utmb Health

INFORMED CONSENT FORM (ENROLLMENT)

Title: Randomized order, controlled, double blind, crossover early Phase 1 pilot study to assess safety and pharmacokinetics of a Tenofovir Disoproxil Fumarate and Emtricitabine (TDF-FTC) releasing IVR over 28 days compared to placebo- Version 2.0

Short Title: PrEP-Pod-IVR-02

PRINCIPAL INVESTIGATOR: Kathleen L. Vincent, MD
301 University Blvd, Route 0587
Galveston, Texas 77555-0587
Office: 409-772-2610

STUDY COORDINATOR: Lauren Dawson
301 University Blvd, Route 0587
Galveston, Texas 77555-0587
409-354-9792

Source 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 intravaginal rings being used in this study will be provided by the Oak Crest Institute of Science (called "the sponsor").

Questions about the Study: The person in charge of this study at the University of Texas Medical Branch is Kathleen L. Vincent, MD. If you have any questions about the study, concerns or complaints, you can contact the Principal Investigator, Dr. Kathleen L. Vincent (409-772-2610), the study coordinator (409-354-9792).

Why am I being asked to take part in this research study? You are being asked to take part in this study because you are a healthy female participant between the ages of 18-45. Your participation in this study is completely voluntary. You may refuse to participate or stop your participation in this research study at any time without penalty or loss of benefits and without jeopardizing your medical care at UTMB.

You are being asked to participate in this research study investigating the safety of an intravaginal ring (IVR) containing tenofovir (TDF) and emtricitabine (FTC) and a placebo IVR (an IVR without the TDF-FTC), because you already completed a screening visit and are eligible to participate.

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.

Study Summary:
The following things you should know about this research study:

- The purpose of the study is to determine if intravaginal rings (IVRs) releasing drugs to prevent HIV are safe, where the drug goes in the body, and what you and other women think about using the IVR.
- If you choose to participate, you will be asked to come to the Clinical Research Center every 1-4 weeks for a total of 14 study visits. It will take approximately 5-6 months to complete all study visits.
- The study visits will involve drawing blood, having pelvic exams with collection of vaginal and rectal samples, using the study IVR, taking surveys about the study IVR, and discussing your experience with the IVR.
- At home, you will be asked to collect vaginal swabs and store them in your freezer, record your symptoms on a study diary, answer daily phone call surveys, be abstinent (not have sex) during different times throughout the study, and use condoms during sex.
- Risks or discomforts from this research include vaginal discharge, irritation, or bleeding and abdominal cramping.
- The study will not directly benefit you except for learning the results of HIV and sexually transmitted infection tests.
- Taking part in this research study is voluntary. You do not have to participate and you can stop at any time.
- Please take your time to read this entire form and ask questions before deciding if you want to take part in this research project.

YOUR PARTICIPATION IS VOLUNTARY

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. You will be asked at the end of this consent form to let us know your decision as to whether or not you agree to have your samples stored for future use.

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 offered 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.

What is the purpose of this research study?
?
This research study will try to find out if the intravaginal rings (IVRs), which are silicone rings inserted into the vagina designed to provide a controlled release of drugs, are safe. In this study, we are investigating IVRs containing the drugs Tenofovir Disoproxil Fumarate and Emtricitabine (TDF-FTC) and the placebo (IVR without the TDF-FTC) to see if they are safe and if there are any bad effects when they are used vaginally for 28 days. The second purpose of the study is to see if the study drugs (TDF and FTC) go into the bloodstream and into the vaginal or rectal tissues. Another purpose of this study is to understand how people feel about using these intravaginal rings.

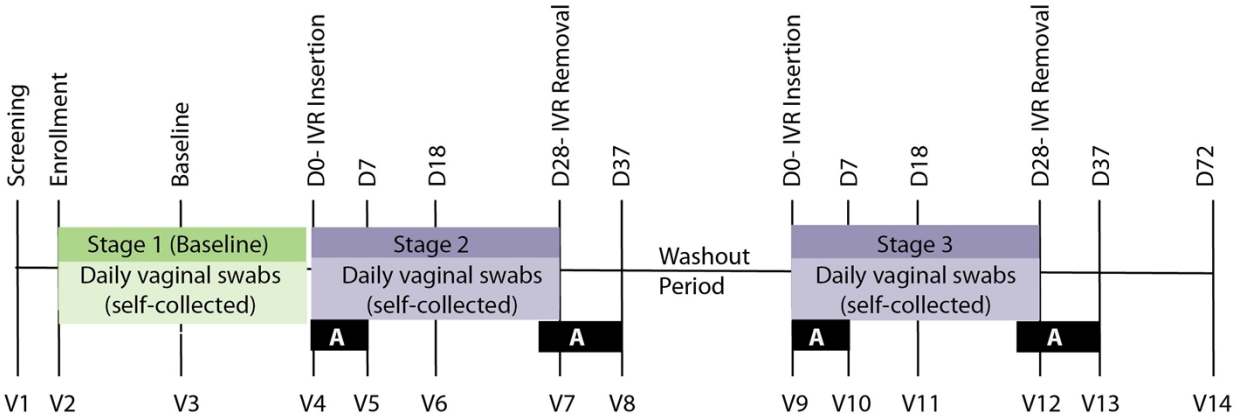
The pill form of TDF and FTC (Truvada®) is approved in the USA by the Food and Drug Administration (FDA) for both the treatment and prevention of human immunodeficiency virus type 1 (HIV-1) infection. **The IVR form of TDF and FTC is "experimental" for HIV-1 prevention. This means we do not know if the IVR will work to protect against HIV-1 infection. The IVR will not prevent other sexually transmitted infections nor will it prevent pregnancy.** In the future, investigators are hopeful that the IVR containing TDF-FTC will be developed to help prevent HIV-1 infection. In order to do this, we need to make sure that the IVR containing TDF-FTC is safe when used this way and to understand how people feel about using it.

