Makerere University Walter Reed Project

CONSENT TO PARTICIPATE IN RESEARCH

Title of Protocol: A Phase I, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of an Ad26.Mos4.HIV and CH505 TF chTrimer (Env) Combination to Mimic Acute HIV Viral Replication Kinetics in Healthy Adults

Sponsor: The Surgeon General, Department of the Army

Principal Investigator: Grace Mirembe, MBChB, MMed

Introduction

Thank you for your interest in this research study. This study will take place at the Makerere University Walter Reed Project (MUWRP) clinic. This study is supported by the United States Department of Defense (U.S. DoD) and funded by the Division of AIDS, National Institute of Allergy and Infectious Diseases, US National Institute of Health. The box below provides important information about the study that you should think about before deciding to join the study. We will provide more detailed information below the box. Please ask questions about any of the information before you decide whether to participate. You may also wish to talk to others (for example, your family, friends, or your doctor) about this study, before agreeing to join. If you decide to take part in this research study, you must sign and date this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information	
Voluntary Participation	You do not have to take part in this research study. It is your choice. You may decide not to participate in the study, or you may decide to stop participating in the study at any time without penalty or loss of benefits to which you are entitled.
Purpose	We are doing this research to see if the immune response produced by your body is improved when combinations of experimental HIV vaccines are given more frequently at increasing doses, as compared to giving standard doses at a slower pace. Immune responses occur when your body recognizes and defends itself against foreign substances such as bacteria and viruses by making proteins that get rid of the foreign substances. These proteins are called antibodies. Vaccines also cause immune responses, but they help teach your body how to defend itself from a virus without infecting you with the virus.
Experimental Products	There are 4 different products used in this study: 1. Ad26.Mos4.HIV – an experimental HIV vaccine that has been tested in both animals and humans and has been shown to be generally safe and well tolerated. 2. CH505 TF chTrimer – a protein that acts like the outer shell of the

	HIV virus, has been tested in animals and humans, and has been shown to be generally safe and well tolerated. This product will be mixed with the Army Liposomal Formulation QS21 (ALFQ) adjuvant. 3. ALFQ – an adjuvant that will be mixed with CH505 TF chTrimer to make it more effective by improving the immune response or causing the immune response to last longer. ALFQ has been tested in both animals and humans and was shown to cause mostly mild to moderate side effects. 4. Normal saline (sterile salt water) will be used as the placebo. The placebo does not contain any of the experimental vaccines. While each product has been separately tested in humans, this is the first time that the combination of products will be administered to humans.
Duration	You will be in this study for about 18 months or 1.5 years.
Procedures	If you participate in the study, you will: • Be randomly assigned both to a study group and to get either the experimental HIV vaccine(s) or a placebo. o Participants will be randomly assigned to either Group 1a or Group 2a until enrollment into those study groups has ended. o Participants who join the study after enrollment into Group 1a and Group 2a has ended will be randomly assigned to either Group 1b or Group 2b. o All enrolled participants will be randomly assigned to get either the experimental HIV vaccine(s) or a placebo. • Receive 1 or 2 vaccine or placebo injections in the same leg muscle (in your thigh) at multiple study visits. o Group 1a will receive two injections per visit on Study Days 1 and 57, and one injection on Study Day 169 (6 months). o Group 2a will receive two injections on Study Day 1; one injection per visit on Study Days 4, 8, and 15; two injections on Study Day 57; and one injection on Study Day 169 (6 months). o Group 1b will receive one injection per visit on Study Days 1, 57, and 169 (6 months). o Group 2b will receive one injection at each visit on Study Days 1, 4, 8, 15, 57 and 169 (6 months). • Record any side effects that you may experience for 7 days after each injection (up to 21 days after the initial injection for Groups 2a and 2b). • Have blood samples collected at each visit. • Have urine samples collected to check your health at screening (all participants) and for pregnancy testing (females only) at multiple visits throughout the study. • Undergo medical and physical examinations. • Be tested for HIV and sexually transmitted infections. • Undergo an optional lymph node biopsy, if you are interested, eligible, and provide consent for the optional procedure.

Risks	In this study, there may be risks associated with the vaccines, blood draws, the optional lymph node biopsy, and from the possibility of false-positive HIV test results due to the immune response to the vaccines. As with all experimental vaccines, not all risks are currently known. The most serious known risk is the possibility of a potentially life-threatening allergic or (rare) autoimmune reaction to the vaccines. The clinic has emergency medical equipment in place to handle both minor and potentially life-threatening allergic reactions if they should occur. There is no guarantee that you will be protected from HIV infection from receiving the experimental vaccines and there is the possibility that you could receive the placebo, so you should continue to practice all HIV infection prevention measures.
Benefits	This study is experimental and there is no guarantee that you will receive any benefit from participating. Some participants may benefit from the general health screenings in this study and the referrals for treatment if the results of these health screenings indicate an infection or are abnormal.
Alternatives	Participation in this study is voluntary and the only alternatives are to not participate or to participate in a different experimental HIV vaccine study.
Compensation	You will receive compensation for your participation in this study. You will not receive compensation for telephonic or missed visits.

