Official Title:

A Randomized, Double-Blind Phase 1 Safety and Pharmacokinetic Study of Q-Griffithsin Enema Administered Rectally to HIV-1 Seronegative Adults

ClinicalTrials.gov ID (NCT number):

NCT04032717

Document Date:

October 21, 2020

University of Pittsburgh

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CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: PREVENT: A Randomized, Double-Blind Phase 1 Safety and Pharmacokinetic Study of Q-Griffithsin Enema Administered Rectally to HIV-1 Seronegative Adults (DAIDS ES-38585) – Version 1.0 December 4, 2018

SHORT TITLE: PREVENT

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SOURCES OF SUPPORT: The study is being paid for by the Division of AIDS, US National Institute of Allergy and Infectious Diseases of the National Institutes of Health. The Griffithsin (Q-GRFT) enema being used in this study will be provided by the PREVENT program.

QUESTIONS ABOUT THE STUDY: The person in charge of this study at the University of Pittsburgh is Ken Ho, MD. If you have any questions about the study, concerns or complaints, you can contact one of the investigators at the numbers listed on the first page of this consent form. You can also call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668 if you have any questions about your rights as a research subject or wish to talk to someone other than the research team.

Key Information Summary

You are being asked to take part in the research study named above. The study team will explain the study to you and help you decide if you want to participate. You can decide not to join.

A microbicide is a product designed to prevent transmission of HIV. Griffithsin, or "GRFT", is an investigational product that is being developed as a microbicide. GRFT is naturally produced by a plant and has been found in laboratory studies to have activity against HIV and other sexually transmitted viruses such as herpes simplex virus type-2, human papillomavirus (HPV), and hepatitis C..

This study will try to find out if a Q-Griffithsin or "Q-GRFT" enema is safe and if there are any bad effects when applied rectally. It also seeks to understand how people feel about using the Q-GRFT enemas.this study

product. Results from this study will help researchers determine if Q-GRFT can be developed as a product to prevent HIV-1 infection.

If you qualify and choose to participate, you will have 5 or 6 study visits over about 12 to 13 weeks. During this time, you will receive one dose of the Q-GRFT enema or a placebo enema without Q-GRFT. After the dose, you will have laboratory tests and clinical evaluations or exams for research purposes and to make sure you do not have any side effects.

The study procedures will include:

- Questions about your health, any medicines you are taking, and any side effects you might have had from the study product or procedures.
- Completion of questionnaires on a computer.
- Physical exams which will include an exam of your rectum. If you are a woman, the exam may also include an examination of your cervix and vagina.
- Urine and blood tests, including testing for HIV infection, other sexually transmitted infections and, if you are a woman, pregnancy
- Collection of fluid and small tissue samples (biopsies) from your rectum.

Q-Griffithsin has never been administered in humans before. The risks are unknown, but similar drugs can cause a hypersensitivity reaction. Symptoms include facial swelling, rash, difficulty breathing, painful joints, diarrhea and anemia.

You may experience discomfort from the blood draws or specimen collection from the rectum. Other less likely risks involve breach of confidentiality.

You should not take part in this study if you are pregnant or intend to become pregnant. If you are a woman who can become pregnant, you must commit to using recommended birth control methods.

You should expect no direct benefit from taking part in this study.

You will be compensated $75 for the screening visit, $150 each for Visits 2, 3, 4, and 4a (if one of the first 3 participants) and an additional $25 each for completing questionnaires at 2 study visits. You will also receive $50 for visit 5. For full complete participation in this study you could receive up to $775.

You may decide you aren't comfortable with the risks involved or don't have the time to commit. Should you decide not to participate in this research, you may be interested in starting the FDA approved drug Truvada®, a pill taken once a day in combination with safer sex practices to reduce the risk of sexually acquired HIV infection in adults at high risk.

INTRODUCTION: You are being asked to participate in this research study investigating the safety of a Griffithsin enema because you are a healthy adult age 18-45. In order to participate in this study, you must not have HIV (human immunodeficiency virus) and will be tested for HIV through this study. You are not required to have the HIV test; however, if you do not have the test, you will not be able to participate in this study. Once you have the HIV test performed, it is a requirement that you be informed of the results. Counseling is available to you before you make the decision to participate in this testing.

Before you decide if you want to join this study, we would like to explain the purpose of the study, how it may help you, any risks to you, and what is expected of you. This consent form gives you written information about

this study, which will also be discussed with you. This study also asks for your permission to store leftover samples for future testing.

Once you read, discuss and understand this study, and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep. Before you agree to participate in this study, it is important that you ask as many questions as possible and know the following:

- Your participation is entirely voluntary;
- You may decide not to take part or to withdraw from this study at any time without losing the benefits of the routine medical care you are otherwise entitled to;
- You will be asked to tell the study staff about any other studies you are taking part in, or are thinking of taking part in. This is very important for your safety.

Your physician may also be involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

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, please let study staff know.

WHY IS THIS STUDY BEING DONE?

A microbicide is a drug or agent designed to prevent transmission of HIV. Griffithsin, or "GRFT", is an investigational product that is being developed as a microbicide. GRFT is naturally produced by a plant and has been found in laboratory studies to have activity against HIV, herpes simplex virus type-2, human papillomavirus (HPV), and hepatitis C.