NUMBER OF SUBJECTS PARTICIPATING AND THE DURATION OF YOUR PARTICIPATION
The number of subjects to complete the study will be ten with all subjects participating at the University of Texas Medical Branch for clinical procedures and completing two video-conference interviews with our research partners at The Miriam Hospital in Rhode Island. A larger number of women, seventy, may be screened in order to achieve this goal. The length of time for your participation is approximately 6 months to complete the study visits after the initial screening visit to check for eligibility.

WHAT DO I HAVE TO DO IF I AM IN THE STUDY?
This study consists of 2 study groups. Both of the groups will have 5 women and both groups will receive the IVR with the placebo and the IVR with TDF-FTC. Approximately 10 healthy, HIV-negative women between the ages of 18 and 45 will participate in this study at the University of Texas Medical Branch (UTMB), including two video-conference interviews with our research partners in Rhode Island. Each group will have the same visit schedule. The only difference is the order you will receive the IVRs. Both of these groups are very important to the results of the study. Your group assignment will be chosen randomly. Randomly means by chance, like flipping a coin or throwing dice. You cannot choose your group. Neither you nor the study staff will know which group you are assigned to until the study is over.

- Group 1- TDF-FTC IVR first; then Placebo IVR
- Group 2- Placebo IVR first; then TDF-FTC IVR

If you are eligible for the study and decide to participate, including this visit, you will have approximately 14 visits, including today, at the UTMB clinic over at about 6 months. During this time, you will insert the first IVR assigned to your group into your vagina where it will remain for about 28 days. Then after taking a break for at least 20 days, you will insert the second IVR assigned to your group into your vagina where it will remain for about 28 days. Abstinence from sexual intercourse is critical at four main time periods - you should remain abstinent from the time of the IVR insertion visits (Visit 4 and Visit 9) until the following study visit (Visit 5 and Visit 10). You should also remain abstinent 2 days before and 7 days after study Visit 7, Visit 12, and Visit 13.



A= Period of Required Abstinence

While on study you will be asked to do the following:

- Be asked questions in person by research staff, via computerized questionnaires (about 30 minutes long), daily automated phone surveys (less than 3 minutes long), and two videoconference calls from UTMB with research staff in Rhode Island (about 45-90 minutes long). The interviewer will be located in Rhode Island and speak to you via videoconference.
- You will be asked to remain abstinent from sexual intercourse from the time you insert the IVR at visits 4 and 9 until you return for the next visit about a week later, visits 5 and 10, and are cleared by the study clinician. You will be asked to remain abstinent 2 days before and 7 days after visits 7, 12, and 13.
- You will also undergo physical exams which may include an exam of your vagina, cervix, and rectum. The exams of your vagina and cervix will include a special exam with pictures taken using a camera called a colposcope and having images taken with an optical coherence tomography (OCT) probe (about the width of a pencil eraser). OCT works like ultrasound, except that it uses light waves instead of sound waves.
- You will have an ultrasound (i.e., a test that uses sound waves to create images); a probe is placed on your lower abdomen or at the entrance of your vagina or inside your vagina to take a picture of where the IVR is in your vagina.
- You will have urine and blood tests, as well as testing for HIV infection, other sexually transmitted infections, and pregnancy
- You will have fluid samples taken from your vagina and rectum.

- You will have small tissue samples (biopsies) taken from your vagina at 3 study visits. If you agree to optional rectal biopsies, you will also have tissue samples taken from your rectum at 3 study visits. Each biopsy is less than  3mm or in size and will feel like a pinch. No numbing medicine is needed to have these biopsies and none will be given. The information from these experiments will be very important in deciding whether or not the study drug might be an effective drug for HIV prevention.
- **You will be required to collect samples with swabs (like long Q-tips) from your vagina every day for 28 days before you receive the first IVR and then every day while each IVR is in place. You will keep these samples in a container, provided by us, in your freezer at home until you can bring them in at your next study visit.**
- You will be required to fill out a study diary to record how you are feeling, changes to any medicines you are taking now, and about any side-effects you might have had from the study product or procedures. You will be required to bring this study diary with you to each study visit.
- You will be asked to invite your male sexual partner(s) to participate in a videoconference call. You will not be present during your partner's videoconference call. During the videoconference your partner(s) will be asked about their experience with the ring, including about what they liked and disliked about the intravaginal rings. You do not have to invite them to participate and even if invited they may choose not to participate.

- 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 sex or put anything into your vagina (for example, medication, finger, penis, or sex toy) for **2 days before and 7 days after** Visits 7, 12, and 13. **Tampons are OK to use while you have your period, except for the 72 hours before a study visit and 7 days after visits 7, 12 and 13.**

- You will also be asked to not insert anything into your rectum (for example, medication, enema, penis, or sex toy) for **2 days before and**, if you have agreed to have rectal biopsies, **7 days after** Visits 7, 12, and 13.

- To decrease the chance of bleeding when tissue samples are taken, you will be asked to avoid taking non-steroidal anti-inflammatory drugs such as ibuprofen, Motrin, Advil, naproxen or Aleve for 1-4 days before and after biopsies are taken (Ask the study staff for specific instructions if you are taking any of these medications). Tylenol is allowed. You should not take any of the following medications the entire time you are on the study:
  - Heparin, including Lovenox®
  - Coumadin® (warfarin)
  - Plavix® (clopidogrel bisulfate)
  - Pradaxa® (dabigatran)
  - More than 81mg of aspirin per day
  - Any other drugs that are associated with increased likelihood of bleeding following biopsies

- To decrease the chance of interactions with medications known to interfere with the study products 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 vaginal and 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 of birth control for women include hormonal contraceptives (such as birth control pill, patch, or injection, but NOT the Nuvaring), an intrauterine device (IUD), or prior surgery (you had your "tubes tied" or your partner had sterilization surgery 'vasectomy').

