KEY INFORMATION FOR ACCELERATED GENITAL TRACT AGING IN HIV: ESTRADIOL CLINICAL TRIAL

We are asking you to choose whether or not to volunteer for a research study that aims to understand how aging of the female genital tract differs in menopausal women living with HIV compared to HIV- menopausal women. Women with and without HIV will participate in 2 study visits (*Table 1, Option 1*). If you have HIV and vaginal symptoms (dryness, irritation, itching, pain with sex), you will also be asked to participate in a clinical trial to examine the effect of vaginal estradiol on these symptoms. If you participate in Part 1 of the study (2 visits), you will have 3 additional visits for a total of 5 study visits (*Table 1, Option 2*). If you have HIV and vaginal symptoms and do not participate in Part 1, you will have a total of 4 visits (*Table 1, Option 3).* This page is designed to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

Estrogen is a hormone that has many effects on the body. It keeps the vagina healthy, moist, with good blood supply and helps to maintain healthy vaginal bacteria, which protect women from infection. During menopause, this hormone decreases, causing undesirable side effects, including aging of the vagina. This aging process can lead to changes in the types and amount of healthy bacteria in the vagina, inflammation and a breakdown of natural barriers that keep the vagina healthy. Some menopausal women develop a condition known as vaginal atrophy, which causes uncomfortable symptoms such as dryness, irritation, pain with sex, and itching. We don't yet know if vaginal aging occurs earlier in women with HIV, HIV-related ithout HIV, or if the use of vaginal estradiol tablet placed inside the vagina may prevent the aging process, lead to fewer changes in the types of bacteria present in the vagina, improve vaginal atrophy symptoms and ultimately keep the vagina healthier for a longer period of time. This is especially important for women with HIV as they are living longer, healthier, sexually active lives because the virus is controlled with medication. We will explain the study visits and possible risks and benefits to you. After all of your questions have been answered, you can decide if you want to take part in the study. If you decide to take part, we will ask questions about your medical and sexual history.

The study has two parts. Part 1 is for menopausal women with and without HIV. It consists of 2 visits over 4 weeks (*Table 1 Option 1*). At the first visit, a clinician will perform a pelvic exam to examine the vagina and collect swabs and fluid. At the second visit, a questionnaire will be used to assess symptoms of vaginal aging, blood will be drawn to measure hormone levels that indicate menopause and CD4 count and HIV viral load for women with HIV and a pelvic exam will be done, including 2 vaginal biopsies. We will apply numbing medication (a gel) before a small piece of skin from inside the vagina is removed. Typically, there is a little bleeding and it may feel like a pinch. Part 2 of the study is only for menopausal women with HIV. If you participate in Part 1 of the study (2 visits), you will have 3 additional visits for a total of 5 study visits (*Table 1, Option 2*). If you do not participate in Part 1 of the study, you will have a total of 4 study visits (*Table 1 Option 3*). Each participant will be randomly assigned (like flipping a coin) to the treatment group (estradiol vaginal tablet) or the non-treatment group. The visits are the same for both groups. There will be pelvic exams and questionnaires at each visit as well as vaginal biopsies at the first visit (if you do not participate in Part 1 of the study) and the last visit. All participants will receive 3 phone calls during the study in addition to the study visits.

Table 1: Study Participation Options

	Part 1 Study of Menopausal HIV- and HIV+ women		**Part 2 Pilot Randomized Clinical Trial of Topical Estradiol in Menopausal Women with HIV**		
	Visit 1 Screening	**Visit 2** (4 week follow up)	**Visit 3** Randomized Estradiol vs. No therapy	**Visit 4** 6 weeks Estradiol vs. No therapy	**Visit 5** 12 weeks Estradiol vs. No therapy
HIV+ and HIV- Participants Option 1 *2 visits*	X	X			
HIV+ Participants Option 2 *5 visits*	X	X		X	X
HIV+ Participants Option 3 *4 visits*		X		X	X

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

Women with HIV who participate in the trial may have direct benefit of vaginal estradiol as symptoms of vaginal atrophy such as itching, burning, and dryness may resolve. Some participants appreciate knowing they have contributed to research that may benefit others in the future. For a complete description of benefits, refer to the Consent Document below.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

Some people feel that a women's health study is too personal for them, due to the pelvic exam. We also ask detailed questions about your medical history and sexual practices. There may also be discomfort associated with blood draws, pelvic exams, and vaginal biopsies. You will not lose any services, benefits or rights or access to care you would normally have if you choose not to volunteer.

