If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. plate

COMBINED PARENTAL PERMISSION / RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: Safety, PK/PD, Acceptability, and Desirability of a Novel HIV Prevention Douche among Adolescent Men (DREAM-ATN)

Application No.: IRB00272468

Sponsor/Supporter/Funded By: The study is being paid for by *The Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) with co-funding from The National Institute on Drug Abuse (NIDA) and The National Institute of Mental Health (NIMH)

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513-225-2884

You are being asked to join a research study. Participation in this study is voluntary. Even if you decide to join now, you can change your mind later.

If you are a parent or legal guardian of a child who may take part in this study, your permission is required for your child to participate. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child.

1. Research Summary (Key Information):

The information in this section is intended to be an introduction to the study only. Complete details of the study are listed in the sections below. If you are considering participation in the study, the entire document should be discussed with you before you make your final decision. You can ask questions about the study now and at any time in the future.

You are being asked to participate in this research because you participated in an online behavioral study (ATN Dream Behavioral Study) and indicated you were interested in participating in an HIV prevention study comparing a rectal douche containing a mixture of saline (i.e., salt water) and the anti-HIV drug

tenofovir. The study is being done to evaluate the safety of tenofovir, where the tenofovir goes in the body after dosing, and the acceptability of the douching product. This is part of a longer-term project to develop a safe and effective tenofovir douche to be used to prevent Human Immunodeficiency Virus (HIV) infection associated with anal sex.

If you join this study you will be asked to attend 6 study visits over 4-5 months and you will receive the study rectal douche once. You will have physical exams and rectal swabs. For participants age 18 and above, there will be collection of rectal fluid and scope procedures to collect rectal biopsies. There are some risks to receiving the study douche and procedures which are described later in this document. There is no direct benefit or cost to you from being in this study.

2. Why is this research being done?

The study is being done to evaluate the safety of tenofovir, where the tenofovir goes in the body after dosing, and the acceptability of the douching product.

The use of the tenofovir douche in this study is investigational. The word "investigational" means the tenofovir douche is not approved for marketing by the US Food and Drug Administration (FDA) for HIV prevention. This means we do not know if it works to protect against HIV. However, the FDA is allowing the use of the tenofovir douche in this study. In future studies, we would like to see if this product could prevent HIV. In order to do this, first we need to make sure that it is safe for use.

We will use a formulation of the douche in this study that will include tenofovir mixed in saline. This product will be administered during your study visit in our clinic or research unit.

Who can join this study?

Healthy, HIV-negative adolescent and young adult individuals who were assigned male sex at birth and identify as male will be enrolled at Johns Hopkins University (JHU). We are asking young adolescent and young adult men to join this study who:

1. Tell us that they have had consensual receptive ("bottom") anal sex in the past.
2. Are HIV negative (uninfected) and agree to use condoms for receptive anal sex for the duration of study

How many people will be in this study?

A total of up to 48 individuals will be enrolled to assure that 16 individuals complete the study.

3. What will happen if you join this study?

If you join the study, you will be asked not to put anything (drug/medication, lube, penis, other object, sex toy, or douche) in your rectum for 72 hours before and after using the tenofovir douche study product, and for participants age 18 and above, 7 days after each flexible sigmoidoscopy (where a flexible tube with a scope is placed in the rectum) with biopsy collection. Participants less than age 18 will not have a flexible sigmoidoscopy. We will give you specific instructions at each visit. You will also be asked to avoid using the following products or medications, which are likely to alter the study results as well:

- Any rectally administered medications other than study product (including over-the-counter products any product containing N-9; N-9 has been shown to change the rectal lining, which could result in injury to you)
- Any other investigational products

There are 6 study visits that you will be asked to attend.

