Study Title MATRIX-003: Trial to Assess Acceptability and Safety of Two Placebo Intravaginal Ring (IVR) Designs

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MATRIX-003
Trial to Assess Acceptability and Safety of Two Placebo Intravaginal Ring (IVR) Designs
USAID
Version 3.0
06MAR2024

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SHORT TITLE: OCIS Placebo Ring Study
SPONSOR: USAID
INFORMED CONSENT: Version 3.0 06MAR2024

INFORMED CONSENT

You are being invited to take part in this research study because you are an 18-45-year-old woman in good health. Approximately 100 women will take part in this study across sites in the United States (US), South Africa, and Zimbabwe. This study is looking at two placebo vaginal rings.

This study is sponsored by the US Agency for International Development (USAID) and conducted by the Oak Crest Institute of Science (OCIS) as part of MATRIX: A USAID Project to Advance the Research and Development of Innovative HIV Prevention Products for Women. The placebo vaginal rings are supplied by OCIS. At this site, the person in charge of this study is Catherine Chappell, MD.

KEY INFORMATION

- The study will assess the acceptability and safety of the two placebo vaginal rings. The placebo rings do not contain any active medication, and do not prevent HIV.
- You would be asked to try two different placebo rings, each for approximately 28 days (4 weeks). You would be randomly assigned which of the two rings to use first. The study involves answering questions, undergoing examinations of your vagina and cervix, and collecting blood, urine and vaginal fluid samples.
- You would be in the study for approximately 9-11 weeks once you are enrolled.
- The study involves a total of 9 visits/contacts, including in person visits and telephone calls.
- There may be no benefit to participating.

- You cannot join this research study if you are living with HIV, pregnant, or breastfeeding. You also may not be able to join this research study if you are already taking part in another research study.
- Taking part in this research study is voluntary. You do not have to participate, and you can stop your participation in the study at any time

Please take the time to read this entire form and ask questions before deciding to join the study. If you are willing to take part in the study, you will sign this form. A copy of this form will be offered to you. Signing this form does not mean you will be able to join the study. You must first complete the screening tests and exams to see if you are eligible. It is important to know that your participation in this research study is your decision and taking part in this study is completely voluntary (see Your Rights as a Research Participant/Volunteer for more information).

WHY IS THIS RESEARCH BEING DONE?

This research study is being conducted to find out how easy and comfortable the vaginal rings are for women to use. The rings used in this study do not dispense any medications and will not prevent pregnancy, HIV, nor other sexually transmitted infections. We want to know what you like and dislike about these rings to help us design future products and research studies. Although the vaginal rings in this study do not dispense any medications, we also want to make sure the ring itself is safe when used by women for 28 days.

WHO WILL BE IN THIS RESEARCH STUDY?

Approximately 100 women who are 18-45 years old will be enrolled in the study across various sites in the United States (US), South Africa, and Zimbabwe.

DO I HAVE TO BE IN THIS STUDY?

You do not have to be in this study. You can still get the care you need even if you do not join the study. If you join today, you can change your mind later.

WHAT WILL I BE ASKED TO DO IF I JOIN THIS RESEARCH STUDY?

You will undergo a screening visit to be sure you are eligible and interested. If you are eligible and decide to enroll in this study, you will be asked to try two different placebo vaginal rings, each for approximately 4 weeks (28 days). You will be randomly assigned which of the two rings to use first. Randomly means by chance, like flipping a coin or throwing dice. Neither you nor investigators can choose the ring you will use first. Both placebo vaginal rings are important to the study.