DO YOU HAVE TO TAKE PART IN THE STUDY?

You are not obligated to take part in the study. If you decide to take part in the study, it should be because you really want to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Kerry Murphy, MD. If you have questions, suggestions, or concerns regarding this study or want to withdraw from the study, you can reach Dr. Murphy at 718-839-7885. Her office address is 1225 Morris Park Ave., Van Etten Building, 6A-04C, Bronx, NY 10461. If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the Einstein Institutional Review Board (IRB) between the business hours of 9am and 5pm EST, Monday-Friday at 718-430-2253 or irb@einstein.yu.edu.

ALBERT EINSTEIN COLLEGE OF MEDICINE
MONTEFIORE MEDICAL CENTER

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

Introduction

You are being asked to participate in a research study called **Accelerated Genital Tract Aging in HIV: Estradiol Clinical Trial.** Your participation is voluntary -- it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." Her name is **Kerry Murphy, MD**. You can reach Dr. Murphy at:
Office Address:
1225 Morris Park Ave.
Van Etten Building, 6A-04C
Bronx, NY 10461
Telephone #: (718) 839-7885
For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right-hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253, by e-mail at irb@einstein.yu.edu, or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg #1002
Bronx, New York 10461

Support for this research study is provided by the **National Institutes of Health and NovoNordisk**

Why is this study being done?

The study has two major goals. The first goal is to compare changes that occur with aging in the vagina between menopausal women with and without HIV. This includes changes in the amount and types of bacteria and the amount of inflammation present in vagina. We want to determine if having HIV is associated with accelerated vaginal aging including earlier changes in the amount and types of vaginal bacteria and inflammation. Some menopausal women develop a condition known as vaginal atrophy, which causes uncomfortable symptoms such as irritation, pain with sex, dryness and itching. The second goal is to study in menopausal women with HIV if use of a vaginal estradiol tablet (Vagifem® 10 µg) for 12 weeks improves vaginal atrophy symptoms and aging associated changes in the vagina (bacteria, inflammation). Vagifem is safe, effective and FDA approved for the treatment of symptomatic vaginal atrophy. Little is known about the use of Vagifem in women with HIV.

Why am I being asked to participate?

You are being asked to participate in this study because you are a woman 45-70 years of age and menopausal, defined as having no periods in the last 12 months. For Part 1 of the study you may or may not have HIV infection. For Part 2 of the study, you must have HIV infection and symptomatic vaginal atrophy. Symptomatic vaginal atrophy will be defined as reporting at least once per week in the past 30 days, 1 or more of the following symptoms of moderate or severe intensity: vaginal dryness, itching, irritation, soreness/pain or pain associated with sexual activity at least once. Study visits will take place at the Clinic Research Center at the Albert Einstein College of Medicine or the Bronx Women's Interagency HIV Study (WIHS) site at

Montefiore Medical Center, which is an ongoing study of HIV+ and HIV- women. If you are a WIHS participant, you may be invited to discuss this study at your semiannual Core WIHS visit. If you are not a WIHS participant, you may be invited to discuss the study through clinics at Montefiore Medical Center.

You do not qualify to take part in either part of the study if you have any of the following:

- Unexplained or unevaluated abnormal genital bleeding
- Current or suspected pregnancy
- If < age 55, had a hysterectomy and has at least one ovary
- Pelvic or vaginal surgery in the prior 60 days
- Used systemic reproductive hormones in the last 2 months
- Used antibiotics in the last 30 days
- Used immunosuppressive medications in the prior 60 days including biologics, chemotherapeutics or post-transplant immunosuppressive medications.
- Used any vaginal or vulvar preparations in the last month
- Current active vaginal infection diagnosed at study entry
- Any serious disease or condition that may interfere with study compliance

You do not qualify for Part 2 of the study (Clinical Trial) if you have any of the following additional conditions:

- Current or previous history of breast cancer or estrogen-dependent cancer (e.g. ovarian, endometrial)
- Current or previous history of deep vein thrombosis or pulmonary embolism
- Current or previous history of myocardial infarction or stroke
- Known clotting disorder including Protein C, Protein S and antithrombin deficiency, Factor V Leiden or prothrombin mutations
- Known severe liver disease including cirrhosis or active Hepatitis BKnown allergic reaction to Vagifem (estradiol vaginal tablet)

How many people will take part in the research study?