This research study will try to find out if a Griffithsin or "Q-GRFT" enema is safe and if there are any bad effects when applied rectally. The second purpose of the study is to understand how people feel about using the study product. This study will also see if Q-GRFT from the enema goes into the bloodstream and rectum.

This is the first research study of Q-GRFT in humans. The Q-GFRT enema is "experimental" for HIV-1 prevention. This means we do not know if it will work to protect against HIV-1 infection. In the future, investigators are hopeful that Q-GRFT will be developed to help prevent HIV-1 infection. In order to do this, we need to make sure that a Q-GRFT enema is safe when used this way and to understand how people feel about using the enema.

WHAT DO I HAVE TO DO IF I AM IN THE STUDY?

Approximately 30 healthy, HIV-negative individuals between the ages of 18 and 45 will participate in this study at the University of Pittsburgh, the only study site.

This study consists of 3 study arms or groups. Two of these groups will receive the Q-GRFT enema while one group will receive a placebo enema of salt water without Q-GRFT. You cannot choose your group. All of these groups are very important to the results of the study.

Arm 1 will include the first 3 participants who will receive the Q-GRFT enema. The remaining 18 participants will be randomly assigned, like throwing dice, to either Arm 2 (Q-GRFT enema) or Arm 3 (placebo enema). Arm 2 will have 12 participants and Arm 3 will have 6 participants. Arms 2 and 3 are blinded, which means neither you nor the study team will know which group you are in until the study is completed.

If you are eligible for the study and decide to participate, including this visit, you will have 5 or 6 visits in the Magee-Womens Hospital Clinical Translational Research Center (Magee CTRC) over approximately 12 to 13 weeks. During this time, you will receive a single dose of either the Q-GRFT or placebo enema administered rectally by a study clinician.

Study Procedures	Visit 1	Visit 2	Visit 3	Visit 4	Visit 4a*	Visit 5	Exit Call
Paperwork (Consent Form)	X						
Group Assignment		X					
Questionnaire		X		X			
Medical History	X	X	X	X	X	X	X
Physical Exam	X	X	Maybe	Maybe	Maybe	Maybe	
Study Product			X				
Samples taken:							
Blood	X	X	2 times	X	X	X	
Urine^	X	X	Maybe		X	Maybe	
Vaginal	Maybe						
Rectal	X	X	2 times	X	X	Maybe	
Rectal enema & biopsies		X	X	X	X		
Post-visit Telephone call		X	X	X	X		

*only for the first 3 participants
^women will have urine pregnancy testing at Visits 1, 2, 3, 4a* and 5

During this study, you will be asked to return to the clinic for evaluations such as:

- Being asked questions by research staff in person or on the phone, and via computerized questionnaires.
- Being asked about your health, any medicines you are taking, and any side effects you might have had from the study product or procedures.
- Physical exams which will include an exam of your rectum. If you are a woman, the exam may also include an examination of your cervix and vagina.
- Urine and blood tests, including testing for HIV infection, other sexually transmitted infections and, if you are a woman, pregnancy
- Collection of fluid and small tissue samples (biopsies) from your rectum. The biopsies will then be taken to our research laboratory where they will be exposed to HIV to see whether or not the study product can stop the biopsies from becoming infected with HIV. The information from these experiments will be very important in deciding whether or not the study product might be an effective drug for HIV prevention.

In addition, study staff will discuss the rules of this study including:

- To decrease the chance of bleeding or infection when tissue samples are taken and allow you to heal, you will be asked to NOT have anal sex or insert anything into your vagina or rectum (for example, medication, enema, penis, or sex toy) for **72 hours (3 days) before and after each biopsy visit**. Within 3 days after each biopsy collection, you will receive a follow-up phone call from study staff to see how you are doing.

- HIV infection from unprotected receptive anal intercourse may be more likely while the rectal biopsy sites are healing (this takes approximately one week).
- To decrease the chance of bleeding after tissue samples are taken, you will be asked to avoid taking any of the following medications while you are on the study:
    - Heparin, including Lovenox®
    - Coumadin® (warfarin)
    - Plavix® (clopidogrel bisulfate)
    - Pradaxa® (dabigatran)
    - More than 81mg of aspirin per day
    - Non-steroidal anti-inflammatory drugs such as Motrin, Advil or Aleve. These medications increase the risk of bleeding. Tylenol is allowed.
    - Any other drugs that are associated with increased likelihood of bleeding following biopsies
- To decrease the chance of interactions with medications that may interfere with Q-GRFT or the interpretation of study results, you will be asked to avoid taking any of the following medications while you are on the study:
    - Multiple dose dexamethasone
    - Any medication that works against HIV
- You will also be asked to avoid using any products vaginally or rectally that contain the chemical nonoxynol-9 (N-9). A list of some products containing N-9 is attached to this consent form. This list is not complete. You should check the label of any products you use vaginally and rectally to be sure that they do not contain N-9. N-9 has been shown to damage the rectal lining, which could result in injury to you. Use of N-9 is likely to alter the study results.
- You must also agree to use condoms and an acceptable method of birth control while on this study.
    - Acceptable methods for men are condoms or surgery (you or your partner have had your "tubes tied").
    - Acceptable methods of birth control for women include hormonal contraceptives (such as birth control pill, patch, or injection), an intrauterine device (IUD), or surgery (you or your partner have had your "tubes tied").

