must agree to have each of your partners use one of the acceptable methods of birth control. If you or your partner cannot get pregnant, then you do not have to use birth control. Examples of this might include if you are exclusively homosexual, or if you have had surgery that makes it impossible for you or your partner to get pregnant.
- Avoid behaviors that could expose you to HIV infection. We will give you HIV prevention counseling that can help guide you to avoid getting infected with HIV. This includes having counseling against unprotected sex, sharing needles, or getting exposed to blood or other body fluids from a person who has HIV. The study doctor or staff will discuss this further with you.

#### WHAT WILL HAPPEN DURING THE STUDY VISITS?

When you come in for your study visits, the study doctor or staff may do any or all of the following:

- Review your medical history.
- Ask about how you have been feeling and what medications you have taken or are currently taking.
- Ask personal questions about your sexual activities and drug use.
- Perform a physical exam.
- Measure your heart rate, breathing rate, and blood pressure and take your temperature.
- Collect blood or urine samples.
- If you are a woman, you will have a pregnancy test done before each shot. If you become pregnant during the study, you will not receive any more shots. We will keep in touch with you until the end of the pregnancy or end of the study; whichever is longer.
- Review with you how to avoid getting infected with HIV.
- Test your blood for HIV. (You will be counseled about the test and your results.)
- You will get a shot with the study vaccine or placebo at Visits 2, 6 and 10. After each shot you will stay at the clinic for about 30 minutes. Clinic staff will watch to see how your body reacts to the shot.
- Teach you how to fill out the Vaccination Report Card.
- Collect your Vaccination Report Card and review with you what you have written.
- About 2 days after the first shot, you will return to the clinic for a visit. A throat swab, rectal swab, and urine culture will be taken. These will be sent to a lab for testing.
- You may have a throat swab taken if you have pink eye or respiratory symptoms such as a common cold, runny nose, or an upper respiratory infection (URI). You may have a rectal swab taken if you have gastrointestinal (GI) symptoms such as diarrhea or vomiting. Based on your urine test results after each shot, you may have another urine sample taken.

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#### WHAT BLOOD TESTS WILL BE DONE?

At most of your clinic visits and depending on the lab tests to be done, we will take about 20 to 120 milliliters of blood (about 4 teaspoons to a half cup). We will take the blood by inserting a needle into a vein.

We will use some of your blood for routine safety testing, to check your health and see if you have side effects. We will tell you the results of routine safety lab tests at your next visit, or sooner if necessary.

We will use some of your blood to test your immune response to the study vaccine or placebo. The immune system protects your body against infection. Tests will be done to see if you have ever been exposed to certain viruses like adenovirus (a virus that causes the common cold), and the HIV virus. Tests of immune response are for HIV-related or vaccine-related research only (not to check your health), so we will not tell you or the clinic the results.

#### WHAT EFFECTS COULD THE TESTS HAVE ON ME?

You may feel discomfort during some of these tests and some may also have risks, such as:

Blood samples: drawing blood from your arm may cause pain, bruising, lightheadedness, and rarely, infection.

#### ABOUT THE STUDY VACCINE

The study vaccines in this study are made from 2 different adenoviruses, adenovirus type 5 and adenovirus type 6. These viruses are similar and cause the common cold and sore throats. The adenovirus has been changed to contain man-made copies of three genes from HIV. It has also been changed so it cannot grow or cause colds and sore throats in people. Scientists call this kind of adenovirus "defective" or "weakened".

When the study vaccine is injected, it may cause your body to make proteins that look like they came from HIV. These proteins may help your body make an infection-fighting response against HIV.

The MRKAd5 and MRKAd6 HIV-1 trigene vaccines have never been given to people; however, the study vaccines have been studied in animals have been generally well tolerated. Merck has done several Phase I studies with similar vaccines (Ad5 HIV-1 gag, MRKAd5 HIV-1 gag, and MRKAd5 HIV-1 trivalent), all of which were generally well tolerated. From those studies, safety data from over 700 subjects has been reviewed. The vaccines were generally well tolerated, and people who received the trivalent vaccines had similar side effects to people who received the Ad5gag and MRKAd5 HIV-1 gag vaccines.

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The most common side effects that were experienced by people who got these study vaccines are in the section below.