You will be one of about 150 people participating in this study. The first part of the study will include 100 menopausal women, 50 with HIV and 50 without HIV. Enrollment in the second part of the study will include 50 HIV+ menopausal women with vaginal atrophy who will be asked to join a clinical trial where 25 women will receive vaginal estradiol tablet and 25 women will receive no treatment for 12 weeks. Women with HIV can choose to participate in the first, second, or both parts of the study.

How long will I take part in this research?

Depending on your HIV status and enrollment group, the study may take from four weeks up to 17 weeks to complete.

What will happen if I participate in the study?

The first visit will take about one hour to complete. During this visit you will have a pelvic exam and will fill out a questionnaire about your medical history and sexual practices. If you are determined to be eligible, you will return for a second study visit in 4 weeks. At the second visit we will repeat the pelvic exam and perform vaginal biopsies, blood tests and ask additional questions regarding any changes to your medical history. If you have HIV and symptoms of vaginal atrophy you will be asked to participate in a clinical trial, which will consist of 3 additional visits over 12 weeks. Symptomatic vaginal atrophy will be defined as reporting at least once per week in the past 30 days, 1 or more of the following symptoms of moderate or severe intensity: dryness, itching, irritation, soreness/pain or pain associated with sexual activity at least once. If you do not have HIV or have HIV but do not want to continue with the second part of the study, the second visit will be your final study visit. If you have HIV, are eligible, and wish to continue, you will be assigned randomly (like flipping a coin) to the treatment (vaginal estradiol)

or non-treatment group (no therapy). The chance of you being assigned to either group is exactly the same. We do not know ahead of time which group you will be assigned to, and you will not be able to choose or change your group.

CHECK 1 (ONE) OF THE FOLLOWING OPTIONS:

☐ I do not have HIV and agree to participate in the first part of the study. I understand that I may not participate in the trial. The second visit will be my final visit.

☐ I have HIV and agree to participate only in the first part of the study. I will not participate in the trial. The second visit will be my final visit.

☐ I have HIV and agree to participate only in the trial. I agree to return for a total of four visits. I understand that I will be assigned at random to either the vaginal estradiol treatment group or to the group with no treatment.

☐ I have HIV and agree to participate in the both parts of the study, including the trial. I agree to return for a total of five study visits. I understand that I will be assigned at random to either the vaginal estradiol treatment group or to the group with no treatment.

Visit 1

The screening visit for the first part of the study (Visit 1) will take about one hour to complete. During this visit, we will do some tests and procedures to see if you eligible to take part in this research study. The study doctor will review the results of these tests and procedures. If you are not eligible, the study doctor will tell you why.

At this visit:

- You will be asked questions about your background (e.g. age, education, etc.), your medical and sexual history.
- You will have a pelvic exam. A speculum (small plastic instrument) will be inserted into your vagina by the clinician to view the vagina. You will have samples collected from your vagina using a swab (like a Q-tip®). Swabs will be collected to measure the pH (how acidic the

vaginal fluid is), to measure types and quantity of vaginal bacteria present and to examine your fluid under a microscope to look for vaginal infections, including bacterial vaginosis, candida (yeast) and trichomonas. If you have a vaginal infection, you will be notified and referred to your primary doctor for treatment prior to enrollment in the study. After treatment, you may return for repeat testing and if the infection has resolved, you may be enrolled in the study.

- Cervical fluid will be collected by using a small syringe to rinse the vaginal area with saline and then immediately collect the fluid. The fluid will be used in the laboratory to measure the amount of cytokines present in the genital tract (cytokines are substances produced by cells to fight infection).
- If you are determined to be eligible, you will return for a second study visit in 4 weeks.