PROCEDURES

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 1-3 hours. You will be in the study for about 5 months from the time of today's visit until your final visit at the end of the study. Please, review all the visits described below and ask questions about anything you do not understand.

Visit 2/Baseline #1 (today)

At today's 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
- Be offered 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 or periods
- 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
    - the meaning of your test results, including your HIV test results; and
    - how to complete the study diary that are given to you at this visit
    - how to collect and store swabs from your vagina
- Receive condoms and menstrual pads from the study staff
- Provide a urine sample to be tested for pregnancy.

- If the study clinician thinks that your health status has changed since your last study visit, you may have some additional blood drawn [up to 30ml, 6 teaspoons] and/or tests
- Have a physical exam, which will include an exam of your vagina.

    - In order to examine your vagina the study doctor will use a speculum (a plastic or metal instrument used to separate the walls of the vagina). The study doctor will check your vagina and cervix for signs of infection, and other problems using a special camera called a colposcope that allows the doctor to see things she might not see with her eyes alone and take pictures.

    - Using 5 swabs, the study doctor will also take some fluids from the vagina and/or cervix to be tested for microbes (small organisms like bacteria and yeast) and for comparison to samples taken at future visits after the IVR is in place.

    - Then the study doctor will squirt a small amount of salt water inside your vagina and remove it. Then this will be repeated one more time with a little more salt water. The liquid that is removed will be tested for signs of vaginal irritation and for comparison to samples taken at future visits after the IVR is in place.

    - Then the study doctor will use a small brush and two small spatulas (just like the ones used during a Pap smear) to collect samples from the surface of your vagina to be tested for microbes (small organisms like bacteria and yeast) and for comparison to samples taken at future visits after the IVR is in place.

    - The study doctor will then insert a small OCT probe (about the width of a pencil eraser) into your vagina to take pictures. These pictures will be used for comparison to pictures taken at future visits after the IVR is in place.

Before you leave you will be given instructions and supplies for collecting swabs from your vagina every day for the next 28 days. These swabs will be tested for microbes (small organisms like bacteria and yeast) and for comparison to samples taken at future visits. You will be asked to store the swabs you collect in your freezer at home until your next study visit. If you would like to bring them to the clinic sooner, you can contact the study staff to make arrangements.

Visits 3/ Baseline #2

About 2 weeks later you will return to the clinic for Visit 3, which may take about 2-3 hours. At Visit 3 you will be assigned to your study group. Neither you nor your doctor will know to which study group you are assigned.

Visit 3 will be just like Visit 2 except that you will not have to complete a computerized questionnaire. At this visit the study staff will collect the swabs you bring in from home and your study diary and provide you with more supplies.

Visits 4 and 9

About 2 weeks after Visit 3 you will return to the clinic for Visit 4. Visit 9 will not occur until at least 20 days after the first IVR has been removed. If more than 45 days have passed between Visits 3 & 4, you will have to complete another Screening Visit (just like Visit 1) before you continue on to Visit 4. If more than 45 days have passed between Visits 8 & 9, you will have to complete another Screening Visit (just like Visit 1) before you continue on to Visit 9.

These visits will take about 2-3 hours. At these visits, you will:

- Let us know if there are any changes in where you live or how we may contact you
- Be offered 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 or periods
- Tell us if there have been changes to any medicines you are taking now
- Learn from study staff how to: Insert the IVR and complete daily phone surveys
    - You will receive a daily automated phone call every day while the IVR is in your vagina. During these calls you will be asked by a computer to answer questions about the IVR, your sexual behaviors, and how you are feeling. These phone surveys take less than 3 minutes to complete.
- Receive condoms and menstrual pads from the study staff
- Drop off the vaginal swabs you have been collecting every day and receive new supplies. (Visit 4 only)
- Provide a urine sample to be tested for pregnancy, gonorrhea, chlamydia, and possibly other infections.
- Have a blood sample [30 ml, 6 teaspoons] taken from your arm to check the health of your blood, liver, and kidneys, to test for syphilis and HIV, and to compare to samples taken at future visits. If the study clinician thinks that your health status has changed since your last study visit, you may have some additional blood and/or tests
    - Reminder: If gonorrhea, chlamydia, HIV, syphilis, hepatitis B, or hepatitis C is identified, we are required to confidentially report this to the State 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.
    - The clinical lab results from your study visits will be shared with you. This includes your HIV, hepatitis B and C, syphilis, gonorrhea, and chlamydia tests as well as your blood tests that evaluate the liver, the kidneys, blood clotting, and the complete blood count.
- If the study clinician thinks that your health status has changed since your last study visit, you may have a physical exam.
- You will have a vaginal exam
    - In order to examine your vagina the study doctor or nurse will use a speculum (a plastic or metal instrument used to separate the walls of the vagina). The study doctor will check your vagina and cervix for signs of infection, and other problems using a special camera called a colposcope that allows the doctor to see things she might not see with her eyes alone and take pictures.

- Using 5 swabs, the study doctor will also take some fluids to be tested for microbes (small organisms like bacteria and yeast) and for comparison to samples taken at future visits after the IVR is in place.

- Then the study doctor will squirt a small amount of salt water inside your vagina and remove it. Then this will be repeated one more time with a little more salt water. The liquid that is removed will be tested for signs of vaginal irritation and for comparison to samples taken at future visits after the IVR is in place.

- Then the study doctor will use a small brush and two small spatulas (just like the ones used during a Pap smear) to collect samples from surface of your vagina to be tested for microbes (small organisms like bacteria and yeast) and for comparison to samples taken at future visits after the IVR is in place.

- The study doctor will then insert a small OCT probe (about the width of a pencil eraser) into your vagina to take pictures. These pictures will be used for comparison to pictures taken at future visits after the IVR is in place.