Why is this research being done?

We are doing this research to see if the immune response produced by your body is improved when combinations of experimental HIV vaccines are given more frequently at increasing doses, as compared to giving standard doses at a slower pace. When an HIV infection occurs, the virus rapidly makes copies of itself and spreads throughout body. It is thought that this rapid replication and spreading of the virus might overwhelm the immune system and prevent experimental HIV vaccines from being able to teach the body how to defend itself before the vaccines becomes ineffective in the body if they are only given at one time or over a very long period of time. To counter this, researchers want to test the idea that administering vaccines more frequently can provide enough of a constant and repeated immune system stimulation that the body can learn to defend itself despite being overwhelmed by an HIV infection. This idea has been previously tested in animals, but not in humans.

The experimental vaccines in this study are: Ad26.Mos4.HIV and CH505 TF chTrimer, which will be mixed with the Army Liposomal Formulation QS21 (ALFQ) adjuvant. An adjuvant is a substance added to vaccines that can help to make the vaccine more effective by improving the immune response or causing the immune response to last longer. Both the Ad26.Mos4.HIV and CH505 TF chTrimer vaccines have been tested in animals and in humans and have been shown to be safe and well tolerated. The ALFQ adjuvant has been tested in both animals and humans and was shown to cause mostly mild to moderate side effects. While each product has been separately tested in humans, this is the first time that the combination of products will be administered to humans.

The products given in this study are not obtained by collecting them from a person and they are not generated from HIV. They are artificial products manufactured under controlled, clean conditions used for drug manufacturing. As they are not generated from HIV and do not contain HIV, **you will not be infected with HIV from receiving these vaccines**. These vaccines have not been approved or cleared by the US Food and Drug Administration (FDA) or the Uganda National Drug Authority (NDA); however, they have allowed the use of the vaccines in this research study.

Who can participate in this study?

You may take part in this study if you are a healthy male or female aged 18 to 50 years, not pregnant or breastfeeding at screening and not pregnant within 12 weeks prior to screening, at low risk for HIV infection, with a body mass index (a ratio based on your weight and height that will be calculated by the study team) between 18 kg/m^2 and 35.1 kg/m^2 who is willing and able to sign and date this informed consent form, can demonstrate an understanding of the study by achieving a passing score on a test of understanding within 3 attempts, is willing and able to comply with the study requirements, is willing to have a photo or fingerprint taken for identification purposes, is available for the duration of the study, and is willing to provide a phone number at which you can reliably be contacted. Study staff will use your phone number to follow-up with you after you receive the vaccine or placebo injection, to remind you of upcoming study visits, and to reschedule any missed visits. We would also like to collect information for an emergency contact person that would be able to help us get in contact with you if we are unable to for any reason. Study staff will only use your emergency contact if we are unable to get in touch with you within 7 days after a missed visit as we want to make sure that you are safe. You must also be free of any significant medical problems and agree to not donate blood or plasma outside of this study for at least the duration of your participation in this study. Female participants are required to undergo pregnancy testing, to not be pregnant, to not be breastfeeding, and to use an acceptable method of contraception from 45 days before enrollment until at least 12 weeks after the last injection (about 10 months in total) if of childbearing potential. Male participants must agree not to donate sperm and to use an acceptable method of contraception from screening until at least 12 weeks after the last injection (about 9 months in total).

After signing the consent form to take part in the study, you will be asked to take a test of understanding to see how much you understand the study. You must answer at least 9 out of 10 questions correctly in order to participate in the study. You may take the test up to 3 times to get a score of 9 out of 10. The physician investigator will then ask you questions and do a physical examination to see if there is any reason you should not join in the study.

You **cannot** join this study if you have:

- HIV, hepatitis B, hepatitis C, or active syphilis infection
- A history of hepatitis B infection
- Autoimmune disease or deficiency
- Diabetes (type I or II) and/or thyroid disease
- Asplenia (lack of normal spleen function)
- A chronic or significant disease or condition including sickle cell anemia, chronic hepatitis or cirrhosis, chronically recurring hives, chronic heart disease, high blood pressure that is not controlled by medication, severe asthma, chronic lung disease, kidney failure, and infection by a parasite that damages lymph nodes