Visit 2

The following will take place at Visit 2 for participants who do not have HIV or participants with HIV who are not participating in the clinical trial:

- The study staff will draw a blood sample for hormone levels (estradiol and follicular stimulating hormone) to confirm you are menopausal. For participants with HIV, blood will also be drawn for CD4 count and HIV viral load. Test results will be drawn for research purposes only. To obtain the blood sample, we will wipe the skin on your arm with alcohol to clean it. Then, we will insert a small needle into a vein and three tubes of blood will be drawn, which is less than three tablespoons of blood.
- You will have a pelvic exam. A speculum (small plastic instrument) will be inserted into your vagina by the clinician to view the vagina. You will have samples collected from your vagina using a swab (like a Q-tip®). Swabs will be collected to measure the pH (how acidic the vaginal fluid is) and to measure types and quantity of vaginal bacteria present.
- Cervical fluid will be collected by using a small syringe to rinse the vaginal area with saline and then immediately collect the fluid. The fluid will be used in the laboratory to measure cytokines and other substances in the genital tract that fight infection.
- Two small samples of tissue will be taken from the vagina in a procedure called a biopsy. The areas where the biopsies will be taken will first be cleaned with saline. A gel (benzocaine) will be put on the biopsy areas to numb them. The small pieces of tissue are taken with forceps (similar to tweezers). You may feel a pinch when the tissue is taken. You may also take Tylenol up to one hour before the procedure if you wish. Instructions on how to care for your biopsies will be reviewed. You will be instructed not to have sex or to use any vaginal products for one week after this visit to give your biopsy sites time to heal. You will be told to contact the study staff if you have any bleeding, more than spotting, and/or pain.
- To measure vaginal atrophy, a visual exam will be done to assess for thin, pale and dry vaginal and vulvar surfaces and a light scraping of the vaginal wall will be performed to collect cells to examine under the microscope.

The following will take place at Visit 2 for participants with HIV who are participating in the clinical trial and will serve as the screening visit for the trial:

- You will be asked questions about your background (e.g. age, education, etc.), your medical and sexual history and whether you have symptoms of vaginal atrophy.
- The study staff will draw a blood sample for hormone levels (estradiol and follicular stimulating hormones) to confirm you are menopausal. Blood will also be drawn for CD4 count and HIV viral load. Test results will be drawn for research purposes only. We will wipe the skin on your arm with alcohol to clean it. Then, we will insert a small needle into a vein and three tubes of blood will be drawn, which is less than three tablespoons of blood.
- You will have a pelvic exam. A speculum (small plastic instrument) will be inserted into your vagina by a physician to view the vagina. You will have samples collected from your vagina using a swab (like a Q-tip®). Swabs will be collected to measure the pH (how acidic the vaginal fluid is), to measure types and quantity of vaginal bacteria present and to examine your fluid under a microscope to look for vaginal infections, including bacterial vaginosis, candida (yeast) and trichomonas. If you have a vaginal infection, you will be notified and referred to your primary doctor for treatment prior to enrollment in the trial. After treatment, you may return for repeat testing and if the infection has resolved, you may be enrolled in the trial.
- Cervical fluid will be collected by using a small syringe to rinse the vaginal area with saline and then immediately collect the fluid. The fluid will be used in the laboratory to measure certain substances in the genital tract that fight infection.
- Two small samples of tissue will be taken from the vagina in a procedure called a biopsy. The areas where the biopsies will be taken will first be cleaned with saline. A gel (benzocaine) will be put on the biopsy areas to numb them. The small pieces of tissue are taken with forceps (similar to tweezers). You may feel a pinch when the tissue is taken. You may also take Tylenol up to one hour before the procedure if you wish. Instructions on how to care for your biopsies will be reviewed. You will be instructed not to have sex or to use any vaginal products for one week after this visit to give your biopsy sites time to heal. You will be told to contact the study staff if you have any bleeding, more than spotting, and/or pain.
- To measure vaginal atrophy, a visual exam will be done to assess for thin, pale and dry vaginal and vulvar surfaces and a light scraping of the vaginal wall will be performed to collect cells to examine under the microscope.
- If you have HIV and symptoms of vaginal atrophy (e.g. irritation, pain with sex, dryness, itching) and are determined to be eligible, you will be asked to participate in clinical trial of vaginal estradiol which will consist of 3 additional visits (Visits 3, 4 and 5) over a 12 week period. The chance of you being assigned to either the estradiol treatment group or the no treatment group is exactly the same. We do not know ahead of time which group you will be assigned to, and you will not be able to choose or change your group.

