HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

CONSENT TO PARTICIPATE IN A RESEARCH STUDY AND RESEARCH SUBJECT HIPAA AUTHORIZATION

Protocol Title:	**A5321, Version 3.0,07/05/2018** Decay of HIV-1 Reservoirs in Participants on Long-Term Antiretroviral Therapy: The ACTG HIV Reservoirs Cohort (AHRC) Study
Principal Investigator:	Pablo Tebas, MD 502 Johnson Pavilion, Philadelphia PA 19104 **(215) 349-8092**
Project Manager:	Eileen Donaghy, MSN, CRNP
24 hr. Emergency Contact:	Immunodeficiency Program Doctor on call (215) 662-6059

Introduction:

You are being asked to take part in this research study because you are infected with HIV (the virus that causes AIDS), because you are taking anti-HIV drugs that have been controlling your infection for at least 1 or 2 years, and because some samples of your blood from years ago are available (through your participation in other studies).This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is: Dr. Pablo Tebas. Before you decide if you want to be a part of this study, we want you to know about the study.

This is a consent form. It gives you information about this study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Why Is This Study Being Done?

This study is being done to try to answer questions about the ways that HIV infection is sometimes well controlled over time. We believe that the following factors may be important:

- viral load (the amount of HIV in your blood),
- CD4 cell count (a measure of your body's ability to fight infection),
- when you started taking anti-HIV drugs (in relation to when you were first infected),
- genetics (features [or traits] that you were born with)
- the amounts of your anti-HIV drugs that are in your blood, hair, or other parts of your body.

How Many People Will Take Part in This Study?

430 people will take part in this study. About 8 people are expected to enroll at the University of Pennsylvania

What Do I Have To Do If I Am In This Study?

If you join this study, you will need to be seen in the clinic about twice a year (about once every 6 months) for up to 7 years. At these clinic visits, you will have a physical exam and some blood and a small sample of your hair will be collected. You will be asked to answer questions about your health and any medications you are or have been taking. You will also be asked questions about your use of alcohol and tobacco. At some point after you join the study, you will be asked whether you are willing to have a spinal tap for the collection of fluid. This is explained later in this document.

If you are currently enrolled in A5354 (A5354/EARLIER [Early ART to Limit Infection and Establishment of Reservoir]), you will be asked to consider also joining A5341s (Longitudinal Reservoir Sampling, A5321 Substudy) and participate in at least one of its reservoir sampling groups. These groups are described in the consent form for that study. You may enroll into A5321 without committing to enroll into A5341s.

You will need to fast (not have anything to eat or drink for 8 hours, except for water and any medications that you need to take) before each visit. The study staff will give you more information about this and will tell you about how long each visit could be. Most visits should take about 1 hour. You will be able to eat and drink as soon as the blood collection part of each visit is finished.

The study staff can answer any questions you have about individual study visits or about the evaluations that will occur or about how long each visit will be. The table below can be used as a quick reference.

Study Schedule

Evaluation or procedure	Screening	Entry	Twice a Year (every 6 months)	Optional Spinal Tap and pre-spinal tap visit	If you leave the study early
Physical exam	√	√	√	√	√
HIV infection confirmed	possible				
Questions about medications, alcohol and tobacco	Medications Only	√	√	Medications Only	√
Blood and hair collected	Blood only	√	√	√	Blood only
Test for syphilis				√	
Special questionnaires and evaluations				√	
Spinal tap				√	
Gender Identity		When you consent to Version 3 of the study			

No more than about 14 tablespoons of blood will be collected from you at any single visit.

At some point after you enter the study, probably within 18 months, you will be asked whether you agree to the following:

- To undergo some neuropsychological tests (or 'neuro tests', for short). These are some exercises that test your memory, coordination, and response time.

AND

- To answer some questions about daily activities. These are questions about what you are able to do for yourself.

AND

- To have some fluid removed from your spine. The procedure for removing the fluid is called a spinal tap or a lumbar puncture (or LP). The fluid that is collected is called cerebrospinal fluid, or CSF.

Neuro tests can help researchers understand more about the effects of HIV and anti-HIV drugs on the brain. Tests of CSF can help researchers understand how much HIV and how much of the anti-HIV drugs you are taking are in the brain. More about the neuro tests and the LP appears under "Neuro Tests, Spinal Tap and CSF Collection" below.

Gender identity: After you consent to Version 3.0 of the study, you will be asked to identify your gender.

