HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

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

Protocol Title:	Imaging and Inflammatory Biomarkers in Anti-Retroviral Neuro-Intensification (SPIRIT)
Principal Investigator:	Dennis Kolson, MD, PhD 280C Clinical Research Building, Philadelphia, PA 19104
Investigator:	Pablo Tebas, MD 502 Johnson Pavilion, Philadelphia PA 19104 **(215) 349-8092**
Lead Study Nurse:	Wayne Wagner, RN, MSW
Research Team:	Mark Bardsley, RN, BSN Yan Jiang, RN, BSN, MSN Aleshia Thomas, RN, BSN Joseph Quinn, RN, BSN Randee Silverman, RN, BSN
24 hr. Emergency Contact:	Immunodeficiency Program Doctor on call (215) 662-6059

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have any questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are participating

in another study called A5324 ("Antiretroviral Intensification, CNS Penetration, and Neurocognitive Impairment"). The primary purpose of this study is to evaluate whether markers in the blood or MRI images show changes when you receive different types of highly active antiretroviral therapy (HAART) for HIV infection. As part of your participation, you will undergo baseline testing and then repeat the same measures in approximately 12 weeks.

WHAT WILL HAPPEN DURING THIS STUDY?

To be eligible for the study:

- you must have a documented history of HIV infection
- you must be enrolled in the ACTG study A5324 ("Antiretroviral Intensification, CNS Penetration, and Neurocognitive Impairment")
- you must be able to have an MRI.

For all participants, to determine your eligibility, you will have a screening evaluation, which includes:

1. Urine pregnancy test (done on the day of the scan and only for females with no documented history of sterilization, menopause, etc.).

2. A urine drug screening test for cocaine, amphetamines, methamphetamine, barbituates, benzodiazepeines, marijuana, opiates, PCP, methadone, and tricyclic antidepressants. A positive result will not necessarily exclude you from the study.

3. The MRI Screening/Safety Form, which asks questions about your feelings about being inside a closed space like the MRI scanner, questions about history of head injuries, and questions about any metal that subjects may have implanted in your body or any metal piercings that cannot be removed. This takes approximately 5 minutes to complete.

4. You will be asked questions about your demographics and other basic information, such as age, race, gender, handedness, years of education, first language, height/weight, date of HIV diagnosis (and date started medications if applicable), as well as information about drug, alcohol, tobacco and caffeine use.

5. You will also be asked to sign a Release of Information form so we can obtain your medical records, including but not limited to medical, hospitalization, HIV, STD, substance use/abuse/dependence and mental health records from your doctors, results from prior blood, diagnostic, imaging and laboratory tests and other information obtained from interviews or questionnaires related to your medical care. We may also review the records of any University of Pennsylvania research study in which you participate. This will allow us to better determine your eligibility, insure and improve your safety, and decrease your burden if the results of tests done in one research study could be used as data for another instead of asking you to unnecessarily repeat a procedure.

6. We will review and document your medical history and records related to any of your HIV/AIDS-related outpatient visits, inpatient hospitalizations, blood/diagnostic/laboratory/imaging tests (such as CD4 count, viral load, nadir CD4 count, duration of infection, thyroid and liver function, creatinine, c-reactive protein, complete blood counts studies, total fasting cholesterol with LDL/HDL and triglycerides, fasting glucose, and glycosylated hemoglobin, STD history, AST, ALT, fibrinogen-4,

GFR, platelets, HCV, IL-6, d-dimer, hsCRP, and any other HIV- or inflammatory-related labs deemed necessary; any abnormal/exclusionary imaging results, etc.), substance use/abuse/dependence, and mental health treatment. Additional information may also be obtained from clinical interviews or questionnaires found in your records related to your medical care. We will also review your research records from other studies (to see if previous results indicate any exclusionary criteria or provide any results that we could use as data for this study so as to not have you repeat procedures and decreasing your burden whenever possible). These records will only be accessed as long as necessary to acquire study data.

If, on the basis of these tests and at the PI's discretion, you are found to be eligible for this study AND if you continue your participation in A5324, you will be asked to complete the following study procedures:

1. Blood draw: We will draw 2, 10 mL tubes of blood from you (approximately 1.5 to 2 tablespoons). This amount of blood will be drawn from you now and when you return for your follow-up visit (see below).

2. MRI -- The MRI scanner is a powerful magnet that uses simple radio waves to take pictures of your brain. There is no pain associated with this procedure. You will be positioned on your back on the scanner bed and made to feel as comfortable as possible. The scanner bed will be moved inside a large tube so that your head and your chest are inside, but you will be able to see out into the room by your feet. During the scan, you will hear loud, rhythmic knocking sounds. Your ears will be covered to keep the noise at a minimum. There is a speaker and a microphone in the scanner so that you can talk to the MRI technician if there is something you need. Once the scan starts, you will need to lie still since moving around will interfere with taking pictures of your brain. You will be able to end the scan at any time if you feel uncomfortable. You may be asked to do a task while in the scanner. The MRI will take approximately 1 hour to complete.

One of the sequences that we will be using for the MRI is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

3. Neuromedical examination -- A doctor will examine the nerves in your face, as well as test your reaction to touch and will test the reflexes in your arms and legs. This will take approximately 10 minutes.

