Official Title:

APT-POCT-01: An Open Label, Pharmacokinetic Study of Plasma/Urine/Salivary Drug Concentrations Over Fourteen Days Following Drug Intake Cessation, In HIV-Uninfected Healthy Volunteers Dosing to Steady-state to Further Development of Point of Care Diagnostic Testing

ClinicalTrials.gov ID (NCT number):

NCT04302896

Document Date:

February 16, 2021

University of Pittsburgh

Department of Medicine
Division of Infectious Diseases

3520 Fifth Avenue
Suite 510 Keystone Bldg.
Pittsburgh, PA 15213-2582

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: APT-POCT-01: An Open Label, Pharmacokinetic Study of Plasma/Urine/Salivary Drug Concentrations Over Fourteen Days Following Drug Intake Cessation, In HIV-Uninfected Healthy Volunteers Dosing to Steady-state to Further Development of Point of Care Diagnostic Testing- (DAIDS-ES ID 38668) Version 1.0 December 9, 2019

SHORT TITLE: APTAMER

PRINCIPAL INVESTIGATOR: Ken Ho, MD
Assistant Professor of Medicine, University of Pittsburgh
3520 5th Avenue, Room 510 Keystone Building
Pittsburgh, PA 15213
412- 383-1675

SUB-INVESTIGATORS:
Deborah McMahon, MD; Sharon Riddler, MD; Bernard Jonas Macatangay, MD; Madhu Choudhary, MD
Stacey Edick, PA-C 3520 Fifth Ave, Room 510 412-383-1675
Rhonda Brand, PhD 204 Craft Avenue, Room B303 412- 641-7960

SOURCES OF SUPPORT: The study is being paid for by the Division of AIDS, US National Institute of Allergy and Infectious Diseases of the National Institutes of Health.

QUESTIONS ABOUT THE STUDY: The person in charge of this study at the University of Pittsburgh is Ken Ho, MD. If you have any questions about the study, concerns or complaints, you can contact one of the investigators at the numbers listed on the first page of this consent form. You can also call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668 if you have any questions about your rights as a research subject or wish to talk to someone other than the research team.

Key Information Summary

You are being asked to take part in the research study named above. The study team will explain the study to you and help you decide if you want to participate. You can decide not to join.

This study will try to find out more about the pharmacokinetics (how drugs move through the body) of several antiretroviral medications through testing of saliva, blood and urine. The outcomes of this study will provide support for the development of a point of care (POC) test for real time results of drug adherence testing.

If you qualify and choose to participate, you will have 11 study visits over the course of one month. It is vital that you attend all of these visits.

The study procedures will include:
- Questions about your medical/medication history
- Physical exam
- Collection of samples
- Taking drugs for 15 consecutive days

You may experience discomfort from the blood draws. Other unlikely risks involve breach of confidentiality. Risks of the drugs are outlined in detail later in the document.

You should not take part in this study if you are pregnant or intend to become pregnant. If you are a woman who can become pregnant, you must commit to using recommended birth control methods.

You should expect no direct benefit from taking part in this study.

You will be compensated $40 for your time and effort for each of the 11 scheduled study visits that you complete except Visit 5 for which you will receive $60 for up to a total of $460.

INTRODUCTION: You are being asked to participate in this research study investigating the pharmacokinetics (how drugs move through the body) of the following drugs: dolutegravir, emtricitabine, tenofovir alafenamide, tenofovir disoproxil, and lamivudine.

Before you decide if you want to join this study, we would like to explain the purpose of the study, how it may help you, any risks to you, and what is expected of you. This consent form gives you written information about this study, which will also be discussed with you. This study also asks for your permission to store leftover samples for future testing.

Once you read, discuss and understand this study, and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep. Before you agree to participate in this study, it is important that you ask as many questions as possible and know the following:

- Your participation is entirely voluntary;
- You may decide not to take part or to withdraw from this study at any time without losing the benefits of the routine medical care you are otherwise entitled to;
- You will be asked to tell the study staff about any other studies you are taking part in, or are thinking of taking part in. This is very important for your safety.

Your physician may also be involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

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

WHY IS THIS STUDY BEING DONE?