WHAT PROCEDURES WILL BE DONE DURING THIS STUDY?

If you decide to take part in the study, your visit will continue today after you read, discuss, understand, and sign this form. All study visits will take approximately 1-5 hours. You will be in the study for about 12 weeks from the time of today's visit until your follow-up phone call at the end of the study. Please, review all the visits described below and ask questions about anything you do not understand.

The procedures performed in this study are done for research purposes and will be performed by a study investigator, clinician, or other trained member of the research team. The results will become part of your research record. During the study, the investigators will review the results of all labs, evaluations, and procedures that monitor your health and safety. You will be notified of any results that might affect your personal health or decisions as soon as they are available.

<u>Visit 1 Screening (today)</u>

At today's visit, which may take about 2 hours, you will:

- Answer questions about yourself, such as your medical history and menstrual history (if you are a woman), any medicines that you may take and how we can contact you.
- Learn from study staff about:
    - how to avoid infections passed during sex;
    - how to use condoms to prevent infections passed during sex; and

    - the meaning of your test results, including your HIV test results
- Receive condoms from the study staff
- Have a physical exam, including an exam of your rectum. If you are a woman, the exam will involve the insertion of a speculum into your vagina to look at your vagina and cervix.
- Provide a urine sample to be tested for routine safety, pregnancy (if applicable), gonorrhea and Chlamydia. If you are required to have a pregnancy test, you will find out the results today. If your pregnancy test is positive, you cannot continue in the study.
- Have a blood sample [70 mL, 14 teaspoons] taken to check the health of your blood, liver, and kidneys, to test for syphilis, hepatitis, and HIV.
    - The HIV test is a test for the antibody to HIV-1. An antibody is a substance that blood cells make to fight infection. A positive HIV-1 test means that your oral or blood sample tested positive for HIV and that repeat testing will be performed to confirm (prove) this finding. If your sample is proved to be positive for HIV, it means that you are a carrier of HIV. It also means that you can pass the virus to others through sexual intercourse, by sharing needles, and through donating blood and organs. A negative HIV test means that at this time, no antibody to HIV was found in your sample based on the result of the initial screening test, repeat screening tests, or a confirmatory test.
    - There can be individuals who have HIV test results that are called "false positive." That means that, for some reason, the test shows that HIV antibodies are present in the blood when they are not. There can also be "false negative" results. That means that the test is negative when HIV-1 is present in the blood. This happens when the person has been infected with HIV, but that person's body has not yet made antibodies to the virus, or HIV antibody is present in the person's blood, but for some reason the test failed to detect it.
    - If you had an HIV test today, you will receive the result of your initial HIV test today. If you test positive for HIV antibody, you may be asked to give another blood sample for a confirmatory HIV test. You will also be counseled about the risks for transmitting HIV to others, risks for developing AIDS, and the available treatments for HIV infection. You will return to the clinic to receive results from this repeat test but will no longer be tested in the clinic for HIV antibody and you cannot continue in the study. If you have HIV, you will learn from the study staff where you can get care or treatment.
- Have a sample of fluid taken from your rectum using a swab to be tested for gonorrhea and Chlamydia.
- If you are a woman, you may have a sample of fluid taken from your vagina using a swab to be tested for Trichomonas, bacterial vaginosis, and yeast infections.

If HIV, gonorrhea, Chlamydia, syphilis, hepatitis B, or hepatitis C is identified, we are required to confidentially report this to the Allegheny County Health Department with your name and contact information. Someone from the Health Department may contact you to be sure that you and your partners have been treated.

Visit 2 (Enrollment/Baseline)

You will return for Visit 2 one to four weeks after Visit 1. At this visit, which may take about 2-3 hours, you will:

- Let us know if there are any changes in where you live or how we may contact you
- Receive a copy of your test results, if appropriate, and review these results with the study staff
- Tell us about any changes in your medical history and menstrual history (if you are a woman)
- Tell us if there have been changes to any medicines you are taking now
- Learn from study staff about:
    - how to avoid infections passed during sex;
    - how to use condoms to prevent infections passed during sex; and

    - the meaning of your test results, including your HIV test results
- Receive condoms from the study staff, if needed
- Be randomly assigned to a study group
- Answer some questions on a computer about your behavior, including your sexual behavior. The questionnaire should take about 20 minutes to complete. This information is confidential and WILL NOT be placed in your medical record. The questionnaire will only be labeled with your study ID number.
- If the study clinician thinks that your health status has changed since your last study visit, you may have a physical exam.
- Provide a urine sample to be tested for gonorrhea, Chlamydia, and pregnancy (if applicable)
- Have a blood sample [~40 mL, 8 teaspoons] taken to compare to samples taken at future visits and to check your HIV status. If the study clinician thinks that your health status has changed since your last study visit, you may have some additional blood taken and/or tests
- Have a rectal exam and samples of fluid taken from your rectum using swabs and sponges to be tested for gonorrhea, Chlamydia, other microbes (small organisms like bacteria) and proteins. In order to collect the fluid an anoscope (a small plastic tube) will be inserted approximately 2 inches into your anus to pass the swab and sponge through.
- Have an enema. This is when a liquid is instilled into your rectum to promote a bowel movement
- Have about 16 biopsies taken from your rectum for comparison to samples taken at future visits. A tube will be inserted into your rectum and advanced approximately 6-12 inches into your colon (flexible sigmoidoscopy) through which the biopsies will be taken.