- **Study product:** You will insert the first IVR into your vagina and the study doctor will check the placement. The doctor may perform an ultrasound by placing a probe on your lower abdomen or at the entrance of your vagina, or inside your vagina to check the placement and take pictures of where the IVR is in your vagina.
- You will be given 1 extra IVR to take home in case there is a problem with the IVR inserted at your visit (e.g., if it comes out and falls in the toilet).
- Study staff will remind you to complete your study diary, complete the daily phone surveys, and collect vaginal swabs every day until the IVR is removed at Visits 7 and 12. Study staff will also remind you not to have sex for at least one week and until the study staff tell you it is OK to have sex again.

Visits 5, 6, 10, and 11

Visits 5 and 10 will occur about 1 week after the IVR has been inserted.

Visits 6 and 11 will occur about 18 days after the IVR has been inserted.

These visits will take about 2-3 hours and be just like Visits 4 and 9, except that

- you will not have a new IVR inserted; the one you inserted previously will stay in place.
- you will drop off the vaginal swabs you have been collecting every day and receive new supplies.
- the exam results and OCT pictures will be compared to those taken at previous visits to see what effects the IVR has had on your body
- you will have an ultrasound to take pictures of where the IVR is in your vagina at Visits 6 and 11 and possibly other visits if you are experiencing discomfort.
- you will have less blood taken (about 10 ml or 2 teaspoons) unless the study doctor thinks there has been a change in your health status

- your urine will only be tested for pregnancy unless the study doctor thinks there has been a change in your health status
- the samples taken will be compared to those taken at previous visits and to see
    - if the TDF and FTC are in your blood, vaginal cells, and vaginal fluids
    - what effects the IVR has had on your body
    - if the IVR may be increasing or decreasing your risk of getting HIV
    - if the IVR is affecting the microbes in your vagina

Study staff will remind you to complete your study diary, complete the daily phone surveys, and collect vaginal swabs every day until the IVR is removed at Visits 7 & 12. **They will also remind you not to have sex or insert anything into your vagina or rectum for 2 days before Visits 7, 12, and 13.**

Visits 7 and 12

About 4 weeks after the IVR was inserted you will return to the clinic to have the IVR removed.

These visits will take about 2-3 hours and be just like Visits 4 and 9, except that

- you will answer some questions on a computer about what you liked and did not like about the IVR. The questionnaire should take about 30 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.
- the doctor may perform an ultrasound by placing a probe on your lower abdomen, or at the entrance of your vagina, or inside your vagina to check the placement and take picture of where the IVR is in your vagina.
- the IVR will be removed and a new one will not be inserted
- you will return any study IVRs that you had at home
- you will drop off the vaginal swabs you have been collecting every day and once the IVR is removed you will not have to collect the daily swabs or complete the daily phone surveys
- the exam results and OCT pictures will be compared to those taken at previous visits to see what effects the IVR has had on your body
- the samples taken will be compared to those taken before the IVR was inserted
- **you will have 3 biopsies (tissue samples) taken from your vagina to be tested for TDF and FTC and how these drugs may be working. Each biopsy will be less than 3mm in size or about .**
- **you will have samples of rectal fluid collected with swabs inserted through something called an anoscope (a small plastic tube inserted approximately 3-4 inches into your rectum)**
- **if you agreed to have rectal biopsies (tissue samples), you will have 5 tissue samples taken from your rectum through the anoscope. Each biopsy will be less than 3mm in size or about .**

Study staff will remind you not to have sex or insert anything into your vagina or rectum for 7 days after these visits.

Visits 8 and 13

Visits 8 and 13 will occur about 1-2 weeks after the IVR has been removed.

These visits will take about 2-3 hours and be just like Visits 4 and 9, except that

- you will not have an IVR inserted
- the exam results and OCT pictures will be compared to those taken at previous visits to see what effects the IVR has had on your body
- the samples taken will be compared to those taken at previous visits
- you will participate in an audio-taped videoconference call with a member of the study staff at our partner institution in Rhode Island to discuss what your experiences were like in using the IVR. The interview should take about 45-90 minutes. The interviewer will be located in Rhode Island and speak to you via videoconference. If the videoconference cannot be scheduled for the same day as your clinic visit the study staff will work with you to find another convenient time
- if your male sexual partner(s) have agreed to have a videoconference call as well they will be scheduled at a separate time
- At visit 13, you will have 3 biopsies (tissue samples) taken from your vagina to be tested for TDF and FTC and how these drugs may be working.
- At visit 13, you will have samples of rectal fluid collected with swabs inserted through an anoscope (a small plastic tube inserted approximately 3-4 inches into your rectum)
- At visit 13, if you agreed to have rectal biopsies (tissue samples), you will have 5 tissue samples taken from your rectum through the anoscope.

Visit 14

Visit 14 will occur about 4 weeks after visit 13. This visit will take about 30 minutes. You will:

- Let us know if there are any changes in where you live or how we may contact you.
- Be offered 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 or periods.
- Tell us if there have been any changes to any medications you are taking now.
- You will have blood taken (about 10 ml or 2 teaspoons) to test for HIV and to compare to samples taken at previous visits. If the study clinician thinks that your health status has changed since your last study visit, you may have some additional blood and/or tests.
- You will have urine samples and/or vaginal swabs taken only if the study doctor thinks there has been a change in your health status.

Follow-up Contact

Study staff may contact you as needed, using the locator information you provide, to provide test results or ask you about any side effects you might have had from the study products or procedures.

Please, tell the study staff about any medical problems you have during the study. You can contact the study staff between your regular visits to report these problems. At each study visit, the study staff will review any side effects you might be experiencing from study products and/or study procedures.

Interim Visits

In some cases, an extra visit or visits (called Interim Visits) might be necessary in between your scheduled study appointments. Sometimes these visits may be necessary to address any questions you might have or to drop off your daily vaginal swabs. At other times, the Interim Visits may occur 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 stop study product early for any reason, you will be asked to continue with all study visits and procedures through the end of the study unless the study doctor thinks that the procedures would not be helpful or would be harmful to you.