STUDY VISITS

Visit 1 – Screening:

The Screening Visit will take about 2 hours. You will be asked to complete the following procedures:

- Sign this form after you have reviewed it carefully and had the chance to ask questions about the study
- Answer questions about yourself, such as your medical history, any medicines that you are taking, where you live, and how we can contact you. We will also ask about any known HIV-infected partners and about your drug and alcohol use.
- Have a physical exam, including a rectal exam
- Have your height, weight, blood pressure, heart rate, and temperature measured
- Provide urine sample for drug screen to test for recreational drugs and prescription medications
- Provide urine sample for gonorrhea and chlamydia testing
- Have rectal swab collected by a study clinician to be tested for gonorrhea and chlamydia
- If ulcers are present on examination, a swab for herpes simplex virus (HSV) will be collected and tested
- Have a blood sample (about 26 mL or ~5 teaspoons) taken to check the following:
  - Health of your blood, liver, and kidneys
  - Hepatitis B status
  - HIV status
  - Syphilis test
- Learn from study staff how to avoid infections passed during sex and proper condom use and receive condoms from the study staff.

The HIV test is a test for a protein and 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 that repeat testing will be performed to confirm (prove) this finding. If your sample is proved to be positive for HIV, it means that you are a carrier of HIV. It also means that you can pass the virus to others through sexual intercourse, by sharing needles, and through donating blood and organs. A negative HIV test means that at this time, no antibody to HIV was found in your sample based on the result of the initial screening test, repeat screening tests, or a confirmatory test.

There can be individuals who have HIV test results that are called “false positive.” That means that, for some reason, the test shows that HIV proteins or 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 actually already 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.

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. If you have HIV, you will learn from the study staff where you can get care or treatment.

We will give you the test results when they are available. If you have any infections, you will learn from the study staff where you can get care or treatment.

If the results of your screening tests show that you are able to continue your participation in this study, the study staff will contact you to schedule Visit 2.

If you are HIV negative and you either: decide you are not interested in participating in this study or if after the medical screening you are not eligible to be in this study, you will be asked to participate in an online-facilitated in-depth interview (IDI). This may happen as part of the Screening Visit or you may be asked to come back at a later time to complete the interview. This interview will examine concerns, perceived barriers and challenges when individuals are invited to participate in a biomedical clinical trial such as this study. The IDI will be conducted by a trained interviewer located at UPenn using video-conferencing. If your HIV test is positive, you will not be asked to participate in the interview.

Visit 2 – Enrollment:

The baseline study visit will take about 3 hours, and will take place no more than 45 days after Visit 1. We will ask that you not have receptive (bottom) anal sex or put anything (drug/medication, penis, other object, sex toy or any enema) in rectum for 72 hours before the visit and for participants age 18 and above, 7 days after the flexible sigmoidoscopy procedure. Additionally, you may be required to undergo pre-procedure COVID-19 testing within 72hrs of any biopsy visit. If the pre-procedure results indicate COVID infection, the procedure visit will be canceled and may be rescheduled at a later time. The following activities will be completed at this visit:

- Confirm that you understood and signed the consent form and want to continue study participation
- You will receive a copy of your test results, if appropriate
- Your medical history, medications and contact information will be updated as necessary
- A physical exam will be performed, as needed
- Your blood pressure, heart rate and temperature will be measured
- Blood samples (about 6 mL or a little over 1 teaspoon) will be taken for:
    - HIV testing
    - Testing for tenofovir medication in your blood
    - You will receive a cleansing douche
- **Flexible Sigmoidoscopy and Rectal Biopsy Collection for participants age 18 and above:** After receiving the cleansing douche in the clinic, you will have a flexible sigmoidoscopy procedure with biopsy collection.

During the flexible sigmoidoscopy procedure, you will be positioned on your left side on an examination table. The doctor inserts a flexible, lighted tube, called a sigmoidoscope or scope, into the anus and slowly guides it through the rectum and into the sigmoid colon. The scope inflates the colon with air to give the doctor a better view. A small camera mounted on the scope transmits a video image from inside the colon to a computer screen, allowing the doctor to carefully examine the tissues lining the sigmoid colon and rectum. The scope is also equipped with a small instrument that allows the doctor to collect tissue samples or biopsies from 10-20 cm (a little less than 8 inches) inside the rectum. Up to 5 small biopsies will be collected during the flexible sigmoidoscopy session. Each biopsy is a small piece of tissue about the size of a grain of rice.

- You will complete a web-based Baseline Behavioral Questionnaire
- You will learn from study staff how to avoid infections passed during sex and proper condom use and receive condoms from the study staff.