Visit 3

At this visit:

- You will be given a questionnaire and a pelvic exam will be performed including vaginal swabs, the saline wash and a visual exam to assess for vaginal atrophy as described for Visit 2. Vaginal biopsies will not be done at this visit.
- You will be randomized to vaginal estradiol treatment group or the non-treatment group.
- If you are assigned to receive Vagifem, you will be instructed by research staff on how to insert the vaginal estradiol tablet using a plastic applicator which is similar to a tampon. The dosing of Vagifem® will be 1 tablet placed in the vagina once daily for 2 weeks followed by 1 tablet inserted twice weekly (i.e., Tuesday and Friday) for a total of 12 weeks. Each dose of Vagifem is packaged with a single plastic applicator. At this visit, you will be given a 6-week supply of Vagifem (22 single dose tablets and applicators). You will be instructed to use Vagifem the same time daily for all applications. It is important that you not use any other vaginal product while using this medication. You will be instructed to keep a diary of the date and time of Vagifem insertion and to return used applicators at your next study visit.

Visit 4

This visit will take place 6 weeks after visit 3. At this visit:

- You will be given the same questionnaire as the last visit.
- You will have another pelvic exam, during which the clinician will collect the same samples described at Visit 2 in addition to the same visual exam of the vagina. There will be no vaginal biopsies at this visit.
- If you are assigned to receive Vagifem, you will be given a 6 week supply of Vagifem (12 single dose tablets and applicators). You will be instructed to use Vagifem the same time daily for all applications. It is important that you not use any other vaginal product while using this medication. You will be instructed to keep a diary of the date and time of Vagifem insertion and to return used applicators at your next study visit.

Visit 5

This visit will take place 12 weeks after visit 3 and will involve the same tests, biopsies, exams and questionnaires as Visit 2.

There will be three phone calls during the study. They will occur at 2 and 8 weeks after starting Vagifem and 1 week after conclusion of the trial. You will be asked questions about dosing and any discomfort or issues related to the use of the estradiol vaginal insert.

A description of this clinical trial will be available on 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.

Will there be testing for HIV?

- Prior to study enrollment, most participants will be aware of their HIV status. If you are unaware of your HIV status, you will be tested for HIV as part of the study.
- If as a result of participation in this study you are diagnosed with HIV, you will be given HIV counseling or a referral for HIV counseling and you will be connected with care.

- The law protects the confidentiality of HIV related test results.
- The law prohibits discrimination based on your HIV status and services are available to address any discrimination.
- If as a result of participation in this study you are INITIALLY diagnosed with HIV, the results must be reported to the New York State Department of Health for contact tracing purposes.

Genetic Testing

This study will not involve genetic research or genetic testing.

Specimen Banking (Future Use and Storage)

We will store your specimens and information about you in a "biobank", which is a library of information and specimens (tissue, blood, vaginal washes) from many studies. These specimens and information can be linked to you. In the future, researchers can apply for permission to use the specimens and information for new studies to prevent, diagnose or treat disease, including genetic research. If you agree to the future use, some of your de-identified genetic and health information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government. Your specimens and information may be kept for a long time, perhaps longer than 50 years. You may remove your consent for future research at any time by contacting the Principal Investigator named on the first page of the consent or the IRB office at 718-430-2237. If you do, we will destroy remaining specimens and information but if these were already shared with other researchers, we cannot get them back.

You can choose not to participate in the biobank and still be part of the main study and this will not affect your treatment at this facility**.**

INITIAL ONE (1) OF THE FOLLOWING OPTIONS

_____ I consent to have my specimens and information about me used for future research studies.

_____ I do NOT consent to have my specimens and information about me used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

INITIAL YOUR CHOICE BELOW

_____ I consent to be contacted in the future to learn about:

_____ New research protocols that I may wish to join.

_____ General information about research findings.

_____ I do not want to be contacted at all.

Will I be paid for being in this research study?

You will receive compensation to help cover your time and travel expenses related to participating in this study. You will receive reimbursement only for visits that you complete.

You will receive a total of $125 ($50 for Visit 1 and $75 for Visit 2) if you complete only the first part of the study (2 visits).

If you have HIV and complete both parts of the study (five visits), you will receive a total of $300 ($50 at Visits 1, 3 and 4 and $75 at Visits 2 and 5). If you have HIV and complete only the second part of the study (clinical trial) you will receive a total of $250 ($50 at Visits 3 and 4 and $75 at Visits 2 and 5).

You will receive cash reimbursement for your participation in the study. If you choose to withdraw from the study before all visits are completed, you will be paid only for the visits you completed.

If any new products, tests, or discoveries resulting from the research have potential commercial value, you will not be compensated or benefit financially.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

There will be no cost to you to participate in the study.

What will happen if I am injured because I took part in this study?