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 have a visit just like Visit 12 and may be asked to complete a videoconference call to discuss what you did and did not like about the study product.

POTENTIAL RISKS AND DISCOMFORTS

This section describes the risks and/or discomforts of participating in the study.

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 drugs 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 drug, 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 drug side effects, please ask the study staff.

Risks from Tenofovir (TDF) and Emtricitabine (FTC):
When taken by mouth, TDF has caused rash, diarrhea, headache, pain, depression, weakness, nausea, and decreased bone mineral density. Severe reactions include kidney problems, liver

problems, worsening of Hepatitis B in patients that were already infected with HIV and Hepatitis B, and problems with your metabolism that can cause a build-up of acid in the body.

When taken by mouth, FTC has caused headache, diarrhea, nausea, fatigue, dizziness, depression, insomnia, abnormal dreams, rash, darkening of the palms and/or soles, abdominal pain, increased cough, runny nose, increases in pancreatic enzymes (substances in the blood, which can be a sign of a problem with the pancreas), increased triglycerides (a type of cholesterol), and increased creatine phosphokinase ([CPK], which can be a sign of muscle damage). Severe reactions include liver problems, worsening of Hepatitis B in patients that were already infected with HIV and Hepatitis B, and problems with your metabolism that can cause a build-up of acid in the body.

These side effects listed above have occurred when TDF or FTC have been taken by mouth in patients infected with HIV. Much less is known about side effects in healthy volunteers using vaginal rings to deliver TDF and FTC.

Three human studies have been completed delivering these drugs via vaginal ring. In two studies the IVR contained only TDF; in the other study the IVR included both TDF and FTC. In all of these studies amounts of these drugs in the blood were lower than when taken by mouth. In two of the studies the vaginal rings were well-tolerated with minimal side effects. The side effects included vaginal discharge, vaginal bleeding, itching, and pelvic pain in some of the participants. In the third study, women used a different IVR that contained only TDF and no FTC for 3 months. After about 23 days, 8 of the 17 women developed mild ulcers in their vaginas and stopped using the IVR. The IVR we are using in this study delivers a much lower dose of TDF and we do not believe women in our study will experience this problem, but we will monitor you closely, keep you informed, and take actions to ensure your health and wellness.

We do not know if the TDF-FTC IVR will prevent you from becoming infected with HIV, which is why we recommend that you use the condoms provided by the study staff. If you become infected with HIV while the using the TDF-FTC IVR, the virus may develop resistance to TDF, FTC, and other drugs in their class. This means that such drugs may not be effective in treating the HIV infection. Although other drugs may be used to treat your HIV infection, this resistance effect may make HIV treatment more difficult. If you become infected with HIV while you are on the study, blood will be drawn to confirm your HIV diagnosis and you will be referred for proper medical care.

There may be risks to an embryo or fetus that are not known at this time. Since we do not know whether an IVR containing TDF and FTC will have any effect on pregnancy, pregnant women may not join this study. If you become pregnant while on the study we will remove the IVR immediately and follow-up with you to check on the health of you, the fetus, and (if applicable) after birth the newborn.

Risks of Vaginal Ring Use: For You

In past studies of vaginal rings women have reported irritation, increased discharge, vaginal bleeding between periods, discomfort (including with vaginal sex). Women using vaginal rings

have also reported urinary tract infections (UTIs), vaginal yeast infections, or Bacterial vaginosis (BV).

Although rare, there is a very small risk of toxic shock syndrome (TSS), which may result in death. Symptoms of TSS include fever, nausea, vomiting, diarrhea, muscle pain, dizziness, lightheadedness, fainting, or a sunburn-like rash on face and body.

It is possible that you may have an allergic reaction to the study product. Symptoms of an allergic reaction include rash or other skin irritation, itching, joint pain, or difficulty in breathing.

Sexual intercourse when study staff tell you not to (e.g., the week after the IVR is inserted or around the time of the biopsies) may lead to an increased risk of infection, including sexually transmitted diseases and HIV.

Relationship problems may occur if your partner does not agree with your participation in the study and use of the ring.

Risks of Vaginal Ring Use: For Your Sexual Partner(s)
Although unlikely, there is a risk of penile irritation from contact with the IVR.

Risk of Exams: You may feel discomfort or pressure when your vagina and rectum are examined, and you may have a small amount of vaginal and/or rectal bleeding which should stop shortly after the examination.

Risk of Blood Draws: You may feel dizzy, faint or lightheaded and feel discomfort or pain when your blood is drawn. You may develop a bruise, swelling, or infection where the needle goes into your arm.

Risks of HIV and STI testing: You may become worried or nervous while waiting for your test results. There may be emotional discomfort or stress 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 the HIV test 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.

Risk of Speculum Exam, Colposcopy, OCT, and Ultrasound: There is a risk of discomfort, cramping, abdominal pressure, bleeding or pain. This is a very small risk or minor injury to the lining of your vagina.

Risk of Collecting Specimens from Vagina and Cervix:

- You may feel discomfort when the swabs or salt water are inserted and removed.
- You may experience discomfort, pain, cramping or pressure in the vagina or abdomen during vaginal biopsies
- After vaginal biopsies are taken,
    - you may experience low blood pressure after the biopsies

- you may experience limited bleeding (1 to 2 days after the procedure). In rare cases, stitches or other treatment may be required to stop the bleeding.
- even though the risk is low, you may experience infection and mild irritation. It is important that you do not put anything in your vagina or have vaginal sex for 2 days before and 7 days after the biopsies because you may be at higher risk for getting or spreading an infection until the biopsy site(s) have healed.