Visit 3 Dosing Visit (Day 1):

Visit 3 will take place at least a week after Visit 2. This visit will take place in the research unit and must occur at least 7 days after the last flexible sigmoidoscopy with biopsy collection. Additionally, you may be required to undergo pre-procedure COVID-19 testing within 72hrs of any biopsy visit. If the pre-procedure results indicate COVID infection, the procedure visit will be canceled and may be rescheduled at a later time. The following activities will be completed at these visits in the research unit:

- You will receive a copy of your test results, if appropriate
- Your medical history, medications, and contact information will be updated as necessary
- You will be asked how you are feeling and about any symptoms you might be experiencing
- Physical exam will be performed, as needed
- Have your blood pressure, heart rate and temperature measured
- You may have an IV placed in your arm to help us easily collect blood samples. It will be removed prior to your leaving the unit.
- Prior to collection of any study specimens or enema administration, have blood samples (about 20 mL or ~4 teaspoons) taken in order to:
    - Check the health of your blood, liver, and kidneys
    - HIV-1 testing
    - Syphilis testing, if your research care provider believes this is needed
    - Check the levels of tenofovir in your blood
- Provide urine sample for gonorrhea and chlamydia testing, if your research care provider believes this is needed
- Have rectal swab collected by a study clinician to be tested for gonorrhea and chlamydia and/or a swab for HSV, if your research care provider believes this is needed
- **Study Product Administration**: You will have the tenofovir douche administered into your rectum by a study clinician.
- **Multiple Blood Samples**: You will have multiple blood samples collected from the peripherally inserted venous catheter (PIV) in your arm or from multiple blood draws at approximately 1 hr, and 6 hr after the douche. We will test these samples to see how much tenofovir is in your blood. Approximately 32 mL or ~2 tablespoons will be collected.
- **Anoscopy and Rectal Fluid Collection for participants age 18 and above and Microbiome Collection for all participants including those who are less than age 18**: Just before the flexible sigmoidoscopy procedure and at the same time as the biopsy collection, rectal fluid will be collected using a swab and a microbiome specimen will be collected using a swab. These swabs draw the sample of the rectal fluid and microbiome and are inserted through a short hollow lubricated tube called an anoscope, which is placed in the rectum for several minutes while the fluid is collected on the swab.
- **Flexible Sigmoidoscopy and Rectal Biopsy Collection for participants age 18 and above:** After receiving the study douche in the clinic, you will have a flexible sigmoidoscopy procedure with biopsy collection. This procedure will be completed at either 1, 6, 24 (on Day 2), or 72 hours (on Day 4) after receiving the tenofovir douche and based on a schedule that we will give you. During this procedure, you will be positioned on your left side on an examination table. The doctor inserts a flexible, lighted tube, called a sigmoidoscope or scope, into the anus and slowly guides it through the rectum and into the sigmoid colon. The scope inflates the colon with air to give the doctor a better view. A small camera mounted on the scope transmits a video image from inside the colon to a computer screen, allowing the doctor to carefully examine the tissues

lining the sigmoid colon and rectum. The scope is also equipped with a small instrument that allows the doctor to collect tissue samples or biopsies from 10-20 cm (a little less than 8 inches) inside the rectum. Up to 20 small biopsies will be collected during flexible sigmoidoscopy session. Each biopsy is a small piece of tissue about the size of a grain of rice.

- You will be asked to complete the web-based Research Unit Dose Acceptability Questionnaire
- Study staff will discuss how to avoid infections passed during sex and proper condom use, and you will receive condoms from the study staff.
- You will be asked not to put anything in your rectum for 72 hours after receiving study enema and completing the flexible sigmoidoscopy procedure.

Visit 4 (Day 2) and Visit 5 (Day 4) – Sampling Visit:

These visits will take place the day after (24 hours) and two days after (72 hours) receiving the tenofovir douche and will also take place in clinic or the research unit. Additionally, you may be required to undergo pre-procedure COVID-19 testing within 72hrs of any biopsy visit. If the pre-procedure results indicate COVID infection, the procedure visit will be canceled and you will be asked to attend one final visit at a later time.