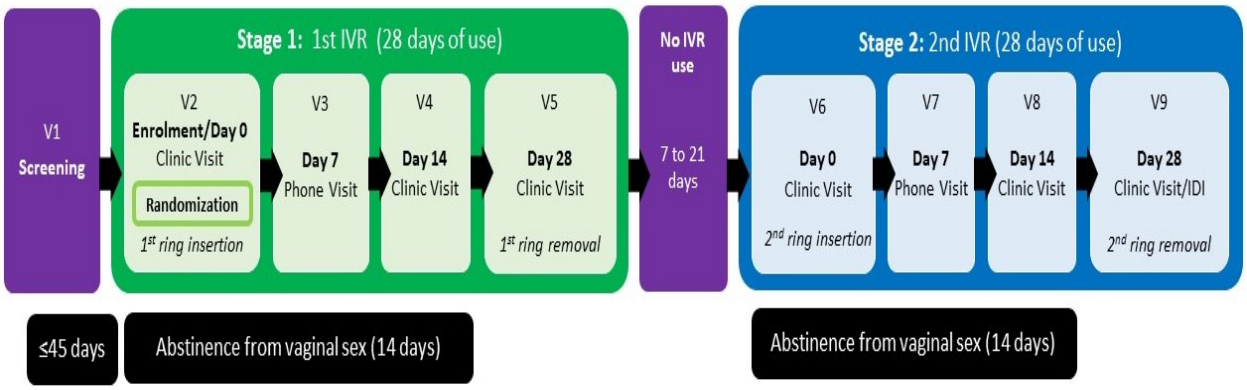
You must be using an effective method of birth control for at least 2 weeks before screening and agree to continue to use the method throughout the duration of the study to qualify.

At the Enrollment Visit (V2) you will be asked to insert the first placebo vaginal ring, undergo evaluations, and answer questions about your experience. While the ring is in place you will have one phone visit about a week later to see how you are doing and then come back to clinic after about 2 weeks of ring use. After about 4 weeks of ring use, you will return to the clinic (V5) to remove the ring and return it to the study team, undergo evaluations, and answer questions about your experience. After a break of about 1 to 3 weeks, you will be asked to

return to the clinic (V6) to insert the second ring and undergo similar evaluations as you did in Visit 2. You will then repeat the same visits over the next 4 weeks until study exit (V9).
You will be asked to not have vaginal sex for the first 2 weeks of each ring use period. You will be asked to abstain from using anything in the vagina during the entire study. For example, this means no tampons, menstrual cups, toys, douches, herbal preparations, or vaginal medications. If you do not think you can agree to this, you should not participate.

WHAT WILL HAPPEN DURING THE STUDY VISITS?
The study includes a total of nine (9) scheduled clinic visits or telephone contacts. Seven (7) visits, including the Screening Visit today, will take place at this clinic. Two (2) visits will be telephone contacts, which may be done through a phone call or via text message. Participants who prefer to complete the telephone contacts in-person may elect to do so.

Study Visit Schedule:



Screening Visit (Visit 1) Procedures:
The procedures done at this visit will let us know if you can join this study and will take about 1 hour.

At the Screening Visit, you will:
- Answer questions related to
  - Demographics: date of birth, race, contact information, etc.
  - Medical and menstrual history: review of any medical problems you may have
  - Medication use: review any medication you take, including start date, dose, etc.
  - Birth control method: you must be using and agree to continue to use an acceptable, reliable method throughout the study to qualify
  - Visit/background questionnaire
- Undergo counseling:
  - HIV and STI (sexually transmitted infection) counseling and how to reduce your risk

  - Abstinence (no vaginal sex and no vaginal product) counseling will be reviewed. For vaginal sex, this would be for the first 2 weeks of each ring use period. For vaginal products, this would be for the duration of the study.
    - It is important that you know if you are not currently using an acceptable method of contraception, or if you do not think you can abstain from vaginal sex for the first 2 weeks of each ring use period or from use of vaginal products for the duration of the study, you will not be eligible to participate in this study.

- Have examinations
  - Physical exam
  - Pelvic exam: To examine your vagina and cervix, the doctor may use a speculum (plastic or metal instrument inserted into the vagina)
- Have baseline testing:
  - Urine pregnancy test: If you are pregnant, you will not be able to join
  - HIV test: A saliva sample will be tested for antibody to HIV. An antibody is a substance that blood cells make to fight infection. Exposure (contact) to the HIV virus produces antibodies. Results take 20 minutes. Study staff will talk to you about the meaning of the result. Sometimes HIV test results are not clearly positive, but also not clearly negative. In that case, blood will need drawn and sent to the lab for further testing. If the test shows you have HIV, you cannot join the study.