Visit 3 (Dosing Visit)

You will return for Visit 3 one to three weeks after Visit 2. At this visit, which may take up to 5 hours, you will:

- Let us know if there are any changes in where you live or how we may contact you
- Receive a copy of your test results, if appropriate, and review these results with the study staff
- Tell us about any changes in your medical history and menstrual history (if you are a woman)
- Tell us if there have been changes to any medicines you are taking now
- Learn from study staff about:
    - how to avoid infections passed during sex;
    - how to use condoms to prevent infections passed during sex; and
    - the meaning of your test results, including your HIV test results
- Receive condoms from the study staff, if needed
- If the study clinician thinks that your health status has changed since your last study visit, you may have a physical exam.
- Have your temperature, blood pressure, heart rate, and respiratory rate (number of times you breathe in a minute) checked several times
- Have a blood sample [~5mL, one teaspoon] taken to check your HIV status. If the study clinician thinks that your health status has changed since your last study visit, you may have additional blood [~5mL, one teaspoon] taken to check the health of your blood, liver or kidneys and/or tests done.
    - May be asked to provide a urine sample for gonorrhea, Chlamydia, and pregnancy (if applicable) testing.
    - May have rectal specimens collected by a study clinician to be tested for gonorrhea and Chlamydia
- **Study product:** A single dose of your assigned study product enema will be brought to room temperature and then administered rectally to you by a study clinician. The fluid you expel after the enema will be collected.
- 1 hour after you receive the study product, you will have:
    - blood samples [~10mL, 2 teaspoons] taken to be tested for Q-GRFT.
    - samples of fluid taken from your rectum using sponges to be tested for Q-GRFT and proteins

- 20 biopsies taken from your rectum to be tested for Q-GRFT and how the Q-GRFT may be working
- 4 hours after you receive the study product, you will have blood samples [~10mL, 2 teaspoons] taken to be tested for Q-GRFT and samples of fluid taken from your rectum using sponges to be tested for Q-GRFT and proteins.

Visit 4

Visit 4 will take place 24 hours after Visit 3. At this visit, which may take about 2 hours, you will:

- Let us know if there are any changes in where you live or how we may contact you
- Answer some questions on a computer about what you think of the study and the study product. The questionnaire should take about 20 minutes to complete. This information is confidential and WILL NOT be placed in your medical record. The questionnaire will only be labeled with your study ID number.
- Receive a copy of your test results, if appropriate, and review these results with the study staff
- Tell us about any changes in your medical history and menstrual history (if you are a woman)
- Tell us if there have been changes to any medicines you are taking now
- If the study clinician thinks that your health status has changed since your last study visit, you may have a physical exam.
- Have blood samples [~40mL, 8 teaspoons] taken to test for Q-GRFT and check the health of your blood, liver, and kidneys.
- Have samples of fluid taken from your rectum using swabs and sponges to be tested for Q-GRFT, microbes, and proteins
- Have an enema without Q-GRFT. The fluid you expel after the enema will be collected.
- Have 20 biopsies taken from your rectum to be tested for Q-GRFT and how the Q-GRFT may be working.

Visit 4a (*first 3 participants only*)

Only the first 3 participants will return for Visit 4a about 48 hours after Visit 4. At this visit, which may take about 2 hours, you will:

- Let us know if there are any changes in where you live or how we may contact you
- Receive a copy of your test results, if appropriate, and review these results with the study staff
- Tell us about any changes in your medical history and menstrual history (if you are a woman)
- Tell us if there have been changes to any medicines you are taking now
- If the study clinician thinks that your health status has changed since your last study visit, you may have a physical exam.
- Have blood samples [5mL, 1 teaspoons] taken to test for Q-GRFT
- Have samples of fluid taken from your rectum using swabs and sponges to be tested for Q-GRFT.
- Have an enema without Q-GRFT. The fluid you expel after the enema will be collected.
- Have 4 biopsies taken from your rectum to be tested for Q-GRFT
- May have urine sample sent to test for pregnancy (if applicable)

Visit 5 (Final Visit)

Visit 5 will take place about 4 weeks after Visit 4 (or 4a). At this visit, which may take up to one hour, you will:

- Let us know if there are any changes in where you live or how we may contact you
- Receive a copy of your test results, if appropriate, and review these results with the study staff
- Tell us about any changes in your medical history and menstrual history (if you are a woman)
- Tell us if there have been changes to any medicines you are taking now
- If the study clinician thinks that your health status has changed since your last study visit, you may have a physical exam.