If you do not enroll into the A5321study
If you decide not to take part in this study or if you do not meet the eligibility requirements, we will still use some of your information. As part of this screening visit, some demographic (for example, age, sex, race), clinical (for example, disease condition, diagnosis), and laboratory (for example, CD4 cell count, viral load) information is being collected from you so that ACTG researchers may help determine whether there are patterns or common reasons why people do not join a study.

While you are in the study
You will remain on your current anti-HIV drugs. The study will not provide any drugs. You will receive the results of any standard laboratory tests that are done during the study, as soon as they are available.

Use of your samples for this study
The blood that is collected from you during this study will be used for routine safety tests, to measure your CD4 count and HIV viral load, and to measure the amount of anti-HIV drugs in your blood. Once a year, some of the blood may also be used for a hepatitis test (a test for a viral infection of your liver). The results of the routine lab tests, the CD4, HIV viral load, and hepatitis tests will be available to you. Beginning at your second on-study visit, site staff will record the results of any viral load testing that you might have had since your last visit; this testing might have been part of another study or part of your regular care.

Some special testing (related either to your HIV viral load and your immune system) may be done on blood samples that were collected from you and stored before you entered this study; some of these samples may have been collected 1 or more years ago. Similar testing will be done on samples that are collected from you during this study.

At each visit, we will collect a small sample of hair (about 100 strands) by cutting some hair from your head, close to your scalp. We will measure levels of anti-HIV drugs in these small hair samples. Drug levels in hair may give us a better idea of a person's long-term exposure to a drug. Humans naturally lose about 100 hairs from their head every day so this amount of hair removal should not be noticeable. If you have no hair on your head or the hair on your head is too short to cut, the collection will not be made.

Some of your blood and hair that is collected during this study will be stored and used for testing that is required for this study. No one will know just from looking at the labels of your stored samples that they came from you. Results from these tests will not be available.

Some of your blood will be used for genetic testing to look at whether your genetics affect your HIV viral load. Your body, like all living things, is made up of cells. Cells contain deoxyribonucleic acid, also known as "DNA". DNA is like a string of information put together in a certain order. Parts of the string make up "genes". Genes contain instructions on how to make your body work and fight disease. Differences or changes in DNA explain some of the physical differences among people. These differences partly explain why some people get diseases like cancer or diabetes while others do not. Genetic testing looks at the differences in people's DNA. This testing also looks at how differences

affect health and the body's response to disease and treatment. Genes may interact with the environment, which can influence the risk of getting a disease. Results of this testing will not be available to you.

Use of leftover samples

Some of your blood and hair that is left over after all required study testing is done may be stored and used for ACTG-approved HIV-related research. No one will know just from looking at the labels of your stored samples that they came from you. Although researchers will not be given your name or any other personally identifying information about you, some information about your medical condition, your race, ethnicity, gender, and age may be shared. These samples may be held for an indefinite length of time. We cannot ensure that you will be told of the results of the research done on these samples.

Storage of Samples

Your samples will be stored at special facilities that are designed to store samples safely and securely. These storage facilities are designed so that only approved researchers can access the samples. The employees at these storage facilities who will store and track the samples will not have information that directly identifies you. An Institutional Review Board or Ethics Committee (EC) will review the storage facility's procedures that show that they protect the rights of research volunteers. Your DNA samples will be stored with coded identifiers that will keep your identity from being known to researchers who may use your samples.

Neuro Tests, Spinal Tap and Collection of CSF

You will be asked separately about taking neuro tests and about the collection, testing, and storage of your CSF. You do not have to decide about this at the same time that you decide whether you want to join A5321. You will be able to remain in A5321 no matter what your decision about the neuro tests and spinal tap.

If you agree to have neuro tests and a spinal tap, you will have up to two extra study visits. At some point up to 4 weeks before the spinal tap, you will be asked questions about medications that you are taking and some blood will be collected for safety tests and to see if you might have syphilis, a sexually transmitted disease. You will be given the results of the blood tests when they are available. If you test positive for syphilis, you will be referred to your provider for appropriate evaluation and therapy. You may be able to have the spinal tap after you complete any required therapy; the study staff will tell you when you may be eligible again for the spinal tap.

Around the time you have the spinal tap (at the same visit or at a different visit), you will have the neuro tests: you will be asked to do some simple tests to measure your coordination, response time and memory. You will also be asked to answer some questions about daily activities that you can do by yourself or that you might need help with.