  - Blood test: Approximately 12 mL (or 2 ½ teaspoons) will be collected to look at the general health of your blood, basic kidney and liver function, and to screen for syphilis
  - STI test for gonorrhea, chlamydia and trichomonas by collecting vaginal fluid using a Q-tip like swab(s)
  - Pap smear: If you have not had a normal result within the required period and/or the report is not available, you will have a Pap smear performed by using a soft brush to collect a sample from your cervix to screen for cervical cancer.
  - Additional tests of your urine and/or vaginal fluid may be done to check for infections if you are having symptoms and as clinically indicated
- Receive test results
  - Results of the tests listed above will be reviewed with you once available. Some tests results may be available while you are at today's visit (urine pregnancy test) while others may take up to a week to result (STI testing). The results of these tests will help to determine if you are eligible to participate.
  - If you are diagnosed with a urinary, vaginal (i.e., yeast or BV) or an STI at Screening, you will be offered/prescribed treatment
  - If there are other clinically significant findings, for example on your blood test or Pap smear, you will be referred for additional evaluations and treatment as needed
- In addition
  - Be provided reimbursement
  - May be scheduled for an Enrollment Visit within 45 days of Screening

It may be necessary to conduct more than one clinic visit to complete all required screening procedures or if a test needs to be repeated.

If you do not join the study, blood and other samples collected at the Screening visit will not be kept or used for any tests other than those listed above.

If you are eligible and decide to enroll in the study, there are common study procedures that will happen at every in person visit (V2, V4, V5, V6, V8, V9), including:

- Review/update your contact information, including address and phone number*
- Review/update your medical and menstrual history*
- Review/update any medications you are taking/using*
- Review/update any sexual activity or intravaginal product use*
- HIV and STI testing and counseling as needed
    - You will be told your test results as soon as they are available. You will talk with the study staff about the meaning of your results, how you feel about them, and learn about ways to prevent HIV and other STIs. Sometimes HIV tests are not clearly positive, but also not clearly negative. In that case, we will do more tests until we are sure of your status. To participate in the study, you must receive the results of your HIV test. If the test shows you have HIV, you cannot join the study. We will refer you to available sources of medical care and other services you may need.
- Review of any new complaints or side effects once you start using the ring*
- Directed physical exam, as clinically indicated based on symptoms/complaints
- Urine pregnancy test
- Pelvic exam with collection of vaginal fluid using a Q-tip like swab(s) to look at the bacteria in the vagina
- As needed tests:
    - Repeat blood tests (general health of blood, kidney and liver function)
    - Microscope exam of vaginal fluid to look for yeast or bacteria
    - Urine tests to check for infections
- Review of test results*
- Treatment or referral for abnormal test results as needed
- Protocol counseling, including HIV and STI risk reduction and contraceptive counseling, as needed*
- Reimbursement for the study visit/contact*
- Schedule next visit/contacts*

*These procedures will also be done at the scheduled Telephone Contacts (V3, V7)

Insertion Visit (Visits 2 and 6) Procedures:
The Insertion clinic visits (the visits where you are given a ring to use) will take about 45 minutes. Visit 2 is the Enrollment Visit, which will take place up to 45 days after the Screening Visit. You will be randomly assigned which of the two rings (A or B) to use first at the Enrollment visit, and you will insert the first assigned ring at the clinic. At Visit 2 you will be asked to remove the ring after it is successfully inserted and then re-insert it to ensure you feel comfortable inserting and removing the ring. At Visit 6, you will insert the second ring at the clinic.