- Have a blood sample [~40 mL, 8 teaspoons] taken to be tested for Q-GRFT, your body's reaction to Q-GRFT, and check your HIV status.
- May have a urine sample to be tested for pregnancy (if applicable), gonorrhea and Chlamydia. If you are required to have a pregnancy test, you will find out the results today.
- May have a sample of fluid taken from your rectum using a swab to be tested for gonorrhea and Chlamydia.

One week after Visit 5, you will receive a follow-up phone call from study staff to see how you are doing.

Interim Visits

In some cases, an extra visit or visits (called Interim Visits) might be necessary in between your scheduled study appointments. Evaluations that may be performed during interim visits include: review/update of locator information, medical history, concomitant meds, and, if female, menstrual history; adverse event assessment, HIV pre-/post-test and HIV/STI risk reduction counseling; physical exam, rectal exam, urine sample, venous blood draw. Sometimes these visits may be necessary to address any questions you might have. At other times, the Interim Visits may occur if you experience a gap between visits due to a pause in the study or if you experience side effects that need to be evaluated by study staff. In such cases, study staff may refer you to appropriate medical care.

Early Discontinuation Visits

If you do not receive study product you will be asked to continue with all study visits and procedures through the end of the study except for counseling on the protocol requirements and study product use, flexible sigmoidoscopy (unless needed to check your health), and collection of biopsies.

If you withdraw or are withdrawn from this study for any reason after receiving the study product, you will be asked to come to the clinic for a final study visit. At this visit, which may take 1-2 hours, you will:

- Receive a copy of your test results, if appropriate, and review these results with the study staff
- Answer some questions on a computer about what you think of the study and the study product. The questionnaire should take about 5-20 minutes to complete. This information is confidential and WILL NOT be placed in your medical record.
- Tell us about any changes in your medical history
- Tell us if there have been changes to any medicines you are taking now
- If the study clinician thinks that your health status has changed since your last study visit, you may have a physical exam
- Have a blood sample [up to 35mL, 7 teaspoons] taken to be tested for Q-GRFT, your body's reaction to Q-GRFT, and possibly to check the health of your blood, liver, and kidneys and to test for syphilis, hepatitis, and HIV.
- May be asked to provide a urine sample for gonorrhea, Chlamydia, and pregnancy (if applicable) testing.
- May have samples of fluid taken from your rectum using swabs and sponges to be tested gonorrhea, Chlamydia, other microbes, proteins, and Q-GRFT

ARE THERE ANY RISKS AND/OR DISCOMFORTS?

As with any research study, there may be adverse events or side effects that are currently unknown, and it is possible that certain of these unknown risks could be permanent, serious, or life-threatening. We may learn new information that might change whether or not you want to continue in the study. If this happens, you will be told in a timely manner. You may decide to stop taking part in the study at any time. If you do, your study doctor will discuss the steps you should follow. If you decide to continue, you may be asked to read and sign a revised consent form containing the new information.

The product used in this study may have side effects, some of which are listed below. Please note that this list does not include all the side effects seen with this product, such as a previously unknown allergic reaction causing a rash, swelling, and trouble breathing. This list includes the more serious or common side effects with a known or possible relationship. If you have questions concerning additional study product side effects, please ask the study staff.

Risks from Study Product Enema Q-Griffithsin: Q-Griffithsin has never been administered to humans before. The risks are unknown. There is a chance that drugs like Q-Griffithsin may cause a hypersensitivity reaction. Symptoms of a hypersensitivity reaction may include facial swelling, rash, difficulty breathing, painful joints, diarrhea, anemia, and inflammation of your kidneys. Use of the Q-GRFT enema rectally may affect normal rectal bacteria. This could cause diarrhea or other unanticipated side effects.

We do not know if the Q-GRFT enema works to protect against HIV-1. You may misunderstand the current experimental status of the study product and as a result increase your HIV risk behaviors while in the study. Because of this, study staff will remind you of the importance of practicing safe sex and using condoms to protect against HIV-1.

Risks from Placebo Enema and Enemas in General: You may experience some mild temporary discomfort and a bloated or crampy feeling, flatulence (gas), or diarrhea.

Risks of Blood Draws: Occasionally, low blood pressure that results in fainting may occur. You may feel dizzy or lightheaded and feel discomfort or pain when your blood is drawn. You may experience bleeding, bruising, swelling, or infection where the needle goes into your arm.

Risks of Rectal and Vaginal Exams and Specimen Collection: You may experience minor discomfort during rectal insertion of the anoscope or vaginal insertion of the speculum. You may feel discomfort or pressure when your rectum and/or vagina are examined and when the swabs and/or sponges are inserted. You may also have a small amount of rectal and/or vaginal bleeding which should stop shortly after the examination.