The following activities will be completed at these visits:

- You will receive a copy of your lab test results, if appropriate.
- Your medical history, medications, and contact information will be updated as necessary
- You will be asked how you are feeling and about any symptoms you might be experiencing
- Physical exam will be performed, as needed
- Prior to collection of any other study specimens, have blood samples (about 10 mL or ~2 teaspoons) taken in order to:
  - Check the health of your blood, liver, and kidneys
  - Check the levels of tenofovir in your blood
- **Flexible Sigmoidoscopy and Rectal Biopsy Collection for participants age 18 and above**: If, based on your assigned schedule, you did not have the flexible sigmoidoscopy on Day 1, you will have a flexible sigmoidoscopy with collection of up to 20 rectal biopsies at approximately 24 hours or 72 hours after you receive the tenofovir douche.
- **Anoscopy and Rectal Fluid Collection for participants age 18 and above and Microbiome Collection for all participants including those less than age 18**: If, based on your assigned schedule, you did not have rectal fluid collection Day 1, you will have an anoscopy during which rectal fluid will be collected using a swab at 24 hours or 72 hours after you receive the tenofovir douche. All individuals will have the microbiome collection again at 24 hours.
- Study staff will discuss with you how to avoid infections passed during sex and will share information about proper condom use, and you will receive condoms from the study staff.
- You will be asked not to put anything (drug/medication, penis, object, sex toy, or enema including take-home enema) in rectum for 72 hours before and after research unit study product exposure and 7 days after the flexible sigmoidoscopy with biopsy collection.

Visit 6 – Termination Visit:

This visit will take place the day after your final biopsy and will also take place in clinic or the research unit.

The following activities will be completed at this visit:

- You will receive a copy of your lab test results, if appropriate.
- Your medical history, medications, and contact information will be updated as necessary
- You will be asked how you are feeling and about any symptoms you might be experiencing
- Physical exam will be performed, as needed
- Have your height, weight, blood pressure, heart rate, and temperature measured
- Provide urine sample for gonorrhea and chlamydia testing
- Have rectal swab collected by a study clinician to be tested for gonorrhea and chlamydia
- If ulcers are present on examination, a swab for HSV will be collected and tested
- Prior to collection of any other study specimens, have blood samples (about 10 mL or ~2 teaspoons) taken in order to:
  - Check the health of your blood, liver, and kidneys
  - HIV status
  - Syphilis test
- Study staff will discuss with you how to avoid infections passed during sex and will share information about proper condom use, and you will receive condoms from the study staff.
- You will be asked not to put anything (drug/medication, penis, object, sex toy, or enema including take-home enema) in rectum for 72 hours before and after research unit study product exposure and 7 days after the flexible sigmoidoscopy with biopsy collection.
- Complete an in-depth interview (IDI) via the HIPAA-compliant video-chat platform, BlueJeans

Exit Follow-Up Phone Call

If necessary, a final exit follow-up call will be made by the study staff to you. This call may be required to provide laboratory test results or post-test counseling.

Interim Visits

In some cases, an extra visit or visits (called an Interim Visit) might be necessary in between your scheduled study appointments. The Interim Visit may occur if you experience adverse events that need to be evaluated by study staff. In such cases, study staff may refer you to appropriate medical care.

Communicable diseases:

The law requires us to report positive tests to the health department. This reporting will include information that identifies you (for example name, date of birth, home address, phone number, etc.) as required by Maryland law. The health department may use this information to contact you for further follow up and/or to help conduct health surveillance activities aimed at preventing or controlling diseases.

Interview recordings (conducted by BlueJeans):

As part of this research, we will create and use audio recordings of the interview to help answer the research question. The BlueJeans platform will be used to conduct the video sessions, but no video recordings will be made. Only the audio portion of the video session will be recorded. Any recordings will not be used for advertising or non-study related purposes.

You should know that:

- It is possible that your identity may be known from your voice recording.
- You may request that the recordings can be stopped at any time.

- If you agree to allow the recording and then change your mind, you may ask us to destroy that recording. If the recording has had all identifiers removed, we may not be able to do this.
- We will only use these recordings for the purposes of this research.
- The audio recording will be transcribed by the study team at UPenn that has agreed to keep all data confidential.