This research study will try to find out how these drugs move through the body, and if we can detect the drugs in a test that could be performed at the point of care (like a pregnancy test), rather than having to send samples

such as blood or urine to a laboratory and wait for results. The results of this study would provide support for the development of a POC device that monitors drug adherence.
The drugs we are testing (dolutegravir, emtricitabine, tenofovir alafenamide, tenofovir disoproxil, and lamivudine) are approved by the U.S. Food and Drug Administration (FDA) alone or in combination to treat, and in some cases prevent, HIV infection. This point of care test (POCT) may help tell us if people have actually been taking these medications so we can better treat their HIV. People who have HIV are on these medications for a long time, but in this study, people will be taking these drugs for only 15 consecutive days. For that reason, we are only allowing people that do NOT have HIV to participate in the study. The use of these drugs in this study and the point of care test are investigational, or not approved by the FDA.

WHAT DO I HAVE TO DO IF I AM IN THE STUDY?
Approximately 30 healthy, HIV-negative men and women at least 18 years old will participate in this study at the University of Pittsburgh, the only study site.

If you are eligible for this study and decide to participate, you will have a total of 11 study visits in the Magee-Womens Hospital Clinical Translational Research Center (MWH CTRC), including today's Screening Visit 1. After a screening period of up to 28 days (4 weeks), you will be in this study for about 29 days (4 weeks). Each study visit may take about 1-2 hours, except for Visit 5 which may take about 5 hours. If you commit to doing this study, it is very important that you attend each and every study visit.

During these visits, you will discuss with study staff the rules of the study and your understanding of the rules, including, but not limited to:

- To decrease the chance of interactions with medications that may interfere with the drugs or the interpretation of study results, you will be asked to avoid taking any of the following medications and products while you are on study:
    - Any medication that works against HIV
    - Sorbitol
    - Dofetilde
    - Rifampin
    - Carbamazepine
    - Phenytoin
    - Phenobarbital
    - St. John's Wort
    - Midazolam
    - Antacids
    - Multivitamins or supplements containing iron, calcium, magnesium or zinc
    - Metformin
    - Sertraline
    - Experimental or investigational products
- You must also agree to use condoms and an acceptable method of birth control while on this study and for 8 weeks after your last dose of study drug. Acceptable methods of birth control for female participants include:
    - Hormonal contraceptives (such as birth control pill, patch, vaginal ring, implant or injection)
    - Intrauterine device (IUD)
    - Prior sterilization surgery such as hysterectomy or "tubes tied"
    - Your partner had sterilization surgery such as a vasectomy
    - Menopause

You will also undergo physical exams and have saliva, urine and blood collected for study tests, including tests for your general health, Hepatitis and HIV infection, and if you are a woman, pregnancy. Some of your samples will be shipped to the University of Liverpool for study testing.

At Enrollment Visit 2, you will be randomly assigned (like the flip of a coin) to one of two study groups. Both of these groups are important to the results of the study. You cannot choose your group, but you will know which group you are in.

- Group 1 will receive dolutegravir 50mg tablet + emtricitabine 200mg with tenofovir alafenamide 25mg tablet by mouth once daily for 15 consecutive days
- Group 2 will receive dolutegravir 50mg tablet + tenofovir disoproxil 300mg tablet + lamivudine 300mg tablet by mouth once daily for 15 consecutive days

You will be asked to fill out a study diary to record when you take your dose of study medication, changes to any medicines you are taking now, and about any side affects you might experience. You will be reminded to bring this study diary with you to each study visit.

WHAT PROCEDURES WILL BE DONE DURING THIS STUDY?

If you decide to take part in the study, your visit will continue today after you read, discuss, understand, and sign this form. The study staff can answer any questions you have about individual study visits and evaluations.

The procedures performed in this study are done for research purposes and will be performed by a study investigator, clinician, or other trained member of the research team. The results will become part of your research record. During the study, the investigators will review the results of all labs, evaluations, and procedures that monitor your health and safety. You will be notified of any results that might affect your personal health or decisions as soon as they are available.

Visit 1/Screening (Today)

At today's visit you will:

- Answer questions about yourself, such as your medical and menstrual history (if female), about any medications that you may take, and how we can contact you.
- Learn from the study staff about:
    - how to avoid infections passed during sex, including HIV
    - how to use condoms to prevent sexually transmitted infections
    - what to expect from HIV testing
- Receive condoms from study staff
- Have a physical exam
- Provide a urine sample for pregnancy testing (females only). If your pregnancy test is positive you cannot continue with the study.
- Have a blood sample (20 ml or about 4 teaspoons) taken to check the health of your blood, liver and kidneys and to test for HIV and hepatitis B and C.

If you test positive for HIV, you may be asked to give another blood sample for a confirmatory HIV test. You will also be counseled about the risks of transmitting HIV to others, the risks for developing AIDS, and the available treatments for HIV infection. If you test positive for HIV, you cannot continue in the study and the study staff will help you arrange care or treatment. Medical care for HIV infection will not be part of this study.