Taking part in this research study may result in injury or harm to you. In the event of an injury resulting from your participation in this study, you should seek appropriate medical care and inform the study doctor. In the event of an emergency you should go to an emergency room. If you are injured or harmed as a result of participating in the study and receive medical care through the Montefiore Medical Center, a Montefiore doctor, or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance.

Albert Einstein College of Medicine and Montefiore Medical Center are not offering to provide you the drug/device after the termination of the study or to pay you for pain, worry, lost income, the cost of your medical care or non-medical care costs that might occur as a result of your taking part in this study. However, you do not waive any of your legal rights in signing this form.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Dr. Kerry Murphy at (718) 839-7885.

What else do I have to do?

- You must tell the research study doctor about any past and present diseases or allergies you are aware of and about all medications you are taking including “over-the-counter” remedies and nutritional supplements or herbs.
- You must take your study drug as instructed, returning any unused study drug (including any empty bottles), at every visit.
- If you do not feel well at any time, call your doctor or the research study doctor immediately.

- ***Drugs may cause a reaction that, if not treated promptly, could be life-threatening. It is important that you report all symptoms, reactions and other complaints to the research study doctor.***
- If any other doctor recommends that you take any medicine, please inform him/her that you are taking part in a research study. You should give the other doctor the research study doctor's name and phone number.
- You may carry out all your normal daily activities.

Confidentiality

The researchers and study staff follow federal and state laws to protect your privacy. This part of the consent form tells you what information about you may be used and shared in the research described in this form. You do not have to sign this form but, if you do not, you may not participate in the research.

The health information that we may use or disclose for the research described in this form includes information from your entire medical record, such as your name, phone number, email, medical diagnoses, dates, test results, social security number, medical record numbers, etc. In addition, the researchers wish to review information pertaining to your HIV records. By law, you must specifically authorize access to these records.

☐ Yes, I authorize the use and disclosure of my information pertaining to HIV testing and HIV status.

Initial: _____ Date: _____

Your information and research records will be kept confidential. Your study information will be kept as long as they are useful for the research described in this form.

The only people who can see your research records are:

- Researchers and other individuals who work with the researchers
- Organizations and institutions involved in this research, including the National Institutes of Health and NovoNordisk.
- Groups that review research such as Einstein Institutional Review Board, Montefiore Medical Center, the Office for Human Research Protections, the US Food and Drug Administration, and the National Institutes of Health

The purposes of these uses and disclosures are to (1) conduct the study and (2) make sure the study is being done correctly. The information covered under this form may no longer be protected by federal privacy laws (such as HIPAA) once disclosed, and those persons who receive your health information may share your information with others without your additional permission. All of these groups have been asked to keep your information confidential.

Medical information collected during the research, such as test results, may be entered into your Montefiore electronic medical record and will be available to clinicians and other staff at Montefiore who provide care to you.

To maintain the integrity of this research study, you generally will not have access to your research-related personal health information. If it is necessary for your care, your research-related health information will be provided to you or your physician.

Certificate of Confidentiality

As a way to protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health, which is funding this study. If information from this study were requested or subpoenaed by government agencies or the courts, we would use the Certificate to attempt to legally refuse to provide that information. These requests are rare – in only a few cases did researchers have to use the Certificate, and it was honored most of the time, but not every time. There are several kinds of situations to which the Certificate does not apply. For example, we are still required to report child abuse and some diseases, and we must make data available to the government for review or evaluation of our research. The Certificate does not prevent you or a member of your family from voluntarily sharing information. Similarly, if an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Are there any risks to me?

Blood Draw

Rarely, the vein where we inserted the needle will become sore or red. Sometimes, a temporary harmless “black and blue” may develop. There is a small risk of blood clots or infection from drawing blood. Very rarely, fainting may occur.

Pelvic/Speculum Exam and Procedures

Having a pelvic/speculum exam may cause some discomfort. You may feel some discomfort when the vaginal speculum is inserted. There is a very small risk of injury to the lining inside your vagina from the speculum or vaginal scraping. There is no risk to cervicovaginal lavage or vaginal swab collection.