Risk of Collecting Specimens from your Rectum:

- You may feel discomfort when the swabs are inserted.
- If you have rectal biopsies taken,
  - you may experience low blood pressure right after the procedure
  - you may experience limited rectal bleeding (1-2 days after the procedure)
  - you may experience (the risk is low) infection, mild rectal irritation, or 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 on average about 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 for 2 days before and 7 days 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 Collecting and Storing Vaginal Swabs at Home: You may experience inconvenience or embarrassment from keeping specimens in your freezer or bringing them to and from the clinic. Theoretically, there is a small risk of food contamination from swabs stored in your freezer, but this risk is mitigated by the secure specimen containers provided by the study team. Your roommates or family members may not want you to store the vaginal swabs in the freezer.

Risks from Computerized Questionnaires, Phone Surveys, and Videoconference Calls: 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. There could be discomfort or embarrassment if someone else answers the phone when you receive the call for your daily phone survey.

Risks of Loss of Confidentiality: Any time information is collected there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks of Social Harm: It is possible that your participation in this study may cause problems in your personal and professional relationships (e.g., your male sexual partner(s) may not like the IVR or your boss may not like you taking time off from work for study visits). Your sexual partner, may accidentally discover that you have other sexual partners. In order to decrease the chance of this happening, we will make sure that your partners are not scheduled to come in for an interview at the same time. We will not reveal any information to your partners without your permission. It is possible that your involvement in the study could become known to others, and

that you may experience stigmatization or discrimination as a result of being perceived as being HIV-infected or at risk for HIV infection. For example, you could be treated unfairly, or could have problems being accepted by your family and/or communities.

Frequency Table:

	Frequent 30% of subjects	Occasional 15% of subjects	Rare Less than 1% of subjects
Serious	n/a	n/a	Toxic shock syndrome Allergic reaction Sexually transmitted infection or HIV Tear in intestine from biopsies (1 in 1000) Kidney or liver problems including worsening of pre-existing Hepatitis B
Less Serious	n/a	n/a	Infection at site of blood draw Diarrhea, nausea Depression Decreased bone mineral density
Minor	Vaginal discharge or irritation Pelvic pain or cramping	Vaginal/rectal discomfort Vaginal/rectal bleeding Discomfort/bruise/swelling with blood draw	Dizzy/faint/lightheaded with blood draw Vaginal or urinary tract infection Rash/darkening of palms or soles Headache Fatigue/weakness Insomnia/abnormal dreams Embarrassment/anxiety Relationship problems Penile irritation (partner)

ARE THERE RISKS RELATED TO PREGNANCY?

Pregnant and breastfeeding women are excluded from study participation. The effects of the study drug 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. If you are able to become pregnant, it is important that you use an effective method of birth control that you discuss with the study staff. For this study, effective, acceptable, methods of birth control include hormonal contraceptives (such as birth control pill, patch, or injection, but NOT the Nuvaring), an intrauterine device (IUD), or prior surgery (you have had your "tubes tied" or your partner had sterilization surgery 'vasectomy'). **If you become pregnant while on the study we will remove the IVR immediately and follow up with you to check on the health of you, the fetus, and (if applicable) after birth the newborn.** We will report this information, but not your name nor the newborn's name, in the Antiretroviral Pregnancy Registry (a database of safety information for women taking drugs like TDF and FTC while they are pregnant).

This research study may involve risks that are currently unforeseeable.

WHAT ARE THE BENEFITS?

If you agree to take part in this study, there may be no direct benefits to you. We hope the information learned from this study will benefit others with HIV in the future. You may get no direct benefit from being in this study. **We do not know if tenofovir (TDF) and emtricitabine (FTC) delivered by an intravaginal ring will work 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 vaginal and 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 screening tests and exams. 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 UTMB Patient Billing Services.

WILL I RECEIVE ANY PAYMENT?

You will be compensated for your time and effort for your scheduled study visits as follows:

- You have already received $50 for the Screening Visit
- You will receive $100 for each of the 12 additional study visits that include vaginal samples that you complete and
    - an additional $50 for each visit that includes vaginal biopsies and
    - an additional $50 for each visit that includes rectal biopsies.

- You will receive $50 for completion of each of the 2 audio-recorded in-depth interviews.
- You will receive $50 for Visit 14
- You will receive an additional $15 for any extra visits that take less than 30 minutes and $50 for any extra visits that take more than 30 minutes.
- A parking voucher will be provided for each of the study visits that you complete, if needed.

In total, you may receive up to $1700 for your participation in this research study, not counting payment for any extra visits.

You will be issued a UTMB Clincard, which is a debit card that your funds are loaded onto following completion of the screening visit. When a study visit is completed, funds will be approved and loaded onto your card. The funds will be available within 48 hours and can be used at your discretion. You will be issued one card for the duration of your participation. If your card is lost or stolen, you can contact customer service at 1-866-952-3795. We will collect some information about you, including name, address, telephone number, date of birth, email address, if applicable, and your social security number (if a US citizen) in order to issue the debit card. All information is stored in a secure fashion and will be kept confidential. You will also receive a parking token at the end of each visit if needed. 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 specimens with all identifiers removed may be used for commercial profit. You will not share in this commercial profit.

WHAT HAPPENS IF I AM INJURED (EXPERIENCE HARM)?

It is important that you report any illness or injury to the research team listed at the top of this form immediately. Compensation for an injury resulting from your participation in this research is not available from the University of Texas Medical Branch at Galveston. If you are physically injured because of any of the study products or procedures, your injury will be treated. You or your insurance company or health care plan, will be billed and you will be responsible for any charges. You will be responsible for paying any costs related to illnesses and medical events not associated with being in this study. There are no plans to provide other forms of compensation. However, you are not waiving any of your legal rights by participating in this study. Questions about compensation may be directed to the study doctor. The U.S. National Institutes of Health (NIH) does not have a program to pay money or give other forms of compensation for injuries.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?
USE AND DISCLOSURE OF YOUR HEALTH INFORMATION

Study records that identify you will be kept confidential as required by law. Federal privacy regulations provided under the Health Insurance Portability and Accountability Act (HIPAA) provides safeguards for privacy, security, and authorized access of your records. These regulations require UTMB to obtain an authorization from you for the use and disclosure of your health information. By signing this consent form, you are authorizing the use and disclosure of

your health information for the purpose of completing the research study. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of the University of Texas Medical Branch (UTMB). For records disclosed outside of UTMB, you will be assigned a unique code number. The key to the code will be kept in a locked file in Dr. Kathleen Vincent's office.