In addition to the common study procedures listed above, at these visits you will:

- Answer questions
  - About the vaginal ring
  - About sexual behaviors and risk factors
  - About the vaginal ring following insertion
- Undergo counseling
  - Abstinence (not have vaginal sex or use vaginal products) counseling
- Have HIV testing and counseling
- Be assigned to the group using Ring A first or to the group using Ring B first
- Have a blood sample, approximately 10 mL (or 2 teaspoons) taken at Visit 2 in case there is a question about your test results at a later time
- Have examinations
  - Pelvic exam before inserting the ring
    - Vaginal fluid will be collected using a Q-tip like swab(s) at Visit 2 in case there is a question about your test results at a later time
  - Digital genital exam (clinician places finger inside vagina) after insertion of the ring to check ring position
  - You will be asked to walk around the room after insertion of the ring to make sure the ring is comfortable. If you experience any discomfort while walking, the digital genital exam may be repeated.
- Review instructional materials
  - You will be provided with vaginal ring instruction materials to review before inserting the ring. Study staff will be available to answer any questions you may have.
- Insert the vaginal ring given to you by the study team
  - You will have 2 attempts to insert the vaginal ring
  - If after 2 attempts, you are having difficulty, a clinical team member can insert the ring for you

Telephone Contact (Visits 3 and 7) Procedures:
Visits 3 and 7 will take place approximately 7 days (1 week) following the Insertion Visits. These telephone contacts will take approximately 5 minutes to complete.

In addition to the common study procedures with Telephone Contacts listed earlier, you will be asked about concerns and comfort with ring use.

Mid-point Clinic Visit (Visits 4 and 8) Procedures:
The Mid-point clinic visits will occur approximately 14 days (2 weeks) after the Insertion Visits and will take about 45 minutes to complete.

In addition to the common study procedures listed earlier, at these visits you will be asked about concerns and comfort with ring use, and you will have a pelvic exam. You will also be reminded there are no restrictions on sex for the second 14 days of ring use and be offered male condoms.

Removal Visit (Visits 5 and 9) Procedures:
The Removal clinic visits (the visits where you remove the vaginal ring in the clinic) will occur approximately 28 days (4 weeks) after the Insertion Visits. These visits will take about 45 minutes to complete. Your participation in this study will end after Visit 9.

In addition to the common study procedures listed earlier, at these visits you will:

- Answer questions
  - About your experiences using the vaginal ring
  - About sexual behaviors and use of vaginal products
  - Up to 30 participants (of the total 100) will be chosen to do an in-depth interview ideally at or within 1 week of Visit 9 but no later than 3 weeks after Visit 9
    - If chosen, the interview will be performed remotely by a behavioral researcher. The interview will be conducted at the study office using a secure platform like Zoom to connect you with the in-depth interviewer.
    - Study staff will make every effort to ensure your privacy and confidentiality, and information you provide during the interview will not be shared with your partner
    - The interviewer may take notes, and interviews will be audio-recorded to make sure we record your words exactly how you said them
    - The interview will be focused on your experiences using the ring and behaviors during the study and could take up to an hour to complete
- Have examinations
  - Pelvic exam
- Remove the vaginal ring. It is important that you return the ring to the study team.
  - You will have 2 attempts to remove the vaginal ring
  - If after 2 attempts, you are having difficulty, a clinical team member can remove the ring for you
- Offer male condoms
- In addition
  - Investigators will ask you to confirm if you are willing to have your partner contacted to participate in an in-depth interview about your partner's experience while you were in the study.
    - This is optional and you should only agree if you (and your partner) feel comfortable. If you don't feel comfortable including or asking your partner to participate, you will not be disqualified.
  - If you agree and feel comfortable, you will be asked to provide our contact information to your partner so they can call us if interested in participating.
    - You will be given information to share with your partner to see if your partner would be comfortable participating in an interview
    - Your partner would need to sign a separate consent

Additional Visits and Procedures

In addition to the procedures listed above, it is possible that study clinicians may need to perform additional exams or tests, if necessary. For example, you may be asked to make additional clinic visits to perform these exams/tests if you report having symptoms and/or other issues, if there are abnormal test results, or due to mistakes during the collection, processing and/or shipping of your samples. These exams/tests might include the following:

- Physical and/or pelvic exam
- Test vaginal fluid for STIs

- Test your urine for STIs or other infections
- Test your blood for STIs
- Test your blood to check the health of your blood, liver and kidneys
- Give you treatment or refer you for treatment of STIs or other issues, if needed.