If at any time during this study HIV, hepatitis B or hepatitis C is identified, we are required to confidentially

report this to the Allegheny County Health Department with your name and contact information. Someone from the Health Department may contact you to be sure that you and your partners have been treated.

Visit 2/Enrollment (Day 1)

Visit 2 will occur any time up to 4 weeks after Visit 1 and will be scheduled on a Monday. At this visit you will:

- Let us know if there are any changes in where you live or how we may contact you
- Be offered a copy of your test results, if appropriate, and review these results with the study staff
- Tell us about any changes in your medical, menstrual and medication history
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit
- Have a saliva (spit) sample taken with a swab to compare to samples at future visits
- Provide a urine sample to compare to samples at future visits, and for females, to test for pregnancy. If the pregnancy test is positive, you cannot continue in the study.
- Have a blood sample (10ml or about 2 teaspoons) taken to compare to samples at future visits
- Be randomly assigned to a study drug group
- Take the first dose of your assigned study drugs (2-3 tablets) by mouth in front of the study staff.

Visit 3 (Day 2)

Visit 3 will occur the day after Visit 2. At this visit you will:

- 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, menstrual and medication history
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit.
- Have a saliva (spit) sample taken with a swab to test for study drug
- Provide a urine sample to test for study drug
- Have a blood sample (10ml or about 2 teaspoons) taken to test for study drug
- Take the second dose of study drug (2 -3 tablets) by mouth in front of study staff
- Receive 13 doses of study drugs with instructions to take one dose by mouth once a day and to bring the drugs with you to Visit 4 (Day 8) to be taken in front of study staff.
- Be given a study drug diary with directions to record the date and time you take your daily dose of study drugs on non-visit Days 3-7 and to bring this diary with you to Visit 4.

Visit 4 (Day 8)

Visit 4 will occur 6 days after Visit 3. AT this visit you will:

- Let us know if there are any changes in where you live or how we may contact you
- Tell us about any changes in your medical, menstrual and medication history
- Have your study drug diary reviewed by study staff and be reminded to record the date and time you take your daily dose of study drugs on non-visit Days 9-14 and to bring this diary with you to Visit 5 (Day 15).
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit.
- Provide a urine sample to test for study drug, and for females, to test for pregnancy. If the pregnancy test is positive, you will stop taking the study drug, but are asked to remain on study until the pregnancy outcome is determined
- Have a blood sample (10ml or about 2 teaspoons) taken to test for study drug

- Take the eighth dose of you assigned study drugs (2-3 tablets) by mouth in front of study staff and be reminded to bring the last dose of study drugs with you to Visit 5 (Day 15) to take in front of study staff.

Visit 5 (Day 15)

Visit 5 will occur 7 days after Visit 4 and may take about 5 hours. At this visit you will:

- 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, menstrual and medication history
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit.
- Return any missed doses of study drugs and turn in your diary for review by study staff
- Have a saliva (spit) sample taken with a swab 3 times (before your last dose, 1 hour after your last dose, and 4 hours after your last dose) to test for study drug
- Provide a urine sample 3 times (before your last dose, 1 hour after your last dose, and 4 hours after your last dose) to test for study drug, and for females, to test for pregnancy. If the pregnancy test is positive, you will stop taking the study drug, but are asked to remain on study until the pregnancy outcome is determined
- Have a blood sample (12ml or about 2.5 teaspoons) taken to check the health of your blood, liver and kidneys
- Have a blood sample (10ml or about 2 teaspoons) taken 3 times (before your last dose, 1 hour after your last dose, and 4 hours after your last dose) to test for study drug.
- Take the last dose of your assigned study drugs (2-3 tablets) by mouth in front of study staff.

Visits 6, 7, 8 and 9 (Days 16, 17, 18 and 19)

These visits will start the day after your last dose of study drugs and occur every day for 4 days in a row. At each of these visits you will:

- 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, menstrual and medication history
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit
- Have a saliva (spit) sample taken with a swab to test for study drug
- Provide a urine sample to test for study drug
- Have a blood sample (10ml or about 2 teaspoons) taken to test for study drug

Visit 10 (Day 22)

Visit 10 will occur 7 days after your last dose of study drugs. At this visit you will:

- 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, menstrual and medication history
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit
- Have a saliva (spit) sample taken with a swab to test for study drug
- Provide a urine sample to test for study drug, and for females, to test for pregnancy
- Have a blood sample (20ml or about 4 teaspoons) taken to test for study drug and HIV-1