Incidental Findings

As part of this research study, you will undergo a flexible sigmoidoscopy. A qualified professional will review your flexible sigmoidoscopy. This flexible sigmoidoscopy will not include the full diagnostic information that you would get if your primary doctor referred you for this procedure.

There is a possibility that while conducting the flexible sigmoidoscopy we may see an unexpected abnormality. This is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by mail, email, or phone. In the case of a potential serious emergency, someone may go to your home.

A qualified person (usually a member of the research team) will talk to you if there is an incidental finding. You do not have an option to decline information about an incidental finding from this procedure.

If you want, we will give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

What could happen if there is an incidental finding?

- An incidental finding may cause you to feel anxious.
- Since a report of the incidental finding will be part of your medical record, it will be available to those accessing your medical record for your clinical care and may affect your current or future life or health insurance coverage. This risk will vary depending on the type of insurance plan involved.

The costs for any care that may come from the incidental finding, such as the need to see a doctor to diagnose or treat an incidental finding, will not be paid for by this research study. These costs would be your or your insurance company's responsibility.

Will research test results be shared with you?

This study involves research tests that may produce information that could be useful for your clinical care. We will share this information with you. The following results will be shared with you, if appropriate (depending on the visit):

- Health of your blood, liver, and kidneys
- Hepatitis B status
- HIV test
- Syphilis test
- STI screening results

How long will you be in the study?

You will be in this study for up to 4-5 months.

4. What happens to data and biospecimens that are collected in the study?

If you join this study, your data and biospecimens will be used to answer the research question and your data will be used to publish the findings of this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

You will not own the data and/or biospecimens collected from you as part of this research study. If researchers use them to create a new product or idea, including those that may have commercial value, you will not benefit financially from those efforts.

Johns Hopkins researchers and their collaborators may use the data/biospecimens collected in this study for future research purposes and may share some of the data/biospecimens with others.

Because science constantly advances, we do not yet know what future use of research data or biospecimens may include. This future research may be unrelated to the current study and may include outside collaborators.

Sharing data and/or biospecimens is part of research and may increase what we can learn from this study. Often, data/biospecimen sharing is required as a condition of funding or for publishing study results. It also is needed to allow other researchers to validate study findings and to come up with new ideas. Your data and/or biospecimens may be shared with researchers at Johns Hopkins and other institutions, for-profit companies, sponsors, government agencies, and other research partners. Your data and/or biospecimens may also be put in government or other databases/repositories.

We (Johns Hopkins) will do our best to protect and maintain your data/biospecimens in a safe way. One of the ways we protect data/biospecimens is by limiting the uses of the information and the type of information that is shared, especially your personal information. This may occur through data/specimen sharing agreements and review by oversight groups within Johns Hopkins.

If data/biospecimens are used or shared with types of information that may be likely to identify, you such as your name, address or medical record number, further institutional review and approval would be required. In these cases, Johns Hopkins will review whether additional consent from you is required. Generally, if your data/biospecimens are used/shared without any personal identifiers or with information that is less likely to identify you (such as the date of a procedure), further review and approval is not needed.

Data/biospecimen sharing could change over time, and may continue after the study ends.

The use and sharing of your data and biospecimens is required for participation in this research study. If you are not comfortable with the use and sharing of your data/biospecimens in future research without further consent, you should not participate in this study.

5. What are the risks or discomforts of the study?

POTENTIAL RISKS AND DISCOMFORTS

General Risks of Douching

The main risk from having enema douche is temporary discomfort. A hollow plastic tube about the thickness of a pencil will be used to administer approximately 120-125 mL of fluid into the rectum. You

may experience some mild discomfort and a bloated or "crampy" feeling. If you have any hemorrhoids or other painful conditions, you might feel anal or rectal discomfort or have anal or rectal bleeding (see handout for more information).

Some air may be pumped into the rectum as well, causing gas to pass from your rectum. The tube is small, but it might cause some anal or rectal discomfort if the subject has any hemorrhoids or other painful conditions. There is a remote possibility that the enema tip could cause perforation.