It is important for you to complete every study visit/contact. If you cannot make a scheduled visit/contact, please tell the study staff as soon as possible so that the visit/contact can be rescheduled.

It is important that you remember that at any time during the study, study staff can answer any questions you may have about the procedures mentioned above or any other aspect of this study.

WHAT IF I BECOME INFECTED WITH HIV?

The placebo vaginal rings do not contain medications and will not prevent HIV infection. Persons living with HIV will not be included in this study. Being in this study will not cause HIV infection. However, there is always a chance that you can get HIV through sex or other activities. If you become HIV-positive, you will stop using the study product and will stop taking part in this study. The study staff will refer you for medical care and other available services.

Depending on local and national health requirements, the study staff may need to report certain diseases, including HIV. The reportable diseases at this site are HIV, Gonorrhea, Chlamydia, and Syphilis. We must inform the Allegheny County Health Department (ACHD) if any of these tests are positive. Outreach workers from ACHD may then contact you about informing your partner/s, since they also should be tested. If you do not want to inform your partner/s yourself, the outreach workers may contact them, according to the confidentiality guidelines of the ACHD.

WHAT IF I BECOME PREGNANT?

The placebo vaginal rings are not family planning methods and will not prevent pregnancy. We do not know what effect the study product(s) have on pregnancy, including any effect on the unborn babies. Because of this, pregnant women may not join this study. Also, you must use an effective family planning method (e.g., birth control pills, hormonal-based methods, intrauterine device [IUD], the patch) other than a vaginal ring for at least 2 weeks before screening and for the study duration.

RISKS AND/OR DISCOMFORTS

Risks of Blood Draws

You may feel discomfort or pain when your blood is drawn. You may feel dizzy or faint. You may have a bruise, swelling, small clot, or infection where the needle goes into your hand or arm.

Risks of Pelvic Exams

You may feel discomfort or pressure during the pelvic exam and vaginal fluid collection. You may have a small amount of vaginal bleeding or spotting which should stop shortly after the exam.

Risks of Vaginal Rings

The ring is a placebo and does not contain any medications. You may experience discomfort when inserting or removing the ring, or while the ring is in place. It is possible that you may have an allergic reaction to the ring itself. Symptoms of an allergic reaction include rash or other irritation, itching, joint pain, or difficulty in breathing.

Risks of HIV and Sexually Transmitted Infection (STI) Testing

HIV and STI testing may make you feel anxious regardless of the test results. Finding out your HIV status may also cause problems with your family, friends, or partner.

Other Possible Risks

You may feel embarrassed and/or worried when talking about sexual activities (if you are currently sexually active), your living situation, ways to protect against HIV and STIs, and your test results. You can choose not to answer questions at any time. Trained study staff will help you with any feelings or questions you have.

We will make every effort to protect your privacy and confidentiality during the study visits. Your visits will take place in private. Reports via computer will be stored in computers that are password-protected and will not include personal information that could identify or link information to you; only your study ID number will be recorded. However, it is possible that others may learn of your participation in this study, and because of this, may treat you unfairly or discriminate against you. If you have any problems, study staff will talk with you and try to help you.

There may be a breach of confidentiality from sending/receiving text messages for appointment reminders. Text and data rates may apply based on carrier.

If you participate in the in-depth interviews, they will be performed in the study office via Zoom.. The interviews will be audio recorded and questions of a personal nature may be asked. Responding to these questions may make you uncomfortable. The audio files will be put into writing by the person conducting the interview or by another person who does not know you and does not have your personal information. You should NOT identify anyone in the interviews and any names that might be mentioned on the recording will only be noted in the transcript

using a generic description. The audio files will be stored in computers that are password protected. The data that is collected during the interviews will be linked to data collected as part of the main study. This data is all labeled by study code only.

BENEFITS

This study involves a placebo, so you are not expected to receive direct benefit from study participation.

NEW INFORMATION

You will be told about any new information learned during this study that may affect your willingness to stay in the study. For example, we will let you know if we learn that the study product may be causing bad side-effects. We will also tell you when study results may be available, and how to learn about them.