Visit 11 (Day 29)
Visit 11 will occur 14 days after your last dose of study drugs. At this visit you will:

- 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, menstrual and medication history
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit
- Have a saliva (spit) sample taken with a swab to test for study drug
- Provide a urine sample to test for study drug, and for females, to test for pregnancy
- Have a blood sample (30ml or about 6 teaspoons) taken to test for study drug; to check the health of you blood, liver and kidneys; and to test for HIV-1

Interim Visits
In some cases, an extra visit or visits (called Interim Visits) might be necessary in between your scheduled study appointments. Sometimes these visits may be necessary to address any questions you might have. At other times, the Interim Visits may occur if you experience side effects that need to be evaluated by study staff. In such cases, study staff may refer you to appropriate medical care.

Early Discontinuation Visits
If you stop taking the study drugs early for any reason, you will be asked to continue with all study visits and procedures though the end of the study.

If you withdraw or are withdrawn from this study for any reason after receiving the study drugs, you will be asked to come to the clinic for a final study visit. At this visit, which may take 1-2 hours, you will:

- 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, menstrual and medication history
- Have a physical exam, if the study clinician thinks your health status has changed since your last study visit
- Turn in your study diary and any missed doses of study drug
- Have a saliva (spit) sample taken with a swab to test for study drug
- Provide a urine sample to test for study drug, and for females, to test for pregnancy
- Have a blood sample (30ml or about 6 teaspoons) taken to test for study drug; to check the health of your blood, liver and kidneys; and to test for hepatitis and HIV-1.

Final Contact
After your Final Study Visit or Early Termination Visit, study staff may contact you to provide laboratory test results, and, if applicable, post-test counseling.

ARE THERE ANY RISKS AND/OR DISCOMFORTS?
As with any research study, there may be adverse events or side effects that are currently unknown, and it is possible that certain of these unknown risks could be permanent, serious, or life-threatening. We may learn new information that might change whether or not you want to continue in the study. If this happens, you will be told in a timely manner. You may decide to stop taking part in the study at any time. If you do, your study doctor will discuss the steps you should follow. If you decide to continue, you may be asked to read and sign a revised consent form containing the new information.

The product used in this study may have side effects, some of which are listed below. Please note that this list does not include all the side effects seen with this product, such as a previously unknown allergic reaction causing a rash, swelling, and trouble breathing. This list includes the more serious or common side effects with a known or possible relationship. If you have questions concerning additional study product side effects, please ask the study staff.

Risks from Tivicay® (dolutegravir; DTG): Dolutegravir can cause serious, life-threatening side effects. These include allergic (hypersensitivity) reactions and liver problems.

Allergic reaction may cause a rash. You may develop a rash with any of the following signs or symptoms:

- Fever
- General ill feeling
- Extreme tiredness
- Muscle or joint aches
- Blisters or sores in your mouth
- Blisters or peeling skin
- Redness or swelling of your eyes
- Swelling of your mouth, face, lips, or tongue
- Trouble breathing

Liver problems may cause:

- Yellowing of your skin or whites of your eyes (jaundice)
- Dark or tea-colored urine
- Pale-colored bowel movements
- Nausea or vomiting
- Loss of appetite
- Pain, aching, or tenderness on your right side below your ribs
- Changes in liver test results, more common in people with hepatitis B or C

People with pre-existing history of depression or other mental health illness may be at greater risk for suicidal thoughts, or attempts, which may lead to death. If your mental health illness worsens or you developm suicidal thoughts, contact your healthcare provider right away.

Additional side effects include:

- Trouble sleeping
- Abnormal dreams
- Tiredness
- Headache
- Anxiety (fear, worry)
- Muscle and joint aches
- Dizziness
- Nausea/Vomiting

Risks from Tivicay® (dolutegravir) and Pregnancy: Early results from a large study of pregnant women in Botswana showed a possible increased risk of certain types of serious birth defects involving the brain and spinal cord in babies born to women who received DTG for HIV treatment at the time of becoming pregnant or

early in their pregnancy. No cases of babies born with these types of birth defects have been reported amount women who started DTG later in pregnancy. You cannot be in this study if you are pregnant. If you become pregnant while on the study, we will continue to follow you in the study until the outcome of your pregnancy is determined.