- A history of cancer, other than skin cancer, unless there has been surgical and/or medical treatment that is considered to have achieved a cure
- A major surgery within 28 days prior to screening or plans to have a major surgery during the study
- A personal or family history of a bleeding problem or disorder
- A personal or family history of a blood clotting problem or disorder
- A condition known to increase the risk of blood clotting
- A history of a serious allergic reaction to any vaccines, vaccine component, or latex
- Tattoos, scars, or other marks that would, in the opinion of the investigator, interfere with the assessment of the injection sites
- Current or history of substance abuse within 12 months prior to enrollment that, in the physician investigator's opinion, could interfere with reliable participation
- Have received or plan to receive any of the following:
    - Drugs that modify your immune system within 14 days prior to enrollment or at any time during your participation in this study
    - Blood products within 120 days prior to enrollment or at any time during your participation in this study
    - Blood products that modify your immune system within 90 days prior to enrollment or at any time during your participation in this study
    - Drugs for treating active tuberculosis within 90 days prior to enrollment, unless the drugs have achieved a cure, or at any time during your participation in this study
    - A licensed or authorized vaccine from 30 days prior to enrollment in this study until at least 42 days (6 weeks) after your last study injection
      Note: You are allowed to get a flu shot or COVID-19 shot during your participation in this study as long as it is not received within 14 days before or 6 weeks after each study injection
    - An experimental vaccine or drug for conditions other than HIV within 90 days prior to enrollment or at any time during your participation in this study
    - An experimental HIV vaccine or certain experimental HIV preventative drugs at any time prior to or during your participation in this study
    - Medications that increase the risk of bleeding or blood clots within 30 days prior to enrollment or at any time during your participation in this study

In addition to the above, you may not participate in the study if you are currently in or planning to participate in another study that requires blood draws or exposure to investigational or non-investigational drugs or devices, if you are employed at the study site, or if you have a history of any condition(s) that, in the opinion of the investigators, may interfere with your full participation in the study or that may impair your ability to provide informed consent. Blood and urine will be collected to verify that you are eligible to participate in the study. If the investigator determines that you are ineligible for participation due to a temporary condition or receipt of any substances listed above, then your eligibility can be reassessed once the condition resolves and/or the window after receipt of the substances expires. Your eligibility will only be reassessed one time. The final determination of your eligibility will be based on the medical judgement of the investigator.

How many people will be in the study?
A total of 78 people will take part in this study. Of the 78 people enrolled, 62 will receive the experimental HIV vaccines and 16 will receive placebo.

How long will I be in the study?
About 18 months (1.5 years).

What will happen during this study?
If you are selected to participate in the study, you will be randomly assigned (by chance) both to a study group and to get either the experimental HIV vaccine(s) or placebo. The placebo is a sterile saltwater injection that contains no vaccine. Neither you nor the study investigator and study staff will know whether you have received the experimental HIV vaccine(s) or placebo until the end of the study. Once the last participant has completed their final study visit, we will provide a letter to you that will contain information about the group that you were in and whether you received the experimental vaccine(s) or placebo.

The injections will be administered into your leg (thigh) muscle. In clinical care, the leg (thigh) muscle is often used when giving vaccines to young children or to adults who are unable to receive an injection in their arm as it is one of the largest muscles in the body and has a large surface area. This muscle has also been used for vaccine injections in other studies without any safety issues or complaints from participants.

Participants will be randomly assigned to either Group 1a or Group 2a until enrollment into those study groups has ended. Participants who join the study after enrollment into Groups 1a and 2a has ended will be randomly assigned to either Group 1b or Group 2b. You will remain in your assigned group for the duration of your participation in this study.

- **Group 1a:** One injection of the Ad26.Mos4.HIV vaccine and one injection of the CH505 TF chTrimer+ALFQ vaccine at each visit on Study Days 1 and 57, and one injection of the CH505 TF chTrimer+ALFQ vaccine on Study Day 169 (11 participants) OR two injections of Placebo at each visit on Study Days 1 and 57, followed by one injection of Placebo at Study Day 169 (3 participants)
- **Group 2a:** One injection of the Ad26.Mos4.HIV vaccine and one injection of the CH505 TF chTrimer+ALFQ vaccine on Study Day 1; one injection of the CH505 TF chTrimer+ALFQ vaccine on Study Days 4, 8, and 15; one injection of the Ad26.Mos4.HIV vaccine and one injection of the CH505 TF chTrimer+ALFQ vaccine on Study Day 57; and one injection of the CH505 TF chTrimer+ALFQ vaccine on Study Day 169 (11 participants) OR two injections of Placebo on Study Day 1; one injection of Placebo at each visit on Study Days 4, 8, and 15; two injections of Placebo on Study Day 57; and one injection of Placebo on Study Day 169 (3 participants)
- **Group 1b:** One injection of the CH505 TF chTrimer+ALFQ vaccine at each visit on Study Days 1, 57, and 169 (20 participants) OR one injection of Placebo at each visit on Study Days 1, 57, and 169 (5 participants)
- **Group 2b:** One injection of the CH505 TF chTrimer+ALFQ vaccine at each visit on Study Days 1, 4, 8, 15, 57, and 169 (20 participants) OR one injection of Placebo at each visit on Study Days 1, 4, 8, 15, 57, and 169 (5 participants)

If you agree to take part in this research, you need to agree to the following:

After the screening visit, there are at least 13 required clinic visits and up to 10 scheduled phone visits over approximately 18 months. The first visit must be completed within 45 days after the screening visit. If the investigator determines that you are eligible to participate in the study but your first study visit is not completed within 45 days, then the screening visit must be repeated to confirm that you are still eligible. The screening visit will only be repeated one time.