WHY YOU MAY STOP USING THE STUDY PRODUCT EARLY OR BE ASKED TO LEAVE THE STUDY

You may need to leave the study early without your permission if:

- The study is cancelled by USAID, OCIS, the US Office for Human Research Protections (OHRP), MATRIX, the local government or regulatory agency, or the Institutional Review Board (IRB)/Independent Ethics Committee (IEC). An IRB/IEC is a committee that watches over the safety and rights of study participants.
- You are not able to keep appointments.
- Other reasons that may prevent you from completing the study successfully.

The study doctor will ask you to stop using the study products if:

- You acquire an HIV infection (see "If You Become Infected With HIV" section).
- You become pregnant or are breastfeeding (see "If You Become Pregnant" section).
- You use drugs for HIV prevention or to prevent infection after HIV exposure.
- You use injectable drugs for reasons other than treating disease.
- You experience a serious adverse event while on study.
- You fail to follow study requirements in a manner judged by the study doctor to significantly put you at risk of an adverse reaction or otherwise affect study outcomes.
- A study clinician decides that using the study product would be harmful to you, for example, you have a bad reaction to the vaginal ring(s).

If a study doctor asks you to stop using study product, we will ask you to come in for an interim visit during which some/all of the procedures scheduled to occur on Visit 9 will be completed. You will then exit the study, unless otherwise informed by study staff.

If you are removed from the study or choose to leave, we will ask you to come back for one final clinic visit. It is important that you come to the clinic to remove the ring if you are still using it. If you do not have the study products with you when you come to the clinic, staff members will make every effort to assist you in returning them as soon as possible

ALTERNATIVES TO BEING IN THE STUDY

This is a placebo study enrolling healthy, adult women. You can choose not to participate in this study without affecting your care at this or other facilities or your ability to participate in other studies.

COSTS TO YOU

There is no cost to you for study visits, study products, physical/clinical exams, laboratory tests or other procedures. We can give you treatments for STIs (other than HIV) at no cost while you are in the study, or we can refer you for available treatment.

REIMBURSEMENT

You will receive compensation for your time, effort, and travel to and from the clinic for each scheduled study visit.

If you complete all study visits and contacts on time, you will receive an additional $60 incentive. If you are selected for and complete the In-depth Interview you will receive $60. If you are asked to return for an interim visit, you will receive $20. All payments are processed at the completion of each study visit. On the day of your visit, you may also be offered a free parking pass for the garage at UPMC Magee-Womens Hospital (worth approximately $5).

Visit	Payment
V1 Screening	$40
V2 (Enrollment)	$60
V3 (1 week phone call)	$20
V4 (2 week clinic visit)	$40
V5 (4 week clinic visit)	$40
V6 (2nd IVR insertion)	$60
V7 (1 week phone call)	$20
V8 (2 week clinic visit)	$40
V9 (Final clinic visit/IDI)	$40 + $60 incentive
TOTAL	$420 (included $60 incentive)

Since you are being compensated for you participation in this study, your name, address, and social security number will be released to the Accounting Office. Your study payments will be loaded onto a UPMC cash card at the completion of each visit. Payment to participants is considered taxable income regardless of the amount. If a participant receives $600 or more in a calendar year from one organization, that organization is required by law to file a "Form 1099-Miscellaneous" with the IRS and provide a copy to the taxpayer. We are required to give your name and social security number to the Accounting Office. Participants who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 76% of the expected payment.

CONFIDENTIALITY

We will make every effort to keep your information private and confidential. But we cannot guarantee it.

Study visits will take place in private. We will keep the information about your study visits in a secure place that only certain people can access for the purposes of this study. We will only enter your information into computers protected by passwords and will not include information that could identify you. Your identity on these records will be indicated by a number rather than by your name, and the information linking these numbers with your name will be kept separate from the research records. You can choose not to answer questions at any time. We will keep the audio recordings and materials from all interviews and discussions confidential and will only use study numbers or fake names. We will store the original records, including the audio recordings, for at least three years after completion of the study. These records will be stored in a secure, locked location.