Risks of Lamivudine; 3TC: The following side effects have also been associated with use of lamivudine:

- Headache
- Feeling tired
- Dizziness
- Numbness, tingling, and pain in the hands or feet
- Depression
- Trouble sleeping
- Rash
- Upset stomach, vomiting, nausea
- Loose or watery stools
- Pancreatitis (inflammation of the pancreas), which may cause death. If you develop pancreatitis, you may have one or more of the following: stomach pain, nausea, and vomiting.
- Abnormal pancreatic and liver function blood tests

If you are infected with both Hepatitis B and HIV, you should be aware that your liver function tests may increase, and symptoms associated with hepatitis (an acute inflammation of the liver) may worsen if lamivudine is stopped. Although most of these cases have resolved without treatment, some deaths have been reported. If you test positive for HIV or Hepatitis B, you will not be allowed to participate in the study.

Risks of Viread® (tenofovir disoproxil fumarate; TDF): The following side effects have been associated with the use of tenofovir:

- Upset stomach, vomiting, gas, loose or watery stools
- Generalized weakness
- Dizziness
- Depression
- Headache
- Abdominal pain
- Worsening or new kidney damage or failure
- Liver problems. If you are developing liver problems, you may have one or more of the following symptoms:
  o Yellowing of the skin or whites of your eyes,
  o Dark urine,
  o Pain on the right side of your stomach,
  o Loss of appetite, upset stomach or vomiting,
  o Pale colored stools,
  o Itchy skin.
- Shortness of breath
- Rash
- Allergic reaction: symptoms may include fever, rash, upset stomach, vomiting, loose or watery stools, abdominal pain, achiness, shortness of breath, a general feeling of illness or a potentially serious swelling of the face, lips, and/or tongue.
- Bone pain and bone changes such as thinning and softening which may increase the risk of breakage

- Muscle pain and muscle weakness
- Sleeping problems

If you have hepatitis B virus (HBV) infection and take tenofovir DF and then stop using it, you may have worsening of your HBV infection. Tell your health care provider about any new or unusual symptoms after you stop taking tenofovir DF. If you test positive for hepatitis B, you will not be allowed to participate in the study.

Risks of Descovy® (tenofovir alafenamide/emtricitabine; TAF/FTC): The reported side effects include:

- Headache
- diarrhea
- nausea
- decreased kidney function
- feeling tired
- dizziness
- depression
- difficulty sleeping
- abnormal dreams
- rash, abdominal pain
- increased cough
- runny nose.

Severe reactions include kidney failure, a build-up of lactic acid in the body making the other side effects worse, worsening of Hepatitis B, and hepatomegaly (enlargement of the liver). If you test positive for hepatitis B, you will not be allowed to participate in the study.

Risks of Combination Antireretroviral Drugs: The use of potent antiretroviral drug combinations may be associated with an abnormal placement of body fat and wasting. Some of the body changes include an increase in fat around the waist and stomach area; an increase in fat on the back of the neck; thinning of the face, legs and arms; and breast enlargement
Lactic acidosis (elevated lactic acid levels in the blood) and severe hepatomegaly (enlarged liver) with steatosis (fatty liver) that may result in liver failure, other complications or death have been reported with the use of antiretroviral nucleoside analogues alone or in combination. The liver complications and death have been seen more often in women on these drug regimens. Some nonspecific symptoms that might indicate lactic acidosis include unexplained weight loss, stomach discomfort, nausea, vomiting, fatigue, cramps, muscle pain, weakness, dizziness and shortness of breath.

Risks of Sample Collection: You may feel dizzy or lightheaded and feel discomfort or pain when your blood is drawn. You may experience bleeding, bruising, swelling, or infection where the needle goes into your arm. There is no risk associated with urine collection. There is the risk of mild discomfort during saliva collection, in addition to a slight risk of bleeding.

Risks of Collecting Genetic Information There are risks to collecting genetic information. Genetics are about DNA. DNA can confirm who your parents are by blood tests and if you are more likely to get certain diseases. This is confidential information. Whenever this information is stored, there is always a small chance someone can view it that is not supposed to. This is called breach of confidentiality and is against the law. In some cases, it could be used to make it harder for you to get or keep a job, or insurance. Genetic information about diseases that some people have negative opinions about could be used in ways that could cause you or your family distress.

Risks of Discussing Sexual Behaviors: You may become embarrassed, worried, or nervous when discussing personal questions about your sexual behavior and ways to protect against HIV and other infections passed during sex.

Risks of HIV-1 and STI testing: You may become worried or nervous while waiting for your test results. There may be emotional discomfort, sadness, depression, stress, problems in relationships with sexual partners, and increased HIV risk behaviors associated with knowledge of the results of this test. A trained counselor will help you deal with any feelings, questions, or concerns you may have. There is a possibility that if the results of these tests were to become generally known this information could impact future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in stigmatization.