Over the first 6 months, you will receive 5 (Group 1a), 8 (Group 2a), 3 (Group 1b), or 6 (Group 2b) injections into the same muscle of your leg (in your thigh). You will remain under observation for at least 30 minutes after the injections for safety. The study team will collect blood samples from you at each clinic visit for the duration of your participation. The amount of blood drawn at clinic visits will vary from about 2 teaspoons (11 mL) to less than 8 tablespoons (113 mL), depending on the visit. You might also be asked to have laboratory tests completed between regular visits if needed to check your health. The total amount of blood drawn during the study will be between 3-4 cups (up to 845 mL). All participants will give a urine sample at the screening visit, but female participants will also give a urine sample to check for pregnancy before each study injection. The Vaccine/Placebo Injection visits will take about 2-3 hours, follow-up visits will take up to an hour, and telephonic follow-up visits will take up to 15 minutes.

The scheduled phone visits will be completed in the days following each study injection visit, 8 days after the Study Day 15 injection visit (Groups 2a and 2b only), 28 days after the last study injection visit, and at months 15 and 18 so that the study team can collect information about any side effects that you may have experienced as well as ensure your safety. Since participants who are in Groups 1a and 1b will have fewer injection visits, they will have fewer scheduled phone visits. You may be asked to return to the clinic for unscheduled visits if you develop symptoms that are concerning to you or the study team, or if repeat testing is needed.

You will also be given the opportunity to participate in an optional lymph node biopsy at Study Day 71 (Visit 7). If you are willing and eligible to participate in this optional procedure, that visit will take longer than the usual visit. The lymph node biopsy procedure is optional, so you can refuse the procedure and still participate in the main research study. Additional information about the optional lymph node biopsy will be provided in a separate informed consent form.

What are my responsibilities during the study?

If you participate in this study, you will be asked to:

- Sign the informed consent form and achieve a passable score (9 out of 10 correct) on the Test of Understanding within 3 attempts.
- Provide complete and accurate information about any current or past medical conditions and any medications you have been taking or are taking now. For your safety, you must inform study staff of any new medical conditions or medications that begin during your participation in the study.
- Attend all scheduled visits and follow all of the study team's instructions.
- Be available for telephone calls from the study staff. If you cannot keep an appointment, contact the study clinic immediately to reschedule.
- Quickly inform the study investigator or study staff of any health problems, even if you think the vaccine did not cause them. This includes but is not limited to a fever of 38.5˚C

or higher that lasts more than 24 hours, a rash, hives, or difficulty in your usual daily activities (such as going to work, fixing a meal, laundry, etc.). You will be given an emergency contact card with phone numbers that you can call at any time.
- Have blood samples taken at every clinic visit.
- Complete the diary card daily during the seven days after each injection (up to 21 days after the initial injection visit for participants in Groups 2a and 2b), as instructed by the study investigator and staff. You will get a ruler to measure any injection site reactions and a thermometer to measure your body temperature. If you feel ill beyond the seven days after an injection visit, you need to inform the study investigator and continue to record any symptoms. Bring the diary card to each visit.
- Not enroll in ANY other clinical research study in which you would have blood drawn or receive an investigational or non-investigational vaccine/product while you are in this study.

You will be given a study schedule that contains details about what will happen at each visit. Except for the lymph node biopsy, the procedures and tests described in the schedule are part of the study; therefore, if you do not agree to these procedures and tests, you cannot participate in this study.

What precautions do I need to take?

There are several precautions that you need to take during this study to reduce possible risks and to ensure that the scientific study results are accurate.

- Female participants must not be pregnant or breastfeeding and, if of childbearing potential, must use an effective form of contraception for at least 45 days before starting this study. This contraceptive method must be used until at least 12 weeks after the last study injection (about 10 months in total).
- Male participants who have not had a vasectomy must agree not to donate sperm and to use an acceptable method of contraception from screening until at least 12 weeks after the last injection (about 9 months in total). Male participants who have undergone a vasectomy and who have a partner of known HIV-uninfected status, provided that the partner is the only sexual partner, are not required to use an acceptable method of contraception.
- Acceptable contraceptive methods for female participants who are of childbearing potential and for non-vasectomized male participants who have a partner of childbearing potential include:
    - Hormonal contraceptives (such as pills, injections, patches, implants, and others) that inhibit ovulation
    - Intrauterine device
    - Intrauterine hormone-releasing system
    - Prior surgical procedure in which the fallopian tubes were blocked
    - A male partner who has previously undergone a vasectomy, provided that the male partner is your only sexual partner and has a known HIV-uninfected status
    - Use of male or female condoms in combination with another method listed above
    - Abstinence from penile-vaginal intercourse
- You should use multiple methods of contraception together to ensure that they are effective at preventing pregnancy. We can provide male condoms to you at no cost. Other forms of contraception are available, at no cost to you, from any of the Health Centre 2, 3, and 4

facilities in the area as well as at the China-Uganda Friendship hospital in Naguru and the National Referral Hospital. The trained providers at these facilities can give information about the different forms of contraception and provide guidance on the proper use of each type of contraceptive. While you are able to access these services at any time, we can also provide a referral, if necessary.