Your personal information may be disclosed if required by law. For example, if we learn something that would immediately put you or others in danger, the study staff must take steps to keep you and others safe. This means that we have to share any information with the authorities (hospital, police, or social services) that tells us you may be in danger. For example,

if you tell us that you plan to hurt or kill yourself, hurt or kill someone else, or if you tell us that someone is abusing or neglecting you.

The study staff may use your personal information to verify that you are not in any other research studies. This study will not use your name or identify you personally in any publication.

In clinical studies where study products or other medical devices are being assessed, it is important that volunteers are enrolled in only one clinical study at a time. Using more than one study product may lead to drug interactions and side effects that could potentially be harmful to your health. In addition to compromising the health of the study participant, this can affect the outcome of the study. The study staff will ask you about any other studies that you are or are planning to participate in.

Your records may be reviewed by:

- Representatives of the US Federal Government, including US OHRP, USAID and/or USAID contractors, and other US, local or international regulatory authorities
- Representatives of Pitt/MWRIF
- Representatives of OCIS
- MATRIX representatives
- University of Pittsburgh Office of Research Protections
- Study monitors
- Site IRB/IEC
- Study staff

Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders made by the investigators for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance)

Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form, you provide your authorization for the use and disclosure of information protected by the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. This includes things learned from the procedures described in this consent form. Study staff may also collect other information including your name, address, date of birth, and information from your medical records.

People outside the study team may need to see or receive your information for this study, such as those listed above. We cannot do this study without your authorization to use and give out your information to them. You do not have to give us this authorization. If you do not, then you may not join this study.

The use and disclosure of your information has no time limit. You may cancel your authorization to use and disclose your information at any time by notifying the Principal Investigator of this study in writing. 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 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.

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

RESEARCH-RELATED INJURY

It is unlikely that you will be injured by being in this study. If you are injured or get sick from being in this study, please tell study staff immediately.

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. If you become ill or injured as a result of participation in this study, medical treatment for the adverse reaction or injury will be provided to you by the hospitals of UPMC. The site staff will refer you for ongoing treatment for the injury, if needed. Clinical trial insurance purchased by the site will be responsible for compensating you for appropriate medical expenses for treatment of any such illness or injury. An HIV infection that occurs during the course of the trial will not be considered an injury or illness caused by trial participation. The research center or sponsor is not responsible for any loss, injuries and/or damages that are caused by any of the following things:

- Any injury that happens because you used other medicine during the study that you did not tell us about.
- Any injury that happens because you did not follow instructions given by the study doctor or nurse.
- Any injury that happens because of negligence on your part.

You are not giving up any legal rights by signing this form.

CLINICALTRIALS.GOV

A description of this research study will be available on https://www.ClinicalTrials.gov, as required by U.S. 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.

YOUR RIGHTS AS A RESEARCH PARTICIPANT/VOLUNTEER

Being in this study is completely voluntary. You may choose not to join this study or leave this study at any time. If you choose not to join or to leave the study, you can still join other studies and you can still access non-study services you would normally get at this or another clinic. If

you leave the study, your specimens will be destroyed when all protocol-specified testing has been completed and your study records may be kept for at least seven years after study completion. If you want the results of the study after it is over, let the study staff members know.

PROBLEMS OR QUESTIONS

If you ever have any questions about the study, or if you have a research-related injury, you should contact the Principal Investigator, Catherine Chappell, MD at 412-641-4242.

If you have questions about your rights as a research participant, you should contact the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668.

CONSENT FOR LONG-TERM STORAGE AND FUTURE TESTING OF SPECIMENS and RELATED HEALTH INFORMATION

There might be a small amount of blood or vaginal fluid left over after we have done all of the study-related testing. We would like to ask your permission to store these leftover samples and related health information for use in future studies, such as future research to fight HIV and other related diseases. This health information may include personal facts about you such as your race, ethnicity, sex, medical conditions and your age range. This health information will not include your name or any other personal identifying information. The samples will be stored by your participant number only.

