utmb Health

The University of Texas Medical Branch at Galveston
Screening Consent Form

Protocol 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

IRB Number: 17-0131

Sponsor: National Institutes of Health – NIAID DAIDS
Oak Crest Institute of Science

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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 woman 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.

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.

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 the 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. The last 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. Also, 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 procedures are involved as part of the screening process?

If you agree to take part, you will be asked to sign this screening consent form and have the following tests and procedures. The procedures are being done only because you are taking part in this research study and not as standard of care. In order to determine if you qualify for the study, the study doctor will need to perform the following tests:

At today's visit, which may take about 1-2 hours, you will:

- Answer questions about yourself, such as questions about your period, your medical history, any medicines that you may take and how we can contact you.
- Answer some questions on a computer about your health and 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.
- 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, which may include an exam of your vagina, cervix, and rectum.
    - 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 4 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), as well as for comparison to samples taken at future visits.

    - The study doctor may also collect samples from your cervix for a "Pap test" or "Pap smear" if you are unable to provide results from a Pap test done in the past 36 months. The results of your Pap test may affect whether or not you can continue in the study. If the test is abnormal, it could mean you have cervical cancer, or that you should have more tests or treatment to lower your chances of having it turn into cervical cancer. If the test is abnormal the study doctor will discuss the results with you and refer you back to your primary doctor or another provider to do further testing or treatment.

- Provide a urine sample to be tested for routine safety, pregnancy, gonorrhea, chlamydia, and possibly other infections. You will find out the results of the pregnancy test today. If your pregnancy test is positive, you cannot continue in the study.
- 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, hepatitis, and HIV.

    The HIV test is a test for the antibodies to HIV. An antibody is a substance that blood cells make to fight infection. A positive HIV test means that your blood sample tested positive for HIV and testing will be performed to confirm (prove) this finding by looking for copies of the virus itself. 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 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 at your next visit. 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.

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.

If you are eligible to participate in the study after the results of this screening exam have come back, you will be asked to return for a study visit in which you will give informed consent to enroll in the study. Today, you will be given a fact sheet with more information on the study.

The clinical lab results from this screening visit 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.

What are the possible risks for choosing to participate in this screening process?

This section describes the risks and/or discomforts with the screening exams and tests. If you are eligible, the risks and/or discomforts of participating in the study will be described in the consent form for study participation.

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.

Risk of Collecting Specimens from Vagina and Cervix: You may feel discomfort when the swabs are inserted.

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 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 (being discriminated against).

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

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). 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. You may experience inconvenience or embarrassment from keeping swabs your freezer or carrying the swabs to and from the clinic. Your roommates or family members may not want you to store the vaginal swabs in the freezer.

Frequency Table:

	Frequent 30% of subjects	Occasional 15% of subjects	Rare Less than 1% of subjects
Serious	n/a	n/a	n/a
Less Serious	n/a	n/a	Infection at site of blood draw
Minor	n/a	Vaginal/rectal discomfort Vaginal/rectal bleeding Discomfort/bruise/swelling with blood draw	Dizzy/faint/lightheaded with blood draw Embarrassment/anxiety Relationship problems

What are the 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 a woman and 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 had your "tubes tied" or your partner had sterilization surgery 'vasectomy').

What are the potential benefits for participating in this research study?

You may be eligible to participate in a clinical research study, there may be no direct benefits to you. Possible benefits to you may include knowledge of results of the kidney and liver function tests as well as the HIV and sexually transmitted disease tests. This screening is provided for your information only and does not take the place of seeing your primary care physician or specialist. If these tests show that you might have any health problems, you will be referred for medical care and other services available to you.

What are the benefits to society?

This research is designed to study a new medicine that is not approved by the FDA to see how much TDF and FTC is delivered to the genital tract when released from an IVR and to see if it is safe. The results of the research may contribute to scientific knowledge and may benefit patients in the future.

What other choice do I have (alternative treatment)?

The alternative is not to participate in this research study. 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 will happen if I am harmed as a result of taking part in this study?
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, Oak Crest Institute of Science, or the National Institutes of Health (NIH). 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 the 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.

Will I be reimbursed for participating in this screening process?
You will be compensated $50 for your time and effort for the screening tests and exams. 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 the 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 voucher at the end of each visit if needed.

Your specimens with all identifiers removed may be used for commercial profit. You will not share in this commercial profit.

Voluntary Consent and Withdraw: Can I be removed without my consent?
It is important to remember that your participation in this screening is voluntary. At any time, you may change your mind and choose not to participate, without penalty or loss of benefit unrelated to the screening. You may withdraw from the screening at any time.

You may be withdrawn from the screening tests and exams 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 considers that having the exams and tests 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 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 screening exams and tests, any identifiable research or medical record information recorded for, or resulting from, your participation in these screening exams and tests prior to the date that you were formally withdrawn from these screening exams and tests without your consent may continue to be used and disclosed by the investigators for the purposes described above.

Will my insurance provider or I be charged for the costs of any part of this research study?

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.

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 recorded. 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. 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.

This study will be reviewed periodically to monitor its conduct. Therefore, as mentioned above, 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)
- 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

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

With the 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 my 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.

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.

Future Use of Specimens

You have decided to take part in a screening exams and tests for the research study, named above. There will be samples of fluid from your vagina taken. At the end of the screening, there may be some leftover samples that might be useful for future research. Even if you are not eligible to participate in the study, your samples from today's visit could still be used.

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). 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

Consent to Participate:

The purpose of this research study, procedures to be followed, risks and benefits have been explained to you. You have been given the opportunity to ask questions, and your questions have been answered to your satisfaction. You have been told who to contact if you have additional questions. By signing this form, you are confirming that you have read this consent form and voluntarily agree to participate as a subject in this study.

Signature of Subject	Date and Time

Using language that is understandable and appropriate, I have discussed this project and the items listed above with the subject.

Signature of Person Obtaining Consent	Date and Time Consent Obtained

Printed Name of Person Obtaining Consent