#### WHAT SIDE EFFECTS COULD THE STUDY VACCINE(S) CAUSE?

The MRKAd5 and MRKAd6 HIV-1 trigene vaccines have never been given to people; therefore it is not known what side effects the vaccine may cause. However, Merck has done several studies with similar vaccines (Ad5 HIV-1 gag, MRKAd5 HIV-1 gag, and MRKAd5 HIV-1 trivalent). In those studies, the most common side effects that people had were:

- Fever
- Headache
- Fatigue or feeling tired
- Chills
- Muscle aches and pains
- Other aches and pains
- Pain, swelling, and/or redness where the injection was given

Most of these side effects were mild and did not last more than a few days. Other less common side effects have also been reported. The study doctor or staff can discuss these with you.

There is also the risk of you having an allergic reaction to the study vaccine components. You should tell your doctor if you ever had a bad reaction after receiving a shot. The study doctor or staff can discuss this with you.

There may be other side effects or risks that are not known at this time.

We do not know if the study vaccine will affect an unborn baby.

You will be told in a timely manner about significant new information that might affect your decision to stay in the study.

#### Have there been severe side effects in other studies using a similar vaccine?

As mentioned above, the study vaccine is made with a weakened adenovirus. Other experimental medicines made from weakened adenoviruses (not the study vaccine) have been used to try and treat cancer, cystic fibrosis, and other diseases.

The risks are more serious when a high dose of the weakened adenovirus is injected into a blood vessel instead of a muscle. In fact, one person died after a very high dose of a weakened adenovirus was injected into a blood vessel going to the liver during a gene therapy study. The dose was about 500 times higher than the strength of the highest dose of study vaccine that you might get in this study. In this study, you will get shots in a muscle only.

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#### **Will the study vaccine protect me from getting infected with HIV?**

If you are exposed to HIV at some time after getting the study vaccine, we do not know what will happen. The study vaccine could have a positive or negative effect or no effect on:

- Your risk of becoming infected with HIV if exposed
- The time it takes to develop AIDS after being infected
- The course of HIV infection

You might not get the study vaccine. You might just get the placebo which will not protect you. Because we do not know the effect of the study vaccine, you should avoid behaviors that could expose you to HIV infection. The study staff will talk to you about ways to lower your risk of HIV infection.

#### **Will I be able to be in studies of other HIV vaccines in the future?**

Studies of HIV vaccines are usually limited to people who have never gotten an HIV vaccine before. Being in this study may keep you from being in other HIV vaccine studies in the future.

#### **Will the study vaccine make future vaccines based on weakened adenoviruses less effective?**

If you get the study vaccine now, a future HIV vaccine may not work as well for you. Even though there are no approved vaccines made with weakened adenovirus right now, there are several other experimental vaccines similar to this one that are being tested. Someday they may turn out to be good vaccines to prevent AIDS or some other disease. If you get the study vaccine now, you may develop antibodies to adenovirus which will make these other vaccines less likely to help you.

#### **What happens if I test positive on standard HIV antibody tests?**

It is likely that the study vaccine will cause you to have a "false-positive" on standard HIV antibody tests. This means that the test results make it look like you are infected with HIV even if you are not. This occurred in about half of the people who got vaccines similar to the ones used in this study.

We will use a special combination of tests to check you for HIV infection during the study. This means we will know if you are really infected with HIV or not.

If you get tested for HIV outside of the study, the test may be the standard antibody test only, and you may get a "false positive" result.

If you have a "false-positive" test, you could be treated unfairly or be discriminated against. People may think that you are HIV infected, when really the study vaccine has given you a "false-positive" result. This misunderstanding may cause problems for you. Some problems you may have are:

- *Problems with health care.* You may have problems getting health or life insurance, or being admitted to a hospital

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- *Problems with travel and employment.* You could also have problems traveling to some other countries; immigrating to another country; entering the military, Job Corps, or Peace Corps; or getting a new job.
- *Problems with donating blood.* HIV testing is required for blood donation. If you have a positive test from the study vaccine, you may not be able to donate blood again. You should not try to donate blood during the study.
- *Problems in your personal relationships.* It may be hard for some people to understand that a study vaccine can cause a positive HIV test. It may be hard for you to explain that you really are not infected with HIV.

Because of these possible problems, you should only get tested for HIV at the study clinic. If you have to get HIV testing outside this study, talk to the study staff. You can get an identification card (ID) that shows you joined the study. The card also lists a phone number that you can call for help or information.

We can help you with any discrimination you may experience by being in this study. With your written permission, we can talk or write to insurance companies, employers, and others to explain that you are or were in the study, or to help prevent discrimination.