As part of the study, Dr. Kathleen Vincent and her study team will report the results of your study-related laboratory tests to the following recipients: FDA, National Institutes of Health, and Oak Crest Institute of Science. The sponsor of this study may further disclose this information to regulatory agencies or other recipients. While the sponsor and other recipients may understand the importance of protecting the confidentiality of your health information, UTMB cannot guarantee the confidentiality of your health information or protect from further disclosures once these recipients receive your health information.

If you sign this form, you are giving us permission to collect, use and share your health information. You do not need to sign this form. If you decide not to sign this form, you cannot be in the research study. We cannot do the research if we cannot collect, use and share your health information. Whether or not you agree to the research project or give us permission to collect, use or share your health information will not affect the care you will be given at UTMB. Dr. Kathleen Vincent will use and disclose your study related test to complete the research study. These would include blood tests for complete blood count, kidney and liver function, blood and vaginal and rectal fluid tests for drug concentration, HIV and Hepatitis B tests and vaginal fluid tests for sexually transmitted diseases, bacterial and viral pathogen levels, and images from the pelvic exam and optical coherence tomography. The test results for complete blood count, kidney and liver function, HIV and Hepatitis B tests, and tests for sexually transmitted diseases will be recorded in your medical record. All of the above tests may be reported to Oak Crest Institute of Science, National Institutes of Health, and/or the FDA. You will be offered a copy of any research information (results from blood count, kidney and liver function, HIV and Hepatitis B testing, and sexually transmitted disease screening) that will be included in your medical record. For all other health information we collect on you (results from the blood and vaginal fluid tests for bacteria levels and drug concentration, and images from the pelvic exam and optical coherence tomography), will not be included in your medical record and you will not receive a copy of the information. Additionally, the results of this study may be compared to results obtained in other studies that you may have participated in with Dr. Vincent's team.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include, for example, representatives of Oak Crest Institute of Science, the Food and Drug Administration, UTMB, UTMB IRB, and the National Institutes of Health. This authorization for the use and disclosure of your health information as described above expires upon the conclusion of the research study except for FDA regulated studies. This study is an FDA regulated study and for FDA regulated studies, the study sponsor and government agencies, such as the FDA may review your records after the study ends.

If you change your mind later and do not want us to collect or share your health information, you need to contact the researcher listed on this consent form by telephone. You need to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it. The results of this study may be published in scientific journals without identifying you by name.

This study is being conducted according to ethical guidelines. Efforts will be made to keep your personal information private. Only your study ID, **NO** personal identifiers (e.g., your name, address, date of birth, social security number), will be collected as part of the questions you will answer by computer, automated phone surveys, or video conference call. Videoconference calls will be conducted in private via a secure connection and audiotaped; no video will be saved. You should NOT identify anyone during the videoconference calls. The audio files will be transcribed (put in writing) by the person interviewing you or by another person who does not know you and does not have your identifying information. All records, including audiotapes, will be kept in a secure, double locked location and only study staff will have access to the records. The audio recordings will be destroyed at the end of the study.

Your physical exams, including vaginal and rectal exams will be done in private. However, we cannot guarantee absolute confidentiality. In some situations, including emergencies, legal and professional rules may force us to share confidential information about you. If this study is published, your name will not be used and you will not be personally identified. You are encouraged but not required to tell your sexual partner(s) about your participation in this study.

- If gonorrhea, chlamydia, HIV, syphilis, hepatitis B, or hepatitis C is identified, we are required to confidentially report this to the State 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.
- In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical record information) related to your participation in this research study in response to an order from a court of law. 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 Texas law, the appropriate agencies.
- Once this information has been disclosed, it may be further disclosed by the recipient of the information and no longer protected by privacy laws.

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form, you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical

records. This could include information about HIV and genetic testing, or treatment for drug or alcohol abuse or mental health problems.

The research team will know your identity and that you are in the research study. Other people at UTMB, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety. If you think this study might affect your clinical care, please inform your doctor.

People outside of UTMB may need to see or receive your information for this study. This study will be reviewed periodically to monitor its conduct. Therefore, as mentioned above, your records may be reviewed by government agencies and the groups listed below as part of routine audits:

- US National Institutes of Health (NIH)
- Food and Drug Administration (FDA)
- Office for Human Research Protections (OHRP)
- Oak Crest Institute of Science (OCIS)
- University of Texas Medical Branch 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

We cannot do this study without your authorization (permission) to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form; however, people outside UTMB who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

Finally, please specifically authorize the use of your private health information relating substance abuse, psychiatric information, or HIV/AIDS, if applicable, for the above-described purposes.

Initial: _____

Certificate of Confidentiality: To help us further protect your privacy, the investigators have obtained a Confidentiality Certificate from the National Institutes of Health (NIH) a branch of the Department of Health and Human Services (DHHS).

With this Certificate, the investigators cannot be forced (for example by court subpoena) to disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Note however, that if an insurer or employer learns about your participation, and obtains your consent to receive research information, then the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by US Law. 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.

WHAT ARE MY RIGHTS AS A RESEARCH PARTICIPANT?

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

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

WHY MIGHT I BE WITHDRAWN FROM THE 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, OCIS, IRB, FDA, OHRP, or the local government or regulatory agency
- Study staff believes that participating in this study would cause injury that could be harmful to you.
- You do not want to learn your HIV test result.
- You are not able to complete the study procedures.
- 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, 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 THE 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 Texas Medical Branch, on your current or future

medical care at a UTMB hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

WHO CAN I CONTACT WITH QUESTIONS ABOUT THIS RESEARCH STUDY?