Risks of Flexible Sigmoidoscopy with Rectal Biopsy Collection:

- You may experience some discomfort and the feeling of having a "bloated stomach".
- You may experience low blood pressure after the tissue samples (biopsies) are taken.
- After biopsies are taken you may experience limited bleeding (1 to 2 days after the procedure). In rare cases, the bleeding may be heavy enough to require blood transfusion and a visit to the operating room to stop it.
- Even though the risk is low, after the biopsies you may experience infection, mild irritation, and may feel a sudden urge to have a bowel movement. Even though the risk is very rare, there is a very small chance that you may have a hole or a tear in the intestine from the biopsies. This only happens once out of every 1,000 procedures. If this were to happen, surgery to repair the tear may be necessary. It is important that you do not put anything in your rectum or have anal sex for 72 hours **before and after** the biopsies because you may be at higher risk for getting or spreading an infection until the biopsy site(s) have healed.

Risks of Discussing Sexual Behaviors: You may become embarrassed, worried, or nervous when discussing personal questions about your sexual behavior and ways to protect against HIV and other infections passed during sex.

Risks of HIV-1 and STI testing: You may become worried or nervous while waiting for your test results. There may be emotional discomfort, sadness, depression, stress, problems in relationships with sexual partners,

and increased HIV risk behaviors associated with knowledge of the results of this test. A trained counselor will help you deal with any feelings, questions, or concerns you may have. There is a possibility that if the results of these tests were to become generally known this information could impact future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in stigmatization.

Risks from Web-based Questionnaires: There may be discomfort or embarrassment related to questions dealing with sexual behaviors and personal habits. If some of the questions upset you or make you uncomfortable, you may choose not to answer them.

ARE THERE RISKS RELATED TO PREGNANCY?

Pregnant and breastfeeding women are excluded from study participation. The effects of the study product on a pregnant woman, unborn baby, or breastfeeding infant are not known. If you are having sex that could lead to pregnancy, you must agree not to become pregnant or make your partner pregnant. If you or your partner are able to become pregnant, it is important that you use an effective method of birth control that you discuss with the study staff. If pregnancy occurs, study product will be stopped, you will be exited from the study, and you will be referred for further services. If it is determined that you are pregnant at the end of the study you will continue to be followed in the study until the outcome of the pregnancy is known. For this study, effective, acceptable, methods of birth control for female participants include hormonal contraceptives (such as birth control pill, patch, or injection), an intrauterine device (IUD), or surgery (you or your partner have had your "tubes tied"). For male participants, condoms, as well as partner use of IUD or hormonal contraception, are considered acceptable methods of birth control.

WHAT ARE THE BENEFITS?

You may get no direct benefit from being in this study. **We do not know if the Q-GRFT enema works to protect against HIV-1.** Because of this, study staff will remind you of the importance of using condoms to protect against HIV-1.

You or others may benefit in the future from information learned in this study. You may also get some personal satisfaction from being part of research on HIV prevention.

- You will have physical exams, including rectal exams. You will have tests to check on the health of your blood, liver, and kidneys. If these tests show that you might have any health problems, you will be referred for medical care and other services available to you.
- You will have tests for sexually transmitted infections. These tests may detect infections without obvious symptoms. If you have a sexually transmitted infection, other than HIV infection, you will be offered access to treatment.
- You will get counseling and testing for HIV. You will be given condoms at no charge to you. This study does not provide medication for treatment of HIV/AIDS. If you become infected with HIV, you will be referred for medical care, counseling, and other services available to you.

WHAT TREATMENTS OR PROCEDURES ARE AVAILABLE IF I DECIDE NOT TO TAKE PART IN THIS RESEARCH STUDY?

In July 2012, the US Food and Drug Administration approved Truvada®, a pill that must be taken once a day, to be used in combination with safer sex practices to reduce the risk of sexually-acquired HIV infection in adults at high risk. The only other known way to protect against HIV during sex is to use a condom every time you have sex. There may be other research studies here or in the community that you may be eligible for. If you wish, we will tell you about other research studies that we know about. There also may be other places where you can go for HIV counseling and testing, STI testing, and contraception. We will tell you about those places if you wish.

WHAT ARE THE COSTS TO ME?
There is no cost to you for the study product, clinic visits, procedures, or any laboratory tests. These services will be paid for by the study and will not be billed to you or your health insurance company. If you receive a bill or believe that your health insurance has been billed for something that is part of the research study, notify a member of the research team or UPMC Patient Billing Services.

Any procedures performed for routine medical care, such as treatment for STIs, will be billed to you and/or your health insurance company. You will be responsible for paying any deductibles, co-payments or co-insurance that are a normal part of your health insurance plan. If you do not have health insurance, you will be responsible for those costs.

WILL I RECEIVE ANY PAYMENT?
You will be compensated for your time and effort for your scheduled study visits as follows:

- Visit 1 Screening: $75
- Visits 2, 4, and 4a (if one of the first 3 participants): $150 each + an additional $25 each for completing the questionnaires at Visits 2 and 4
- Visit 3: $200
- Visit 5: $50

In total for full complete participation in the research study, you may receive $675-$825. If you have to return to clinic for any unexpected visits you will receive $50 for the visit.

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

Your data or specimens used in this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or outside agencies may receive.