Risk of HIV Seroconversion and Antiretroviral Drug Resistance
HIV seroconversion, or new HIV infection, on this study is expected to be rare. However, as study drug level declines, the protective effect of antiretroviral drugs also wanes. Should HIV seroconversion occur, there is a risk of the virus developing resistance to the antiretroviral drugs. Given that in this study there is such a short exposure to the antiretroviral drugs, the risk of resistance is thought to be very low.

Risks of Social Harm: You may feel embarrassed or uncomfortable when self-administering doses of study drug under observation. It is possible that your participation in this study may cause problems in your personal and professional relationships (e.g., your boss may not like you taking time off from work for study visits). It is possible that your involvement in the study could become known to others, and that you may experience stigmatization or discrimination as a result of being perceived as being HIV-infected or at risk for HIV infection. For example, you could be treated unfairly, or could have problems being accepted by your family and/or communities.

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

ARE THERE RISKS RELATED TO PREGNANCY?
Pregnant and breastfeeding women are excluded from study participation. The effects of the study product on a pregnant woman, unborn baby, or breastfeeding infant are not known. If you are having sex that could lead to pregnancy, you must agree not to become pregnant or make your partner pregnant. If you or your partner are able to become pregnant, it is important that you use an effective method of birth control that you discuss with the study staff. If pregnancy occurs, study product will be stopped, you will be exited from the study, and you will be referred for further services. If it is determined that you are pregnant at the end of the study you will

continue to be followed in the study until the outcome of the pregnancy is known. For this study, effective, acceptable, methods of birth control for female participants include hormonal contraceptives (such as birth control pill, patch, or injection), an intrauterine device (IUD), or sterilization surgery ("tubes tied" in women, or vasectomy in men).

In one ongoing birth outcome study, early results show that 4/426 (0.9% or nearly 1 in every 100) pregnancies of women who were taking dolutegravir at the time they became pregnant had babies with serious brain and spine defects, compared to 0.1% (one in every 1000) pregnancies of women who were not taking dolutegravir. These defects happen early in pregnancy, within the first month, before many women even know they are pregnant. It is recommended that you use the above recommended methods of birth control while on this study and for 8 weeks after your last dose of study drug.

If you decide that you want to become pregnant and start trying to become pregnant or you think that you may be pregnant at any time while you are participating in this study, tell your study doctor or coordinator right away. If you are pregnant or trying to become pregnant, you must immediately stop taking the study drugs and will be asked to continue to be followed on-study/off-study drugs with all of the visits and some of the evaluations listed above through the end of the study. You will be asked about the outcome of your pregnancy even if delivery occurs after the study is over. This study will not provide care related to your pregnancy, the delivery of your baby, or the care of your baby. You must arrange for your care and your baby's care outside of this study.

Long-term follow-up is recommended for a baby whose mother takes antiretroviral drugs during pregnancy. Your study doctor or coordinator will talk to you about your choices for long-term follow up. Your pregnancy will be reported to The Antiretroviral Pregnancy Registry, www.apregistry.com Phone: (800) 258-4263; Fax: (800) 800-1052. These reports will not use your name or other information that could be used to identify you.

Breastfeeding

It is unknown whether the study drug passes through the breast-milk and may cause harm to your infant. You must not breast-feed if you are in this study.

WHAT ARE THE BENEFITS?

There is no prospect of direct benefit from being in this study.

There may be some ancillary benefit, in that results of study tests could alert you to an undiagnosed health issue.

• You will have physical exams and tests to check on the health of your blood, liver, and kidneys. If these tests show that you might have any health problems, you will be referred for medical care and other services available to you.

• You will be tested for hepatitis B and C. These tests may detect infections without obvious symptoms. If you are diagnosed with hepatitis B or C you will be referred for medical care, counseling, and other services available to you.

• You will get counseling and testing for HIV. This study does not provide medication for treatment of HIV/AIDS. If you become infected with HIV, you will be referred for medical care, counseling, and other services available to you.

WHAT TREATMENTS OR PROCEDURES ARE AVAILABLE IF I DECIDE NOT TO TAKE PART IN THIS RESEARCH STUDY?

There may be other research studies here or in the community that you may be eligible for. If you wish, we will tell you about other research studies that we know about. There also may be other places where you can go for HIV counseling and testing, STI testing, and contraception. We will tell you about those places if you wish.