If the test results show that it is safe, then you will have the spinal tap. On the day of the spinal tap, you will have a brief physical exam. Then you will be asked to lie down on your side or to sit 'backwards' in a chair (so that you are facing the back of the chair). An area on your lower back will be sterilized with fluid. You will get an injection to numb the skin in the sterilized area. You may feel a burning sensation from the fluid that is injected. When the area is numb, the doctor will insert a thin needle between two of the bones in your spine. A small amount of fluid will be collected through the needle. The entire spinal tap procedure to this point will take about 30 minutes.

After the collection, you may be asked to lie flat for up to 30 minutes to reduce the chance that you will get a headache.

It is possible that after your CSF is evaluated, a re-test for syphilis will be done. You will be told the results of the syphilis test when they are available.

Use of Your CSF Samples for This Study
If you agree to have CSF collected, then the amount of HIV and the amount of anti-HIV drugs in your CSF will be tested.

Why Would The Doctor Take Me Off This Study Early?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician or, the study Sponsor .without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- you stop taking your anti-HIV drugs for more than 21 days
- You have not followed study instructions.
- The Sponsor or the study Principal Investigator, has decided to stop the study.

If you leave the study early, you may be asked to complete one more study visit. The Study Schedule chart on page 2 shows what will happen at this visit.

What Are The Risks Of The Study?

Most of the study procedures (blood collection and physical examination) are the same as you would have when seeing any health care provider.

Having blood drawn may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting, or infection.

You might get a slight cut when the hair sample is being collected.

Risks of Sample Storage

There is a risk that your stored samples 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.

Your genetic information is unique to you. There is a risk in genetic research that someone using your samples may identify you. However, this risk is very small, but may increase with the progress of science. Researchers will inform you of any newly identified risks.

Risks of the spinal tap

Headache, sometimes severe
Back pain, slight
Bruising, soreness at collection site
Dizziness, nausea
Fever
Numbness
Paralysis (extremely rare)

Are There Risks Related To Pregnancy?
There are no study-specific risks to you or your baby if you become pregnant. Your pregnancy will be reported to the Antiretroviral Pregnancy Registry an international database that collects information about pregnancies in women taking anti-HIV drugs. This report will not use your name or other information that could be used to identify you. Your doctor may ask you to stop being in the study if you become pregnant.

Are There Benefits to Taking Part in This Study?
If you take part in this study, there may be no direct benefit to you. Information learned from this study may help others who have HIV.

What Other Choices Do I Have Besides This Study?
This study does not provide any anti-HIV treatment. You may choose not to participate in it. If you are interested in treatment studies, the clinic staff may be able to help you find other options.

What About Confidentiality?
We will do everything we can to protect your privacy but cannot guarantee absolute protection. In addition to the efforts of the study staff to help keep your personal information private, we have gotten a Certificate of Confidentiality from the US Federal Government. This certificate means that researchers cannot be forced to tell people who are not connected with this study, such as the court system, about your participation. Also, no publication of this study will use your name or identify you personally.

People who may review your records include the AIDS Clinical Trials Group (ACTG), Office for Human Research Protections (OHRP), or other local, US or non-US regulatory entities as part of their duties, University of Pennsylvania institutional review board (IRB), National Institutes of Health (NIH), study staff, and study monitors. Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.

Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to yourself or others, we will be required to tell the proper authorities.

Your personal information may be given out if required by law. If you test positive for HIV, by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government. Please note that it is likely that this information has been already reported to the PA Health Department as the HIV test being done for this study is not the first test for you. In addition, if you have Hepatitis B or C, this will also be reported to the health department.

HIPAA AUTHORIZATION
The authorization part of the consent gives more detailed information about how your personal health information may be used and disclosed by the University of Pennsylvania Health System (UPHS), the School of Medicine and the individual Principal Investigator, subject to University of Pennsylvania procedures.

What information about me may be collected, used or shared with others?
The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, email address, dates directly related to you such as date of birth and clinic visits.
- Personal and family medical history
- Current and past medications or therapies
- Information from questionnaires administered in the study and from the other HIV studies in which you have participated.
- Results of tests and procedures you will undergo during this research study and from the other HIV studies in which you have participated.
- Social Security Number, Medical record number

Why is my information being used?
Your information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- evaluate and manage research functions.

Who may use and share information about me?

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need access to your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.)
- Authorized members at the University of Pennsylvania, School of Medicine who coordinate this study and support research operations.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB.