Tenofovir Douche
We do not yet know all the effects of the tenofovir douche, including the ways in which it might affect pregnant women or an embryo/fetus. Therefore, it is especially important that you do not father a child while on the study. In addition, we do not yet fully know what effects the douche will have on the rectum. In previous studies using tenofovir rectally as a gel, the following side effects have been reported:

- Dryness, itching, burning, or pain in the rectal area
- Mild burning, irritation, and discomfort and pruritus (itch)
- A temporary increase in rectal leakage or sense of urgency when having a bowel movement
- When using gel for seven days, more participants experienced gastrointestinal problems
- In a previous study with male volunteers, a few mild side effects on urinary and genital organs occurred; they happened to only a few volunteers and did not need any treatment. The most common symptoms were penile burning, irritation, discomfort, and itching.

Since we do not yet know how the tenofovir douche might influence the HIV virus, it might be possible that if you become infected with HIV while the tenofovir is still in your system, the virus could change and become resistant to tenofovir, which means that tenofovir may not work as well if you need to take it for HIV infection.

Risk of blood draws and insertion of a peripheral venous catheter (PIV)
You may feel discomfort when your blood is drawn. You may also feel dizzy, faint, and lightheaded and/or may have bruising, swelling, or infection at the site of injection. You may experience vein irritation, or leakage of fluid into the surrounding tissue from the PIV. Very rarely, there could be clotting of the vein, or a venous air embolism, where air enters the vein and can travel to your heart, brain, or lungs, and cause damage. The study team will adhere to infection control guidelines to reduce the risk from these procedures.

Risk of rectal exams
You may feel discomfort or pressure when your rectum is examined.

Risks from the anoscopy
You may experience some mild discomfort and pressure when the anoscope is inserted into your rectum.

Risks from rectal swabs
You may experience some mild discomfort and pressure when the swab is placed against the wall of your rectum. In some cases, a small amount of bleeding may occur.

Risks from flexible sigmoidoscopy
Flexible sigmoidoscopy, the method used to take the rectal samples, is uncomfortable for some people. There is a slight risk of puncturing the lining of the rectum, which can cause fever, infection, and pain in your belly. If this happens, more medical evaluation and treatment may be needed. There is a very small

risk of making a tear in the colon and causing bleeding. This bleeding stops on its own. Taking the tissue samples will not cause any pain because the lining of the colon does not have any nerves.

Risks from collection of rectal biopsies via flexible sigmoidoscopy
You may experience some mild discomfort and pressure while the biopsies are being performed. In some cases, bleeding or infection may occur. In very rare cases, the biopsy can puncture all the way through the colon. We do not expect this, and if it happens we will mobilize the appropriate medical care immediately.

Risks of Computer Assisted Questionnaire
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. You may get tired or bored when we are asking you questions, or you are completing the questionnaires. You do not have to answer any question you do not want to answer.

Other possible risks
You may become embarrassed, worried, or nervous when discussing ways to protect yourself against HIV and other infections passed during sex and/or when reviewing your test results. You may also become worried or nervous while waiting for your test results and/or sad or depressed upon disclosure of your STI status. If you are diagnosed with an STI and others discover this, it is possible that you may face discrimination.

If you have HIV or other infections, knowing this could make you worried or nervous. A trained counselor will help you deal with any feelings or questions you may have. If a sexually transmitted disease has been identified, you will be referred immediately for appropriate treatment to your primary care physician. In the event that you do not have a primary care physician, a list of local STI clinics and their phone numbers will be provided. If any sexually transmitted disease, with exception of herpes, is identified, we are required to report this to the Baltimore City Health Department. The reporting of sexually transmitted diseases is done confidentially. Someone from the public health department may contact you to be sure that you and your partners have been treated.

We will make every effort to protect your privacy while you are having the study exams and tests. Your visits here will take place in private. However, it is possible that others may learn that you are taking part in the study here. Because of this, they may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job, or being accepted by your family or community. Finding out your HIV status could also cause problems between you and your partner. You may also have problems with your partner associated with use or attempted use of study products.

This research study may involve risks that are currently unforeseeable.