If you have any questions, concerns or complaints before, during or after the research study, or if you need to report a research related injury or bad side effect, you should immediately contact Dr. Kathleen L. Vincent at 409-772-2610 or, if after normal office hours the study coordinator Lauren Dawson at 409-354-9792.

This study has been approved by the Institutional Review Board. If you have any complaints, concerns, input or questions regarding your rights as a subject participating in this research study or you would like more information about the protection of human subjects in research, you may contact the Institutional Review Board Office, at (409) 266-9400 or irb@utmb.edu.

****

VOLUNTARY CONSENT: The purpose of this research study, procedures to be followed, risks and benefits have been explained to me and I was given the opportunity to ask questions, and all of my current questions have been answered to my satisfaction. I have been told who to contact if I have additional questions and 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 University of Texas Medical Branch Institutional Review Board Office at (409) 266-9475. By signing this form, I am confirming that I have read this consent form and I voluntarily agree to participate as a subject in this research study. A copy of this consent form will be offered to me.

_____
Participant's Printed Name

_____ _____
Participant's Signature Date and Time

Rectal Biopsy Collection at Visits 7, 12, and 13

I understand that I do not have to agree to have rectal biopsies taken to be able to participate in the study.

____ (initials) **Yes**, I agree to have rectal biopsies at Visits 7, 12, and 13.

____ (initials) **No**, I do NOT agree to have rectal biopsies at Visits 7, 12, and 13.

CERTIFICATION OF INFORMED CONSENT: I certify that I have explained the nature and purpose of this research study using language that is understandable and appropriate to the above-named individual, and I have discussed the project, 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.

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date and Time

Future Use of Specimens

You have decided to take part in the research study, named above. While you are in this research study there will be samples of blood, fluid and tissue from your vagina taken at each study visit with the inclusion of the self-collected daily swabs, and fluid and tissue from your rectum taken at visit 7 and 12. At the end of the study there may be some leftover samples that might be useful for future research.

Your samples will be stored at special 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). The study team will have sole control over these samples, and only approved researchers will have access to your samples. Your samples may be stored indefinitely, and the exact time at which your samples will be analyzed has not been determined. The study team will oversee the storage facilities to protect you and other research volunteers from harm. Your samples will not be sold or used directly to produce products that can be sold for profit.

Your samples will be used to look for ways that your body responds to infection (such as cells, proteins, and other chemicals in your body) and the TDF and FTC you received during the study. 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 or medications. 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.

Any future research performed on these samples will not require any extra involvement from you. 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.

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.

____ (initials) **Yes**, I agree to future use of any leftover samples

____ (initials) **No**, I do NOT agree to future use of any leftover samples

Researchers will need to ask your permission again for other types of research not described in this informed consent. Indicate below if you want researchers to contact you in the future.	
____ (initials) **Yes**, I would like to be contacted about future research	____ (initials) **No**, I would NOT like to be contacted about future research
You may indicate if you want to be contacted in the future if researchers find something that is important for your health. Information is considered important if it would have an impact on your health or wellbeing, or cause you to make different decisions related to your healthcare.	
____ (initials) **Yes**, I would like to be contacted with information that might affect my health	____ (initials) **No**, I would NOT like to be contacted with information that might affect my health

CERTIFICATION OF INFORMED CONSENT: I certify that I have explained the nature and purpose of this research study using language that is understandable and appropriate to the above-named individual, and I have discussed the project, 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.

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent 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) for 1 day or naproxen (Aleve) for at least 4 days before biopsies. 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

PrEP-Pod-IVR-02 SCHEDULE OF STUDY VISITS

		Baseline (~28 days)		**Stage 2 (~37 days)**					**Stage 3 (~72 days)**					
		Collect daily vaginal swabs at home (28 days)		Collect daily vaginal swabs and complete daily phone surveys at home (28 days)					Collect daily vaginal swabs and complete daily phone surveys at home (28 days)					
				No sex until given clearance at V5			**No sex** for 2 days before until 7 days after V7		**No sex** until given clearance at V10			**No sex** for 2 days before until 7 days after V12		
Study Procedures	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**	**Visit 13**	**Visit 14**
Study Day		**Stage 1 Day 0**	**Stage 1 Day 14**	**Stage 2 Day 0**	**Stage 2 Day 7**	**Stage 2 Day 18**	**Stage 2 Day 28**	**Stage 2 Day 37**	**Stage 3 Day 0**	**Stage 3 Day 7**	**Stage 3 Day 18**	**Stage 3 Day 28**	**Stage 3 Day 37**	**Stage 3 Day 72**
Sign Consent Form		X												
Group Assignment			X											
Computer Questionnaire		X					X					X		
Videoconference Call								X					X	
Medical History		X	X	X	X	X	X	X	X	X	X	X	X	X
Bring Study Diary			X	X	X	X	X	X	X	X	X	X	X	
General Physical Exam		Maybe	Maybe	Maybe	Maybe	Maybe	Maybe	Maybe	Maybe	Maybe	Maybe	Maybe	Maybe	
Vaginal Exam with Colposcopy and OCT		X	X	X	X	X	X	X	X	X	X	X	X	
Pelvic Ultrasound				Maybe	Maybe	X	Maybe		Maybe	Maybe	X	Maybe		
Vaginal Ring				Inserted			Removed		Inserted			Removed		
Samples taken:														
Blood		Maybe	Maybe	X	X	X	X	X	X	X	X	X	X	X
Urine		X	X	X	X	X	X	X	X	X	X	X	X	
Vaginal fluid		X	X	X	X	X	X	X	X	X	X	X	X	
Vaginal biopsies							X					X	X	
Rectal fluid							X					X	X	
Rectal biopsies- optional							X					X	X	