If you enroll in the study and agree, your samples and related health data will be stored safely and securely at facilities that are designed so that only approved researchers will have access to the samples. Some employees of the facilities will need to have access to your samples to store them and keep track of where they are, but these people will not have information that directly identifies you.

There is no time limit on how long your samples will be stored. Your samples may be shipped and/or stored outside of the country. The type of testing planned for your leftover specimens is not yet known. However, samples may be used by OCIS to complete additional quality assurance testing, ensuring that the tests work correctly and supply accurate data. No genetic testing on either a limited set or the full set of genes is planned for leftover samples that are stored for the purposes of future research. It is important that you know that any future testing or studies planned for these specimens must be approved by an Institutional Review Board before they can be done. You will not receive the results from any future testing of these specimens.

You can still enroll in this study if you decide not to have leftover samples stored for future studies. If you do not want the leftover samples stored, we will destroy them when all protocol-specified testing has been completed. You can withdraw your consent for the storage and future testing of specimens at any time by providing your request in writing to the person in charge of this study. However, researchers will not be able to destroy samples or information from research that is already underway.

_____ I DO agree to allow my biological specimens and health data to be

Initials and Date stored and used in future research studies. I understand my biological specimens may be shipped and stored outside of the country.

_____ I DO NOT agree to allow my biological specimens and health data

Initials and Date to be stored and used in future research studies.

CONSENT TO PARTICIPATE IN AN IN-DEPTH INTERVIEW

We would like to ask your permission to participate in a conversation-style interview (in-depth interview or IDI) at the end of the study to gather more feedback about the placebo vaginal ring. If you agree and are selected to participate in the IDI, trained study staff will ask you questions about your experiences using the product, about product design, packaging and delivery, and other topics related to product use. Information you provide during the IDI will not be shared with your partner. The IDI will be conducted at the Magee CTRC using a secure digital platform.

The IDI is anticipated to last approximately 45-60 minutes. Study staff will take notes and record the interview. You can choose not to answer questions at any time. We will keep the audio recordings and materials from all interviews and discussions confidential and will only use study numbers or fake names to identify them. These materials will be stored in a secure, locked location for at least seven years after completion of the study.

We will reconfirm the decision you make today at later study visits should you change your mind about participating in the IDI.

You can still enroll in this study if you decide not to participate in the IDI. You can withdraw your consent to participate in the IDI at any time.

_____ I DO agree to participate in an in-depth interview. I understand the

Initials and Date interview will be recorded and notes will be taken.

_____ I DO NOT agree to participate in an in-depth interview.

Initials and Date

PERMISSION TO CONTACT SEXUAL PARTNER

We would like to ask your permission to contact your sexual partner to participate in a conversation-style interview (in-depth interview or IDI) at the end of the study to gather more feedback about the vaginal ring.

If both of you agree and your partner is selected to participate in the IDI, trained study staff will ask your partner questions about their views on the vaginal ring and its characteristics and about your experiences using the vaginal ring. This means that your partner will be aware of your participation in this study and your use of the vaginal ring but no other information will be shared with your partner.

If you give us permission to talk to your sexual partner, you will be asked to provide our contact information to your partner so they can call us if interested in participating.

We will reconfirm the decision you make today at later study visits should you change your mind about us contacting your sexual partner.

You can still enroll in this study if you decide not to give us permission to contact your sexual partner. You can withdraw your permission for us to contact your sexual partner at any time.

_____ I DO give permission for study staff to talk to my sexual partner. I agree

Initials and Date to provide my partner with your contact information so they can call you for more information.

_____ I DO NOT give permission for study staff to talk to my sexual partner.

Initials and Date

SIGNATURE PAGE

The above information has been explained to me and all my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any part of this research study during this study. Any future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the Human Research Protection office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form, I consent to participate in this research study A copy of this consent form will be given to me.

_____

Participant's Name (Print)

_____ _____

Participant's Signature Date

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was started until after this consent form was signed.

_____ _____

Printed Name of Person Obtaining Consent Role in Research study

_____ _____

Signature of Person Obtaining Consent Date