- It is currently unknown if the experimental vaccines will provide protection from getting or transmitting HIV to others through sexual intercourse or exposure to infected blood (example: sharing needles for drug use) and there is the possibility that you could receive the placebo, so it is important that you continue to practice HIV infection prevention measures to stay at low risk for HIV. Information about what you can do to stay at low risk will be given to you during the HIV risk reduction counseling that is conducted prior to testing for HIV. If your risk of HIV infection increases for any reason, please inform the study staff as you may be eligible to receive a medication that can help decrease your risk of getting HIV. This medication is only meant for individuals who are at a higher risk of HIV infection, so if you are eligible to receive it then you will not be able to receive any further study injections. Even though you won't receive any further study injections, we request that you continue to attend study visits so that the study staff can monitor your health and safety. This follow-up will be done only if you are willing and able to continue.

What will happen to my samples during this study?

Blood and urine specimens: The investigators will obtain blood samples to test for any possible side effects as well as evaluate the immune response to the vaccine. Additional blood samples may be collected to ensure your safety if you experience certain side effects, including a blood clot or uncontrolled bleeding. Urine collected at study visits will be used to determine eligibility and for pregnancy tests for female participants.

HLA and other genetic tests: With your permission, part of the blood samples that we collect from you for this study will undergo genetic testing. One type of genetic testing that may be performed will identify the 'Human Leukocyte Antigen' (HLA) type. HLA is a group of proteins present on the surface of all cells in the human body with an important role in the immune response to infection. Determining HLA type is necessary to be able to perform certain research studies. Other genetic testing may be performed to look for "genetic variations" and other factors that affect your immune response. We will not notify you with the results of the genetic tests as they are not normal medical tests, and the results cannot be used for treatment purposes. You will be provided a separate form to consent to or refuse genetic testing on your samples.

What will happen to my samples after this study?

During your participation in this study, blood samples will be collected from you as already explained. Lymph node samples will also be collected, but only if you provide consent for the optional lymph node biopsy procedure. With your permission, we will store leftover samples in a secure central storage site for future research to learn more about HIV, vaccines, the immune system, and/or other medical conditions. You will be provided a separate form to consent to or refuse the storage and future use of your samples and future genetic testing. Only samples from participants who have provided consent for the storage and future use of their samples will be stored at the end of this study. If consent is not provided, the samples will be destroyed upon completion of the testing for this study.

Your samples may also be sent to collaborators outside of MUWRP and/or internationally. Your personal information will not be sent to collaborators, so they will not be able to identify you as an individual. All future research that uses stored samples must be reviewed and approved by an Institutional Review Board (IRB), which is a committee that is responsible for overseeing the safety, welfare, and rights of research participants.

Your samples will be used only for research and will not be sold. The results of this study could lead to the development of new tests, procedures, or commercial products in the future. You will not receive money or other compensation should this occur.

What are the possible risks and discomforts?

This section describes the risks associated with the experimental vaccines and other study procedures. While each product has been separately tested in humans, this is the first time that the combination of products will be administered to humans. As such, there may be additional risks related to the experimental vaccines that are currently unknown. If we learn about new risks during this study, we will tell you.

Risks associated with the optional lymph node biopsy will be described in a separate consent form that is specific to the lymph node biopsy procedure.

Possible **risks from the injection:** Temporary stinging, pain, tenderness, hardness, redness/darkening, soreness, itchiness, swelling or bruising at the injection site on your leg (thigh). There is a very small chance of infection.

Possible **risks from any vaccine:** Fever, chills, rash, aches and pains, nausea/vomiting, headache, fatigue (feeling tired), and dizziness. These types of reactions are usually greatest within the first 24 hours after vaccination and may last 1 to 3 days. While rare, there is also the possibility of a serious, even life-threatening, allergic reaction as may occur with the administration of any vaccine. The clinic has emergency medical equipment available to handle both minor and potentially life-threatening allergic reactions.

Possible **risks of the experimental vaccines:** The risks of the experimental vaccines are unknown. The most common complaints in the first few days after receiving similar vaccines include injection site pain, tenderness, redness/darkening, and itchiness as well as fever, chills, headache, aches and pains, and fatigue.

There is also a possibility that the experimental vaccines or adjuvant could uncover or worsen an immune-related disease or syndrome. A variety of experimental HIV vaccine components, like those in this study, have been extensively evaluated in humans and have not caused immune-related diseases; however, participants in this study will be closely monitored for signs and symptoms of immune-related diseases.