Who, outside the School of Medicine, might receive my information?
As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

- ACTG Data Coordinating Center, Frontier Science Technology Research Foundation (FSTRF): Data for this study will be recorded on case report forms, keyed into a central database and electronically submitted to the Data Coordinating Center. The data will be cleaned and stored at this facility until it is ready to be analyzed.
- Statistical Data Analysis Center (SDAC): Approved data will be downloaded from FSTRF to the statistical data center for the AACTG at the Harvard School of Public Health. Specific study reports will be periodically provided to the study team and data safety review board to monitor if the trial is safe.
- Contract Research Organization (PPD, Inc): Monitors from PPD will visit the AACTG on a quarterly basis to review data and correct mistakes before the data are sent to SDAC for analysis.

Regulatory and safety oversight organizations

- The Office of Human Research Protections
- The Study Monitoring Committee
- National Institutes of Health/Division of AIDS (DAIDS)/National Institute for Allergy and Infectious Disease (NIAID)

IRB APPROVAL FROM: 05/03/2019 TO: 05/02/2020

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name, date of birth or medical record number. Information regarding your health, such as side effects of the study drug you experience will be reported only by code number. All samples collected for analysis will be labeled with your study number, visit number and date of your visit.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my35 personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You must do so in writing to the Principal Investigator at Infectious Disease Division, 502 Johnson Pavilion Philadelphia PA 19104. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

What is an Electronic Medical Record?
An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who

are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What Are the Costs To Me?

There will be no cost to you for study-related visits, physical examinations, laboratory tests or other procedures. You or your insurance company may need to assume the cost of drugs not provided by the study. In some cases, it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

Will I Receive Any Payment?

You will be compensated $50 for each study visit you attend. Compensation for the screening visit will be given as cash; compensation for the remainder of the study visits will be provided on a ClinCard (a debit card). The maximum amount of compensation for the study is $700 (2 visits per year for seven years). If you elect to participate in the spinal tap part of the study, you will be compensated $50 for the pre-visit and $150 for the visit when the spinal tap is done. Compensation for the spinal tap will be on a ClinCard as well. There is no other form of compensation available such as reimbursements for parking, tokens or child care.

Please note that if you receive more than $600.00 compensation in one year for participation in research studies at the University of Pennsylvania, you must provide a Individual Tax Identification number or Social Security Number for tax purposes.

What Happens If I Am Injured Or, If I Become Pregnant, My Baby Is Injured?

If you or your baby is injured as a result of being in this study, you or your baby will be given immediate treatment for your injuries. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There is no program for compensation either through this institution or the NIH. You will not be giving up any of your legal rights by signing this consent form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

What Are My Rights As a Research Subject?

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. Your healthcare provider will treat you the same no matter what you decide.

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, let the study staff know.

What Do I Do If I Have Questions Or Problems?

If you have questions about this study or a research-related injury, please contact the research team listed on page 1 of this consent form.

For questions about your rights as a research subject, contact:

- Director of Regulatory Affairs at the University of Pennsylvania by phoning (215) 898-2614

CONSENT

Optional Components of the study

Allowing your samples to be stored for this use is optional. Please indicate below if you agree to have your blood and hair stored for later use. No matter what you decide, it will not affect your participation in the study.

For blood samples:

_____ (initials) YES, I agree **OR** _____ (initials) NO, I do not agree

For hair samples:

_____ (initials) YES, I agree **OR** _____ (initials) NO, I do not agree

If you decide now that any of your samples can be stored for research to be done at a later date, you may change your mind at any time. If you change your mind, you must contact your study doctor or nurse and let them know that you do not want your samples used for research to be done at a later date. Every effort will then be made to destroy your left-over samples.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information. **Your signature here does not include your decision about having the neuro tests and a spinal tap. To record your decision about participating in these activities, see the next page.**

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date
_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date

IRB APPROVAL FROM: 05/03/2019 TO: 05/02/2020

SIGNATURE PAGE FOR SPINAL TAP FOR ACTG Study A5321

If you have read this consent form (or had it explained to you), all your questions have been answered and you agree to take part in the neuro tests and the spinal tap procedure, please sign your name below.

_____	_____
Participant's Name (print)	Participant's Signature and Date
_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff's Signature and Date

If you agreed to have a spinal tap, then some of your CSF may be stored and used for ACTG-approved HIV-related research. Please indicate below if you agree to have your CSF stored for this research. No matter what you decide, it will not affect your participation in the study. If you agree to have the sample stored and later change your mind, you should let the site staff know. If the sample has not already been used, it will be destroyed.

For CSF samples:

_____ (initials) YES, I agree OR _____ (initials) NO, I do not agree

IRB APPROVAL FROM: 05/03/2019 TO: 05/02/2020