6. Are there benefits to being in the study?

ANTICIPATED BENEFITS TO RESEARCH PARTICIPANTS

You will get no direct benefit from being in this study.

ANTICIPATED BENEFITS TO SOCIETY

Information gathered from this study will help doctors determine if the tenofovir douche is safe and best suited to advance to the next phase of studies. This knowledge may in the future lead to the development of an enema to prevent the spread of HIV associated with anal sex.

7. What are your options if you do not want to be in the study?

You do not have to be in this study. The decision to not be in this study will not affect your care in any way.

If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

The tests and procedures in this study will not cost you anything. The only cost to you is the time you must spend and what it costs you to get to the study visits.

Your insurance company is unlikely to pay for medical care for any injury that you sustain as a result of being in this study. Emergency care will be provided, but you will be responsible for any costs not covered by your insurance. Treatment of a serious injury could be costly. Check with your insurance company before you start this study to find out if your insurance company will pay.

9. Will you be paid if you join this study?

You will be paid for your time and effort for all regularly scheduled study visits.

The reimbursement schedule and amounts are listed below:

Visit	Reimbursement Amount
Screening and Enrollment	$100 each visit
Completion of Dosing	$100
Completion of Visits 4, 5 and Termination	$50 each visit
Completion of Flexible Sigmoidoscopy	$100 each procedure visit
In-depth Interview	$100
Total Potential Amount for Scheduled Visits	$750 for age 18 and above $550 for less than age 18

You will receive $30 for any interim study visits requested by the study staff which may include additional assessments or laboratory tests to monitor safety as a result of an adverse event. All participants who participate in the study will be offered the opportunity to participate in an in-depth interview. This is regardless of which visit is completed. You may be provided food and transportation as needed at each study. If you need to stay overnight for a visit (for example, between visit 3 and 4), the study will also cover your hotel stay.

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

Your participation in this research is voluntary, and if you choose not to participate, that will not affect your relationship with Johns Hopkins Medicine or Hospital or your right to health care or other services at this institution. You are free to withdraw your consent and discontinue participation at any time without prejudice to your future care at Johns Hopkins Medicine or Hospital.

If you leave the study early, Johns Hopkins may use or share your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

The investigators may need to take you off the study early if:

- The decision is made either to protect your health and safety or because you have developed a certain medical condition and according to a research plan people who develop certain conditions may not proceed with the study
- You are not able to attend the study visits or follow the procedures required by the study
- If you become infected with HIV
- The study is cancelled by the Food and Drug Administration (FDA), the National Institutes of Health (NIH), Office of Human Research Protection (OHPR), or the Institutional Review Board (IRB).

If you are taken out of the study before the study is completed or if you decided to discontinue, you will be paid for your participation up to that time. You may also be asked to complete an Early Termination visit which will include the following procedures:

- Let us know if there are any changes in where you live or how we may contact you
- Receive a copy of your test results, if appropriate, and review these results with the study staff
- Tell us about any changes in your medical history
- Tell us if there have been changes to any medicines you are taking now
- May have a physical exam
- Provide urine, blood, and/or rectal samples, if you're willing and if it is determined that they are necessary to assess your health status

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be maintained and how will the confidentiality of your data be protected?

HIPAA Authorization for Disclosure of Protected Health Information

What information is being collected, used, or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Johns Hopkins Medicine and others) may release your private health information to us, and that we may use any and all of your

information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive, or use your private health information include the researchers and their staff who may be a part of Johns Hopkins Health System, Johns Hopkins University or the Johns Hopkins Applied Physics Laboratory. Additionally, we may share your information with other people at Johns Hopkins, for example if needed for your clinical care or study oversight. To improve coordination of your research and clinical care, some information about the study you join will be included in your electronic medical record.

By signing this form, you give permission to the research team to share your information with others outside of Johns Hopkins. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team.

We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

How will your information be protected?
During the study, your study information will be stored on site in locked file cabinets in an area only accessible by study staff. Generally, only people on the research team will know that you are in the research study and will see your information. However, there are a few exceptions that are listed below.