There is a very rare possibility that the experimental Ad26.Mos4.HIV vaccine could cause blood clots and low levels of platelets (blood cells that help your body stop bleeding). Some people have experienced these issues after receiving a COVID-19 vaccine that is made with a modified virus (adenovirus), which is used to transport the vaccine to the cells in your body. While these events were rare (i.e., less than 1 in about 300,000 people), some of the cases have been fatal. The cause

for these events is still being studied. The experimental Ad26.Mos4.HIV vaccine is also made with this modified adenovirus; however, there have been no cases of vaccine-induced blood clots and low levels of platelets reported from clinical trials that use modified adenovirus vaccines for diseases other than COVID-19. Regardless, it is very important that you seek immediate medical care at a local hospital or medical clinic if you experience symptoms like shortness of breath, chest pain, leg pain or leg swelling, severe or persistent abdominal pain, severe or persistent headaches, blurred vision or other vision changes, increased skin bruising and/or a small red or purple spot on your skin that is not at the vaccine injection site, changes in mental status, or seizures. You should also seek medical care if you find that your body is unable to stop bleeding, such as after being scratched, after receiving the experimental Ad26.Mos4.HIV vaccine. If you are unsure of where to go for immediate medical care, please call Dr. Grace Mirembe for a referral at the phone numbers found both on the back of your appointment card and at the end of this document. The costs for your medical care will be paid by the study if the care and treatment is a result of your participation in this study.

Please tell the study staff as soon as possible if you experience these symptoms or required immediate medical attention. You may be asked to return to the study clinic for a small blood draw (about 10 mL) that will allow us to assess if this event is related to the study vaccines and to answer some questions about your health.

Unknown **safety risks:** There may be unknown side effects from the study vaccine – even serious or life-threatening risks – that we do not yet know about. Please tell the study staff as soon as possible about any side effect you think you are having that may be serious or cause concern. This is important for your safety.

Possible **risks to pregnancy:** If you are pregnant, breast-feeding, or planning to become pregnant any time from the screening visit until 12 weeks after the last injection, then you cannot participate in this study. We do not know the possible effects of the study vaccine on the unborn baby or nursing infant; therefore, female participants must have a negative pregnancy test before each injection. Both male and female participants must agree to use an acceptable method of contraception as previously described.

Female participants should notify the clinic staff immediately if there is a possibility of pregnancy and upon confirmation of a pregnancy while participating in the study. Participants who become pregnant will not be eligible to receive further injections but will be asked to continue with the planned study follow-up visits for safety purposes and will be contacted later to learn about the outcome of any pregnancy that starts in the first 12 weeks after a study vaccination. You will also receive referrals to a pediatrician for an annual evaluation of your child and their growth and development. Information from these evaluations will be shared with individuals associated with this study; however, it will not contain any information that could be used to identify you or your child.

Possible **risks of blood draws:** Pain, bleeding, bruising, feeling lightheaded, fainting, or rarely, infection at the site where the blood is taken. To minimize the risks, trained health care providers will draw your blood.

Possible **risks from genetic testing:** The greatest risk associated with genetic testing is to your privacy. Genetic test results can be used to provide information about how susceptible you are to certain diseases. Used inappropriately, this information could be discriminatory (for example, by insurance companies). HLA typing can also be used to figure out who the true parent of a child is (if compared to the child's HLA type). However, the risk of this happening is extremely low because your results will not be part of your medical records, will only be labeled with your study number rather than any of your personal information, will not be sufficient to independently identify you as an individual, and we will not look at your full set of genes. Neither you nor your doctor will be given the results as the tests are for research purposes only and not used to make health-related decisions. You will be provided a separate form to consent or refuse genetic testing on your samples.

Possible **social risks:** For participants who have received experimental HIV vaccines, routine HIV testing will likely give a false positive result. A false positive result is when the HIV test indicates that you have HIV, even when you don't have an infection. This false positivity is the result of an immune response to the vaccines and may last from a period of months to years, with the reactivity decreasing through time. This false positivity will eventually disappear, but the length of time that it takes to disappear is different for each individual. The clinic has specialized HIV tests that can prove that you are not infected with HIV, and that the false positive result is simply a result of the immune response to the vaccine. This test will be completed at your convenience and free of charge, until the false positivity has disappeared. This testing can continue to be done after your study participation has ended if you are still false positive. As such, you should refrain from having any HIV tests outside of the study clinic, but if you want to or must do the HIV test outside of the study clinic, we would like you to discuss this with the investigators before doing the test to prevent possible problems if the test gives a false positive result.

Due to the potential for a false positive result, you cannot donate blood during study participation. However, even after your participation ends it is possible that you will be refused for blood donation because of your participation in an HIV vaccine trial and false positive result.

You may be treated differently by family, friends, colleagues, or other persons since they may think that you have an HIV infection or are at risk of acquiring HIV. You may be refused medical or dental services, employment, insurance, visa, or enlistment as a soldier if you have a false positive HIV result.

After you have given your written permission, the study staff will assist you with any unfair treatment because of study participation. The study team will provide counseling and education to family members, friends, and others to reduce any potential negative social impact which may occur (if you require). This includes discussion on your behalf with a health insurance company, employer, or other persons to confirm that you have participated in the study. In addition, you will be given a letter at the beginning of the study that explains your participation in this study and the possibility of a false-positive test result. All participants will receive a letter, even participants who are randomized to receive placebo injections, so that the investigators can remain blinded to vaccine/placebo assignments.