We do not know how long the HIV test will stay positive. If at the end of the study, you still have an HIV antibody test that is positive because of the study vaccine, you can contact the site for retesting as needed for employment, insurance, or other purposes.

#### **Are there risks from the special cells in which the study vaccine is grown?**

The study vaccine is made from a weakened adenovirus. It has to be grown in special cells in the laboratory. One part of the special cell mixture is fetal calf serum, which is made from the blood of a baby cow. Any product made from a cow raises some concern about a rare but deadly brain disease called "variant Creutzfeldt-Jacob disease" (commonly known as "mad cow disease"). Special tests have been performed to check if the material that causes mad cow disease is in the study vaccine. These tests have not found this material in the study vaccine. We think that the risk of getting mad cow disease from the study vaccine is extremely small.

#### **ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?**

Information learned from the study may help other people in the future. Since this study does not provide treatment, there is no direct benefit to you.

#### **WHAT OTHER CHOICES DO I HAVE BESIDES THIS STUDY?**

Your choice is not to participate in this study and to continue with the medical care you are receiving outside of the study.

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#### HOW WILL MY PRIVACY BE PROTECTED?

If you agree to be in this study, health data that identifies you will be kept confidential. Unless required by law, only those listed below will have direct access to your medical records to check the study information:

- the study doctor and staff;
- the sponsor;
- those working for the sponsor;
- independent ethics committees;
- inspectors from government regulatory agencies.

A more detailed explanation of how health data about you will be used and shared is included in a separate form. If you decide not to sign this separate form, you will not be able to participate in the study.

To help us protect your privacy, the U.S. government has given us a Certificate of Confidentiality. The certificate means that researchers cannot be forced to tell people who are not connected with the study that you are in it. If you would like to read the certificate, ask the clinic study staff. We will use the certificate to refuse to give information that may identify you, even in court proceedings. Sometimes the certificate cannot be used. For example, if someone from the U.S. government wants to review projects that the government pays for, we cannot withhold information. We must also cooperate to meet the requirements of the U.S. Food and Drug Administration (FDA).

Sometimes we may have to release information about you without your permission. For example, we may do this if:

- you have a disease that we must report to the health department, such as certain sexually transmitted infections;
- we suspect that you may be harming yourself or others or planning to do so.

#### WHAT ARE THE COSTS TO ME?

You will not have to pay for the study-related clinic visits, examinations, vaccines or laboratory tests.

#### WILL I RECEIVE ANY PAYMENT?

You will be paid \$50 per study visit for a total up to \$750 if you complete the study.

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#### WHAT HAPPENS IF I AM INJURED?

In the event of any physical injury resulting from the research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise available from the University of Pennsylvania.

If you are injured directly from the study vaccine, the Sponsor will pay for the reasonable costs of medical treatment, to the extent they are not covered by your medical or hospital insurance or governmental or other programs providing coverage. No other form of compensation is available from the Sponsor.

You or your third party payer, if any, may be billed for medical expenses associated with this study only if they are deemed medically necessary and if such expenses would have incurred independent of the study.

#### WHAT DO I DO IF I HAVE QUESTIONS OR PROBLEMS?

If you wish further information regarding your rights as a research subject, you may contact the Director of Regulatory Affairs at the University of Pennsylvania by telephoning (215) 898-2614. If you ever have questions pertaining to your participation in this research study or about research-related injuries, you may contact the investigators or study nurse listed on the first page of this form.

#### WHAT ARE MY RIGHTS AS A RESEARCH SUBJECT?

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. You will be treated the same no matter what you decide.

We will tell you about new information from this or other studies that may affect your health, welfare or willingness to stay in this study. If you want the results of the study, let the study staff know.

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**By signing below, you agree that:**

- You have read this consent form.
- You have had the chance to ask questions and they have been answered.
- You are aware that taking part in this study is voluntary.
- You may choose not to be in the study or to leave the study at any time by telling the study doctor. You will not be penalized or lose any benefits to which you are otherwise entitled.
- You may have to leave the study without my consent if you need other treatment, do not follow the study plan, have a study-related injury, or for any other reason.
- If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests.

**You will receive a signed copy of this consent form.**

_____ Printed Name of Volunteer	_____ Signature	_____ Date (MM/DD/YYYY)
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_____ Printed Name of Person Conducting Review Of Consent	_____ Signature	_____ Date (MM/DD/YYYY)
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