WHAT HAPPENS IF I AM INJURED (EXPERIENCE HARM)?
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. There is no plan for any additional financial compensation either through this institution or the National Institutes of Health (NIH). You will not, however, be giving up any of your legal rights by signing this consent form.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?
There is a possibility that if your participation in this HIV research study were to become generally known this information could impact future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in stigmatization. To minimize this risk, any information about you obtained from this research will be kept as confidential (private) as possible. Pennsylvania state law requires the reporting of positive HIV test results to the Allegheny County Health Department with your name and contact information. All information will be handled in compliance with the Pennsylvania law on HIV-related confidential information.

All records related to your involvement in this research study will be stored in a secure, double-locked area or password-protected computer database at the HIV/AIDS Clinical Research Site (CRS) that is accessible only by members of the research team. Your identity on these records will be indicated by your subject identification number rather than by your name, and the information linking your subject identification number with your identity will be kept separate from the research records. Your research information and data may be shared with investigators conducting other research. This information may be identifiable.

To maintain your privacy during study visits, procedures will be performed in a private exam or interview room in the Magee CTRC. Only you, study staff, CTRC staff and/or other trained personnel will be present during these procedures. For study product administration and collection of rectal or vaginal samples, you will change into a hospital gown in a private restroom connected to the exam room, and the procedures will be performed in the exam room behind a closed door and curtain.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. Finally, you should also understand that this federal Certificate does not prevent investigators from taking steps, including reporting to appropriate authorities, to prevent serious harm to you or others. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

This study will be reviewed periodically to monitor its conduct. Therefore, your records may be reviewed as part of routine audits by:

- US National Institutes of Health (NIH)
- Food and Drug Administration (FDA),
- Office for Human Research Protections (OHRP)
- Intrucept Biomedicine
- University of Pittsburgh Institutional Review Board (an IRB is a committee of volunteers who are responsible for protecting the rights and welfare of research participants)
- Study staff
- Study monitors including members of data safety monitoring boards
- Other local, US, and international regulatory entities, contractors of the NIH, representatives of the sponsor, and PREVENT Program Cores

A description of this clinical trial will be available on www.clinicaltrials.gov . This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WILL THIS STUDY INVOLVE THE USE OR DISCLOSURE OF MY IDENTIFIABLE INFORMATION?
This research study *will not* involve the recording of *current* identifiable medical information from your hospital and/or other health care provider records. This research study *will* involve the recording of *future* identifiable medical information from your hospital and/or other health care provider records. The identifiable information that will be recorded includes adverse event information related to the study enema products or procedures.

Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information related to your participation in this research study for the purpose of scheduling Magee CTRC appointments for each study visit.

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical record information) related to your participation in this research study for a minimum of 7 years and for as long as it may take to complete this research study. Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following final reporting or publication of a project.

You are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

WHY MIGHT I BE WITHDRAWN FROM THIS STUDY WITHOUT MY CONSENT?
You may be withdrawn from the study without your consent for the following reasons:

- The study is cancelled by the NIH, Intrucept Biomedicine, site IRB, the US FDA, OHRP, or the local government or regulatory agency
- Study staff considers that having the exams and tests would cause injury that could be harmful to you.
- You do not want to learn your HIV-1 test result.
- You are not able to complete the medical exams and tests.
- You are unable or unwilling to follow all of the study procedures or instructions.
- You are found to not be eligible for this study.
- Other reasons that may prevent you from completing the study.

If you are withdrawn early from the study, you will be asked to come in for a final visit with all the exams and tests listed for the final visit, if the study doctor thinks the exams and tests need to be done. Any identifiable research or medical record information recorded for, or resulting from, your participation in this study prior to the date that you were formally withdrawn from the study without your consent may continue to be used and disclosed by the investigators for the purposes described above.

MAY I WITHDRAW, AT A FUTURE DATE, MY CONSENT FOR PARTICIPATION IN THIS STUDY?
You can, at any time, withdraw from this study. You can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw from this study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh, on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

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STORAGE AND FUTURE TESTING OF SPECIMENS: There might be a small amount of biological specimens such as blood, rectal fluid, and/or rectal tissue left over after all of the study-related testing is complete. We would like to ask your permission to store these leftover samples for use in future studies. No additional medical examination or testing is required of you.

Your samples may be used to look for ways that your body responds to infection (such as cells, proteins, and other chemicals in your body). Tests may also include checking your genes (material passed from parent to child that determines the make-up of the body and mind), since they might affect how your body responds to disease, and whole genome sequencing of all of your genes. Your genes might make you more or less likely to get an infection, affect your responses to infection, or make your responses to treatment stronger or weaker. No other kinds of genetic tests will be done on your stored samples without first explaining the test to you and getting your permission. The researchers do not plan to contact you or your regular doctor with any results from tests done on your stored samples. This is because research tests are often done with experimental procedures, so the results from one research study are generally not useful for your medical care. If a rare situation came up where the researchers decided that a test result would provide important information for your health, the researchers would tell your study clinician and your study clinician would try to contact you. If you wish to be contacted with this type of test result, you must give the study clinician or nurse any change to your address and/or phone number. If you want your regular doctor to be told about this type of test result, you must provide the study clinician or nurse with your regular doctor's name, address and phone number. Your samples will not be sold or used directly to produce products that can be sold for profit. Research studies using your samples will be reviewed by a special committee at the researcher's institution (an Institutional Review Board) whose purpose is to protect you as a research participant.