WHAT ARE THE COSTS TO ME?

There is no cost to you for the study product, clinic visits, procedures, or any laboratory tests. These services will be paid for by the study and will not be billed to you or your health insurance company. If you receive a bill or believe that your health insurance has been billed for something that is part of the research study, notify a member of the research team or UPMC Patient Billing Services.

Any non-study procedures performed for routine medical care, such as treatment for STIs, will be billed to you and/or your health insurance company. You will be responsible for paying any deductibles, co-payments or co-insurance that are a normal part of your health insurance plan. If you do not have health insurance, you will be responsible for those costs.

WILL I RECEIVE ANY PAYMENT?

You will be compensated $40 for your time and effort for each of the 11 scheduled study visits that you complete except Visit 5 for which you will receive $60for up to a total of $460.

You may also receive $25 for completing any interim visits.

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

Your data or 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 outside agencies may receive.

WHAT HAPPENS IF I AM INJURED (EXPERIENCE HARM)?

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. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. There is no plan for any additional financial compensation either through this institution or the National Institutes of Health (NIH). You will not, however, be giving up any of your legal rights by signing this consent form.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?

There is a possibility that if your participation in this HIV research study were to become generally known this information could impact future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in stigmatization. To minimize this risk, any information about you obtained from this research will be kept as confidential (private) as possible. Pennsylvania state law requires the reporting of positive HIV test results to the Allegheny County Health Department with your name and contact information. All information will be handled in compliance with the Pennsylvania law on HIV-related confidential information.

All records related to your involvement in this research study will be stored in a secure, double-locked area or password-protected computer database at the HIV/AIDS Clinical Research Site (CRS) that is accessible only by members of the research team. Your identity on these records will be indicated by your subject identification number rather than by your name, and the information linking your subject identification number with your identity will be kept separate from the research records. Your research information and data may be shared with investigators conducting other research. This information may be identifiable.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. 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. Finally, you should also understand that this federal Certificate does not prevent investigators from taking steps, including reporting to appropriate authorities, to prevent serious harm to you or others. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

In addition to the investigators listed on the first page of this consent form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical record information) related to your participation in this research study. This study will be reviewed periodically to monitor its conduct. Therefore, your records may be reviewed as part of routine audits by:

- Division of AIDS, US National Institute of Allergy and Infectious Diseases, the National Institutes of Heath
- The Food and Drug Administration (FDA)
- Office for Human Research Protections (OHRP)
- University of Pittsburgh Institutional Review Board (an IRB is a committee of volunteers who are responsible for protecting the rights and welfare of research participants)
- Mologic, LTD
- Other local, US, and international regulatory authorities
- Study staff
- Study monitors including members of data safety monitoring boards

We will protect your privacy and the confidentiality of your research records, as described in this document, but cannot guarantee the confidentiality of your research records including information obtained from your research records, once your personal information is disclosed to others outside UPMC or the University.

A description of this clinical trial will be available on www.clinicaltrials.gov . 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.

WILL THIS STUDY INVOLVE THE USE OR DISCLOSURE OF MY IDENTIFIABLE INFORMATION?
This research study *will not* involve the recording of *current* identifiable medical information from your hospital and/or other health care provider records. This research study *will* involve the recording of *future* identifiable medical information from your hospital and/or other health care provider records. The identifiable information that will be recorded includes adverse event information related to the study enema products or procedures.

Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information related to your participation in this research study for the purpose of scheduling Magee CTRC appointments for each study visit.

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical record information) related to your participation in this research study for a minimum of 7 years and for as long as it may take to complete this research study. Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following final reporting or publication of a project.

You are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

WHY MIGHT I BE WITHDRAWN FROM THIS STUDY WITHOUT MY CONSENT?
You may be withdrawn from the study without your consent for the following reasons:

- The study is cancelled by the NIH, IRB, OHRP, or other local government or regulatory agency
- Study staff considers that having the exams and tests would cause injury that could be harmful to you.
- You do not want to learn your HIV-1 test result.
- You are not able to complete the medical exams and tests.
- You are unable or unwilling to follow all of the study procedures or instructions.
- You are found to not be eligible for this study.
- Other reasons that may prevent you from completing the study.

If you are withdrawn early from the study, you will be asked to come in for a final visit with all the exams and tests listed for the final visit, if the study doctor thinks the exams and tests need to be done. Any identifiable research or medical record information recorded for, or resulting from, your participation in this study prior to the date that you were formally withdrawn from the study without your consent may continue to be used and disclosed by the investigators for the purposes described above.