What are the possible benefits from being in this research?

There is no direct benefit for participating in this study. As part of the study procedures, you will undergo general health screenings, and some participants may benefit from knowing if the results of these tests indicate an infection or are abnormal. In addition, you and others may benefit in the future from the information that will be learned from the study if it leads to a vaccine for the prevention and/or cure of HIV.

What if new information is learned about my health?

As part of the research study, we will take blood and urine samples to check your general health. We will alert you if you test positive for HIV, syphilis, or hepatitis; otherwise, only abnormal results that are of medical concern from tests that are approved for clinical decision making will be shared. You may be asked to return to the study clinic for an unscheduled visit if repeat testing is necessary to confirm results. You will be referred for treatment for any results that are of medical concern, and you may have a copy of these lab results if you wish.

Depending on the results of the initial and repeat testing, you may become ineligible to receive any further study injections. If this happens, we request that you continue to attend study visits so that the study staff can monitor your health and safety. This follow-up will be done only if you are willing and able to continue.

What are my other options if I do not take part in this study?

Participation in this study is voluntary and the only alternatives are to not participate or to participate in a different experimental HIV vaccine study.

Will I have to pay for anything if I take part in this research?

You will not be responsible for any of the costs associated with the study procedures, however you will have to pay for your transportation to and from the clinic and you will need to have access to a phone. There are no plans to provide phones to participants.

Will I be paid to take part in this research?

You will be compensated Ug shs 70,000 for your time, transportation, and inconvenience at each scheduled in-person study visit. You will not receive compensation for phone visits or for missed visits.

You will be compensated Ug shs 30,000 for each unscheduled visit that may be requested by the study investigator, that may be required to repeat lab tests to verify/clarify results or to better evaluate abnormal lab values, to evaluate a research-related injury or illness, or to collect specimens that could not be collected at a scheduled study visit.

If you consent to participate in the optional lymph node biopsy, you will receive an additional Ug shs 70,000 for a pre-lymph node biopsy safety blood draw visit and an additional Ug shs 200,000 as compensation for your time, transportation, and inconvenience associated with the procedure. This compensation will be provided to you even if the safety blood draw is completed during a scheduled visit or the surgeon is unable to find or remove a lymph node.

Compensation for your participation is provided at the end of each in-person visit. Other than medical care that may be provided and other payment specifically stated in this form, there is no other compensation available for your participation in this study.

What happens if I am injured because of taking part in this research?

If you get sick or injured as a result of the study procedures, you will receive appropriate medical treatment and care until cure or stabilization as provided for by a limited fund (set aside for this study) and a clinical trials medical insurance policy for research-related injuries. While we anticipate the combination of the set-aside fund and the insurance policy is more than enough to pay for the costs associated with any study related injuries, there is a limit to the amount of coverage available. The study sponsor, MUWRP, the owners of the experimental vaccines, and the U.S. DoD will not provide long-term medical care for stabilized research-related injuries.

The study team is responsible for the cost without using any personal health care package which belongs to you. MUWRP will pay costs up to the limit from set aside finds or through the insurance. However, you will not receive any other compensation. You should discuss this thoroughly with the Principal Investigator or study staff before making a decision to participate in this study. If you believe you have a research-related injury or if you have any questions, you can contact Dr. Grace Mirembe by telephone at 0312-330400, 0800-200058, or 0772-577768; or you can contact the study coordinator, Dr. Job Kasule by telephone at 0312-330400, 0800-200058, or 0701-772291. An emergency contact card will be provided to you with phone numbers that you can contact at any time.

How will you protect my privacy and the confidentiality of records about me?

We will take measures to protect your privacy, but we can never fully guarantee the protection of your privacy. We will try our best to protect your privacy by doing the following:

All study participants will receive a unique identification number that will be used to ensure the confidentiality of research information. All of your study documents, samples and test results will be labeled with your identification number, rather than personal information such as your name. Only the study investigators, study coordinators, and representatives from certain agencies (listed below) will be allowed to know which codes belong to you and to have access to your study information. Personal identifying information like your name and age collected at the time of enrollment will be stored in a lockable cabinet to which only designated study team members will have access. The same protection will be given to your electronic information or data stored on a computer – only a few authorized staff members have access to the password-protected, secure database. These steps will ensure confidentiality of your personal information and minimize the chances of it becoming known to others.

Authorized representatives of the following groups, all of whom are bound by rules of confidentiality not to reveal your identity to others, may need to review your research and/or medical records as part of their responsibilities to protect research participants:

- Walter Reed Army Institute of Research Human Subjects Protection Branch
- The Department of Defense
- Makerere University School of Public Health Institutional Review Board
- Uganda National Council for Science and Technology

- Uganda National Drug Authority (NDA)
- Uganda Ministry of Health
- U.S. Food and Drug Administration (FDA)
- U.S. Army Medical Research and Development Command (USAMRDC)
- U.S. National Institutes of Health (study funder and owner of CH505 TF chTrimer experimental vaccine)
- Janssen Vaccines & Prevention (owner of Ad26.Mos4.HIV experimental vaccine)

Research and clinical information relating to you will be shared with other investigators and the scientific community through presentation or publication; however, you will not be identified by name or other personal information that could be used to identify you.