Your samples will be stored at facilities that are designed to store samples securely. Your samples will be labeled with a unique identifier (such as specimen and test type, date, your subject identification number, and study visit number) and stored at a designated biorepository. The investigators will have sole control over these samples, and only approved researchers will have access to your samples. If your samples are provided to secondary investigators, all subject identifiers will be removed from your samples, and your samples will be made anonymous. Your samples may be stored indefinitely, and the exact time at which your samples will be analyzed has not been determined. An Institutional Review Board will oversee the storage facilities to protect you and other research volunteers from harm. There is no time limit on how long your samples will be stored.

You will receive no direct benefit from the storage of your samples. When tests are done on the stored samples there is a small but possible risk to your privacy. It is possible that if others found out information about you from tests (such as information about your genes) it could cause you problems with your family (having a family member learn about a disease that may be passed on in families or learning who is the biological parent of a child) or problems getting a job or insurance. There is a risk that your stored samples and/or health information may be misused. There are laws against this kind of misuse, but they may not fully protect you. The chance that this will happen is considered small because of the security taken with your samples and information.

Your genetic information is unique to you. Should you consent to have future genetic testing done on your stored samples, there is the risk that someone using your samples may identify you. This risk is very small but may increase with the progress of science. Researchers will inform you of any newly identified risks. In addition, there is a federal law called the Genetic Information Nondiscrimination Act (GINA) that generally makes it illegal for health insurance companies and group health plans to use genetic information in making decisions regarding your eligibility or premiums. GINA also makes it illegal for employers with 15 or more employees to use your genetic information when making decisions regarding hiring, promoting, firing, or setting the terms of employment. This Federal law does not protect you against genetic discrimination by companies that sell life, disability, or long-term care insurance.

To keep your information private, your samples will be labeled with a code that can only be traced back to your research clinic. Your personal information (name, address, phone number) will be protected by the research clinic. When researchers are given your stored samples to study they will not be given your personal information. The results of future tests will not be included in your health records.
You can still enroll in this study if you decide not to have these samples and associated health information stored for future research. If you do not want to have these samples and associated health information stored, then your samples and associated health information will be destroyed. You can withdraw your consent for the storage and future testing of samples at any time by providing your request in writing to the person in charge of this study. However, researchers will not be able to destroy samples or information from research that is already underway.

_____ Initial & date — I **do agree** to allow my biological specimens and associated health information obtained during this study to be stored for use in future research studies.

_____ Initial & date — I **do not agree** to allow my biological specimens and associated health information obtained during this study to be stored for use in future research studies.

VOLUNTARY CONSENT: All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form. Any questions which I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668). By signing this form, I consent to participate in this research study and provide my authorization to share my medical records with the research team. A copy of this consent form will be given to me.

_____	_____	_____
Participant's Printed Name	Participant's Signature	Date and Time

CERTIFICATION OF INFORMED CONSENT: I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____	_____
Investigator's Printed Name	Investigator's Signature	Date and Time

Products That May Contain Nonoxynol-9 (N-9)

Read the product label! If in doubt, ASK!

N-9 is a spermicide that can be found on condoms and in lubricants, contraceptive gels, and or foams. If you have any question about whether or not a product contains N-9, ask your local pharmacist. Below is a list of common products containing N-9 (This list may not be accurate, because many companies are removing N-9 from their products.):

• Advantage 24 • Because • Conceptrol Contraceptive Gel and Inserts • Delfen • Emko and Emko Pre-Fil • Encare • Gynol II Original and Extra Strength Contraceptive Jelly • Koromex Crystal Clear Gel, Foam, and Jelly • K-Y Plus • Ortho-Creme	• Ramses Crystal Clear Gel • Semicid • Shur-Seal • Trojan-Enz® • Trojan® HER PLEASURE™ • Trojan® Ultra Ribbed • Trojan Ultra Pleasure® • Trojan® Shared Sensation • Trojan® Ultra Thin • Trojan Supra® • VCF

Reminder- You may not take aspirin, any aspirin containing medications, or non-steroidal anti-inflammatory drugs such as ibuprofen (Motrin, Advil) or naproxen (Aleve) during the period of study participation. These medications may increase the risk of bleeding.

Products That May Contain Aspirin - Read the product label! If in doubt, ASK!

Non-Prescription Products	**Prescription Products**	
• Alka-Seltzer Products • Anacin • Ascriptin • Bayer • BC • Bufferin • Doan's • Dristan • Ecotrin • Excedrin • Goody's • Kaopectate • Norwich • Pamprin • Pepto-Bismol • Sine-Off • St. Joseph	• Acuprin 81 • Aggrenox • Butalbital • Carisoprodol • Darvon • Disalcid • Easprin • Endodan • Equagesic • Fiorinal • Fiortal • Gelpirin • Halfprin • Helidac • Lobac • Lortab	• Magan • Magsal • Methocarbamol • Mono-Gesic • Norgesic • Percodan • Propoxyphene • Robaxisal • Roxiprin • Salflex • Salsalate • Soma • Synalgos-DC • Talwin • Trilisate • Vicoprofen