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

Authorized representatives of the Johns Hopkins Institutional Review Board (IRB), Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), the National Institutes of Health, study monitors, DREAM Program Cores, and the organizations that provide the enemas used in this study may need to review records of individual subjects. As a result, they may see your name; however, they are bound by rules of confidentiality not to reveal your identity to anyone.

Any publication of this study will not use your name or identify you personally. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

13. What is a Certificate of Confidentiality?

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

14. What does a conflict of interest mean to you as a participant in this study?

A researcher and Johns Hopkins University have a financial or other interest in this study.

In some situations, the results of this study may lead to a financial gain for the researcher and/or Johns Hopkins University. This financial interest has been reviewed in keeping with Johns Hopkins' policies. It has been approved with certain conditions, which are intended to guard against bias and to protect participants

If you have any questions about this financial interest, please talk to Renata Sanders, MD, MPH, ScM at 410-502-8166 (office) or 513-225-2884 (cell). This person is a member of the study team, but does not have a financial interest related to the study. You may also call the Office of Policy Coordination 410-361-8667 for more information. The Office of Policy Coordination reviews financial interests of researchers and/or Johns Hopkins.

15. What treatment costs will be paid if you are injured in this study?

Johns Hopkins and the federal government, including the U.S. National Institutes of Health (NIH), do not have programs to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form, you will not give up any rights you have to seek compensation for injury.

16. What other things should you know about this research study?

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

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

What is the Institutional Review Board (IRB) and how does it protect you?
This study has been reviewed by an Institutional Review Board (IRB), a group of people that reviews human research studies. The IRB can help you if you have questions about your rights as a research participant or if you have other questions, concerns or complaints about this research study. You may contact the IRB at 410-502-2092 or jhmeirb@jhmi.edu.

For this multi-site study, Johns Hopkins has agreed to serve as the single IRB (sIRB) providing oversight for all sites. You may contact the Johns Hopkins IRB at 410-502-2092 or jhmeirb@jhmi.edu with your questions or concerns.

What should you do if you have questions about the study, or are injured or ill as a result of being in this study?
Call the research nurse manager, Thuy Anderson, RN at 443-287-8942 (office) or 410-459-8249 (cell) or the principal investigator, Renata Arrington Sanders, MD, MPH, ScM at 410-502-8166 (office) or 513-225-2884 (cell). If you wish, you may contact the principal investigator by letter. The address is on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-502-2092.

If you have an urgent medical problem or think you are injured or ill because of this study, call 911 or go to your local emergency department. You should also call Renata Arrington Sanders, MD, MPH, ScM at 410-502-8166 during regular office hours and at or 513-225-2884 after hours and on weekends. If this doctor is not available, the operator will page the “on call physician.”

17. Optional Study Components:

This part of the consent form is about optional component(s) of the study that you can choose to take part in or not. You can still take part in the main study even if you say "no" to this/these optional component(s).

Future Contact

We would like your permission for our research team to contact you in the future. Please note that your decision below does not prevent other researchers at Johns Hopkins from contacting you about other research.

Please sign and date your choice below:

YES ☐ _____ _____
Signature of Participant Date

NO ☐ _____ _____
Signature of Participant Date

18. Assent Statement

This research study has been explained to my child in my presence in language my child can understand. He/she has been encouraged to ask questions about the study now and at any time in the future.

19. What does your signature on this consent form mean?

Your signature on this form means that you have reviewed the information in this form, you have had a chance to ask questions, and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time

Signature of Person Obtaining Consent	(Print Name)	Date/Time

Signature of Parent/Legal Guardian/Court-Appointed Representative **FOR CHILD PARTICIPANT**	(Print Name)	Date/Time

Description of relationship to child research participant (for example: parent, legal guardian, court-appointed representative)

Signature of Child Participant (optional unless IRB required)	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT PROCESS

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider (Print Name) Date/Time

Signature of Participant (Print Name) Date/Time

Signature of Parent/Legal Guardian/Court-Appointed Representative (Print Name) Date/Time
FOR CHILD PARTICIPANT

Description of relationship to child research participant (for example: parent, legal guardian, court-appointed representative)

Signature of Child Participant (optional unless IRB required) (Print Name) Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).