Clinical Trial Information

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law and on http://www.edctp.org/pan-african-clinical-trials-registry/ as recommended by the Uganda NDA. These websites will not include information that can be used to identify you. At most, the websites will include a summary of results. You can search these websites at any time.

What if I decide not to take part in this research?

It is your choice whether or not you want to take part in this research.

If you decide to take part, you can stop taking part in this research at any time without any penalty or loss of benefits to which you are entitled. Deciding not to take part now or withdrawing later does not harm, or in any way affect, your medical care or future relationship with the Makerere University Walter Reed Project clinic. Although you may withdraw from the study at any time, the samples and data collected up to that time will be used in accordance with the protocol.

You will not be penalized for stopping your participation early, but we hope you will continue to take part, and we encourage you to remain in contact with the study staff if your situation changes. If you decide to withdraw from the study, please inform the study staff of your decision. We will ask you to attend one final study visit, if you are willing, so that we can make sure that you are safe and that the experimental vaccine is safe. It is important that you let us know how you are doing and if you have any symptoms that might be related to the experimental vaccine.

What could end my participation in the research?

The study investigator may remove you from the study at any time. This could happen for several reasons; for example, if there is concern about your health, if you do not follow study instructions, or if the sponsor, IRB, UNCST, Uganda NDA, or US FDA stop the study. If the study is stopped, the study team will inform you.

The study injections could be paused if there is a safety concern; for example, if one or more participants has a serious reaction that could be considered related to the vaccine, then the planned study injections for other participants will be temporarily stopped to allow the study team to look at the data and determine if it is safe to continue.

If you miss a study injection for any reason, such as if you are unable to get to the clinic for your study visit, if the investigator doesn't think that it is safe for you to receive the injection, or other

reasons, you will not be eligible to receive the next study injection. If this happens, we would like you to continue your study visits so that we can make sure you are safe. We will continue to collect blood samples at these visits, but the amount of blood may be lower than what would have been collected if study injections hadn't been stopped. In addition, you will no longer be eligible for the optional lymph node biopsy.

What if any new information is found out?

Results of this study or other scientific research may affect your willingness to continue to take part in this study. During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.

Who should I call if I have questions or concerns about this research?

If you have questions about the research, a problem you think may be related to the study, or if you want to withdraw your consent, you can contact Dr. Grace Mirembe by telephone at 0312-330400, 0800-200058, or 0772-577768; or you can contact the study coordinator, Dr. Job Kasule by telephone at 0312-330400, 0800-200058, or 0701-772291. An emergency contact card will be provided to you with phone numbers to contact at any time.

If you have questions about your rights as a research participant, problems or concerns about how you are being treated in this study, or feel that you have not received the appropriate care and treatment for a sickness or injury that occurred as a direct result of taking part in this study, you may contact Dr. Joseph Kagaayi at the Research and Ethics Committee, Makerere University School of Public Health, Mulago Hospital Complex by telephone at 0773-785333 or you may contact The Executive Secretary at the Uganda National Council for Science and Technology by telephone at 0414-705500.

Study volunteer statement:

I have been asked to take part in the study "A Phase I, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of an Ad26.Mos4.HIV and CH505 TF chTrimer (Env) Combination to Mimic Acute HIV Viral Replication Kinetics in Healthy Adults."

The principal investigator Dr. Grace Mirembe or their representative has explained the significance of the testing, the duration of the study, the testing that I will undergo, the methods to be used, and the risks and dangers of participation. I have been informed that by signing this form, I am not giving up any legal rights. I have been given a chance to ask questions about this research study and all questions were answered to my satisfaction. If I have other questions about this research, I can contact Dr. Grace Mirembe, by telephone at 0312-330400, 0800-200058, or 0772-577768; or I can contact the study coordinator, Dr. Job Kasule by telephone at 0312-330400, 0800-200058, or 0701-772291.

I am signing below to indicate my wish to take part in this study and will follow the requirements of the study as much as possible. I will do my best to follow the recommendations of the study team, and I will report all problems occurring from this study to the study team. It has been explained to me that I can quit this study at any time at any time without penalty or loss of benefits to which I am entitled. If I decide to quit this study, I may be examined before leaving the study to ensure my good health. The medical care that I could receive as a result of any sickness or injury that may result from being a part of this study have been explained to me and I have been offered a signed copy of this consent form.

I agree to participate in this study.

_____ _____

SIGNATURE OF PARTICIPANT DATE

_____

PRINT NAME OF PARTICIPANT

_____ _____

SIGNATURE OF PERSON ADMINISTERING CONSENT DATE

_____

PRINT NAME OF PERSON ADMINISTERING CONSENT