MAY I WITHDRAW, AT A FUTURE DATE, MY CONSENT FOR PARTICIPATION IN THIS STUDY?
You can, at any time, withdraw from this study. You can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw from this study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh, on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

****

STORAGE AND FUTURE TESTING OF SPECIMENS: There might be a small amount of biological specimens such as saliva, blood or urine left over after all of the study-related testing is complete. We would like to ask your permission to store these leftover samples for use in future studies. No additional medical examination or testing is required of you.

Your samples may be used to look for ways that your body responds to infection (such as cells, proteins, and other chemicals in your body). Tests may also include checking your genes (material passed from parent to child that determines the make-up of the body and mind), since they might affect how your body responds to disease, and whole genome sequencing of all of your genes. Your genes might make you more or less likely to get an infection, affect your responses to infection, or make your responses to treatment stronger or weaker. No other kinds of genetic tests will be done on your stored samples without first explaining the test to you and getting your permission. The researchers do not plan to contact you or your regular doctor with any results from tests done on your stored samples. This is because research tests are often done with experimental procedures, so the results from one research study are generally not useful for your medical care. If a rare situation came up where the researchers decided that a test result would provide important information for your health, the researchers would tell your study clinician and your study clinician would try to contact you. If you wish to be contacted with this type of test result, you must give the study clinician or nurse any change to your address and/or phone number. If you want your regular doctor to be told about this type of test result, you must provide the study clinician or nurse with your regular doctor's name, address and phone number. Your samples will not be sold or used directly to produce products that can be sold for profit. Research studies using your samples will be reviewed by a special committee at the researcher's institution (an Institutional Review Board) whose purpose is to protect you as a research participant.

Your samples will be stored at facilities that are designed to store samples securely. Your samples will be labeled with a unique identifier (such as specimen and test type, date, your subject identification number, and study visit number) and stored at a designated biorepository. The investigators will have sole control over these samples, and only approved researchers will have access to your samples. If your samples are provided to secondary investigators, all subject identifiers will be removed from your samples, and your samples will be made anonymous. Your samples may be stored indefinitely, and the exact time at which your samples will be analyzed has not been determined. An Institutional Review Board will oversee the storage facilities to protect you and other research volunteers from harm. There is no time limit on how long your samples will be stored.

You will receive no direct benefit from the storage of your samples. When tests are done on the stored samples there is a small but possible risk to your privacy. It is possible that if others found out information about you from tests (such as information about your genes) it could cause you problems with your family (having a family member learn about a disease that may be passed on in families or learning who is the biological parent of a child) or problems getting a job or insurance. There is a risk that your stored samples and/or health information may be misused. There are laws against this kind of misuse, but they may not fully protect you. The chance that this will happen is considered small because of the security taken with your samples and information.

Your genetic information is unique to you. Should you consent to have future genetic testing done on your stored samples, there is the risk that someone using your samples may identify you. This risk is very small but may increase with the progress of science. Researchers will inform you of any newly identified risks. In addition, there is a federal law called the Genetic Information Nondiscrimination Act (GINA) that generally makes it illegal for health insurance companies and group health plans to use genetic information in making decisions regarding your eligibility or premiums. GINA also makes it illegal for employers with 15 or more employees to use your genetic information when making decisions regarding hiring, promoting, firing, or setting the terms of employment. This Federal law does not protect you against genetic discrimination by companies that sell life, disability, or long-term care insurance.

To keep your information private, your samples will be labeled with a code that can only be traced back to your research clinic. Your personal information (name, address, phone number) will be protected by the research clinic. When researchers are given your stored samples to study they will not be given your personal information. The results of future tests will not be included in your health records.

You can still enroll in this study if you decide not to have these samples and associated health information stored for future research. If you do not want to have these samples and associated health information stored, then your samples and associated health information will be destroyed. You can withdraw your consent for the storage and future testing of samples 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.

_____ Initial & date — I **do agree** to allow my biological specimens and associated health information obtained during this study to be stored for use in future research studies.

_____ Initial & date — I **do not agree** to allow my biological specimens and associated health information obtained during this study to be stored for use in future research studies.

VOLUNTARY CONSENT: All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form. Any questions which I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668). By signing this form, I consent to participate in this research study and provide my authorization to share my medical records with the research team. A copy of this consent form will be given to me.

_____	_____	_____
Participant's Printed Name	Participant's Signature	Date and Time

CERTIFICATION OF INFORMED CONSENT: I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____	_____
Investigator's Printed Name	Investigator's Signature	Date and Time