Vaginal Biopsies

You may feel a sharp pinch or have pain when the samples are taken. In order to minimize the pain and discomfort of the biopsy, we will apply a topical numbing medication (benzocaine gel) to the tissue. Benzocaine gel can cause burning, redness, and itching at the application site, which is rare. You may also choose to take Tylenol® up to one hour before the biopsy. The biopsies may also cause light bleeding, which we will make sure is under control before you leave. Sometimes a medication is needed to stop the bleeding, which would be applied directly to the site. This medication can cause a dark- discharge from your vagina, which is temporary. In rare cases a stitch might be needed or a machine (cautery) may be used. You may feel soreness or discomfort for one or two days after the biopsy. You may have some vaginal spotting or bleeding and a slight discharge for up to a week after a biopsy. If needed, you can use a sanitary pad for the bleeding. Rarely, a biopsy can cause infection and/or prolonged bleeding. You should call the study staff if you have vaginal bleeding (more than spotting), foul smelling vaginal discharge, fever, chills or severe pain in your lower belly or pelvis.

Risks of taking Vagifem® 10 µg

Common Side Effects:

- Back pain (7 out of 100)
- Diarrhea (5 out of 100)
- Vulvovaginal fungal infection (8 out of 100)

  Vulvovaginal itching (8 out of 100)

Less Common Side Effects:

- Vagifem applicator may cause vaginal abrasion

Women who use systemic forms (e.g. pills) of estradiol (without progesterone added) who have a uterus may have an increased risk of endometrial hyperplasia, which in some women may be a precursor to endometrial cancer after prolonged use. In this study, you will be using a low-dose topical estradiol vaginal tablet, which does not increase blood levels of estradiol beyond the baseline menopausal levels and has been proven to be safe for the treatment of vaginal atrophy without adverse effects on the uterus lining, including endometrial hyperplasia. Further, low-dose vaginal estrogen has not been shown to increase risk for coronary heart disease, stroke, venous thromboembolism or dementia.

Risks to Women Who Are or May Become Pregnant

The effect of Vagifem on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding or sharing breast milk

Allergic Reaction to Study Drug

Any drug can cause an allergic reaction which could be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you are having trouble breathing, call 911 immediately.

Psychological/Emotional

You may become embarrassed, worried, or anxious during the physical examinations, or when discussing your sexual history. Although the study team makes every effort to protect your privacy and confidentiality, a risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. As a result, it is possible that social harms may occur such as difficulties in personal relationships or discrimination from your family or community. If you experience these kinds of problems during the study, a trained counselor will work with you to address the problem and provide referrals to other service providers if needed. The study team plans to protect your privacy – see the Confidentiality section above for details.

Inconvenience

Participation in the study may cause an inconvenience to your daily schedule because you will need to come to the study clinic for 2-5 visits. You will be asked not to use any vaginal products other than the study vaginal estradiol tablet.

New Findings

If we learn any significant new findings during the study that might influence your decision to continue, we will contact you and explain them.

Unknown Risks

There is always the possibility that you will have a reaction that is currently not known and not expected. All drugs may have the risk of causing an allergic reaction that, if not treated promptly, could be life threatening. It is important that you report any and all symptoms or possible reactions to your doctor. You will be monitored for side effects by the research study staff, and the research study doctor may decide that you should be withdrawn from the research study.

Are there possible benefits to me?

Women with HIV infection experience menopausal symptoms at an earlier age and are more likely to report symptoms compared to women who do not have HIV. Participants may benefit from study participation because the use of low dose topical estradiol, which has been FDA approved since 2009 for the treatment of vaginal atrophy in menopausal women, may relieve symptoms of vaginal dryness, itching, soreness, pain and urinary symptoms in women with HIV. Participants and others may benefit in the future from information learned from this study. Specifically, if we find that HIV accelerates genital tract aging, this may prompt recommendations for earlier treatment of vaginal atrophy in menopausal women with HIV.

What choices do I have other than participating in this study?

You can refuse to participate in the study.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. This will not affect your care and you will continue to be treated by your regular providers. However, some of the information may have already been entered into the study and that will not be removed. The researchers and the sponsor may continue to use and share the information they have already collected. If you decide to stop taking part in the study for any reason, we will ask you to make a final study visit. You will need to return all unused study drug.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and she will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

Can the study end my participation early?

We will not let you participate in the study any more if you are unable to follow study instructions, you become ineligible, or if it is unsafe for you to continue your participation in the study. In addition, your participation will end if the investigator or study sponsor stops the study earlier than expected.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not I participate. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	Time
Printed name of the person conducting the consent process	Signature	Date	Time