4. We will obtain data from your participation in the A5324 study, including but not limited to the following:

- Date you were randomized to/began taking your neurointensification regimen
- What medications/dosages were part of your neurointensification regimen
- Laboratory results (including serum s100B, sCD14, CD4+, and CD8+ and CSF neopterin, MCP-1 and IP-10) and dates of collection
- Neuropsychological testing dates and scores.

Some of this data may not be available to us for several years after you complete this study, but by signing this consent form, you are allowing us to access that data in the future.

5. We may also review/document your medical history and records including any physical exam reports, laboratory and imaging results.

In approximately 12 weeks after your baseline testing, we will ask you to return for a follow up visit to repeat these same screening and testing procedures again. This will allow us to see if there has been any change in your brain's structure and function over time.

Some of the individual results from tests to be performed during this research study might be of interest to you or your primary care physician. At your request, the researchers will share the medical information gained from this study with you and your referring and/or primary care doctors. If we discover significant abnormal test results or an urgent medical condition that requires treatment, we will notify your primary care physician for your health and safety even if you don't request that we do.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining neuroimaging and laboratory data from you, as well as data from your participation in A5324. We would like to use this data for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding HIV/AIDS, memory, thinking, aging, and various neurodegenerative disorders (i.e., Alzheimer's Disease, HIV-Associated Neurodegenerative Disease, Multiple Sclerosis, other types of dementia, etc.), including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your data you give up any property rights you may have in the data. Your data will be analyzed with data collected in this study, as well as with data collected in other studies.

We will share your neuroimaging, laboratory (including unprocessed blood samples), and A5324 data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These investigators may be at University of Pennsylvania or at other research centers and institutions or industry sponsors of research. We may also share you research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

Your neuroimaging, laboratory (including unprocessed blood samples), and A5324 data will be stored without your name or any other kind of link that would enable us to identify which sample(s) or data are yours, and if we share any of your data with other investigators, the information will be sent by coded ID#. Therefore neuroimaging, neuropsychological, and laboratory data it will be available for use in future research studies indefinitely and cannot be removed.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 10 to 15 people will take part in this study conducted by investigators at the University of Pennsylvania. About 100 people will take part in this study total from several different sites.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 2-2.5 hours. We will then ask you to return and repeat these same procedures in approximately 12 weeks.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

RISKS of MRI

Some things may interfere with Magnetic Resonance Imaging (MRI), and some can be potentially dangerous. You should inform the study doctor if you have any of the following:

- Heart problems
- Pacemaker
- Metal implanted under your skin, such as an insulin pump
- Hearing aid or cochlear implant
- Surgical clips or staples
- Any metal prosthesis. A prosthesis is an artificial body part, like an artificial leg.
- Shrapnel of bullet
- Tattooed eyeliner
- Metal dental items
- Braces
- Pregnancy

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Likely:

Metal in or on the body

The MRI scanner functions like a magnet and any metals in your body can be pulled off by the machine. If you have metal implants (under the skin) such as a pacemaker or metal pins or rods) you may be at risk when you are close to the machine. To minimize this risk, we will ask you a series of questions about metal exposure over the course of your lifetime from work experiences and medical procedures.

Claustrophobia (fear of small spaces)
When you have the MRI you will lie on a small bed and the bed will be inserted inside a large tube. The opening of the tube is narrow, and some people can experience claustrophobia (anxiety or nervousness while inside small spaces) when in the scanner. If you believe that you may experience anxiety or nervousness while inside the scanner you should not participate in this study. If you decide to participate in the study and begin to experience claustrophobia while inside the scanner, we will immediately stop the procedure at your request.

Body Stiffness
You may also experience stiffness from lying still for a long time while in the scanner.

Less Likely: The scanner produces a loud repeating knocking noise during the scan that some people find bothersome. To lessen the noise, you will be given head phones.

Rare:

- Occasionally, some people may experience a short period of dizziness or feel faint after being in the scanner.
- There is a rare possibility that a serious abnormality may be discovered by the technician during the MRI picture of your brain. In this event, you will be referred to your primary care physician for clinical follow up and treatment as appropriate
- Some of the pulse sequences are not FDA approved but there are no additional known risks for using this sequence.
- The greatest risk is a magnetic object flying through the air toward the magnet and hitting you. To reduce this risk we require that all people involved with the study remove all magnetic metal from their clothing and all magnetic metal objects from their pockets. No magnetic metal objects are allowed to be brought into the magnet room at any time except by approved personnel. In addition, once you are in the magnet, the door to the room will be closed so that no one inadvertently walks into the room.

RISKS ASSOCIATED WITH BLOOD DRAW
Likely: Pain at the site of needle insertion.

Rare: Infection at the site.

If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor

if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

If you are a sexually active male it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to the unborn child or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you believe or know that your partner has become pregnant during your participation in this study, please contact the research team member identified at the top of this document as soon as possible

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You will not benefit from being in this study. However, we hope that, in the future, other people might benefit from this study because it may provide valuable data to improve the clinical management of HIV+ patients with thinking and memory problems, but also create a greater understanding of immunological changes affect the central nervous system.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.
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The total amount of compensation for being in the study will be up to $200.00. You will be paid in cash at the conclusion of each visit.

First Visit:
$10 for screening
$90 for MRI, neuromedical testing and blood draw.
Visit 12 weeks later:
$10 for screening
$90 for MRI, neuromedical testing and blood draw.

You will be paid for the portion of the study that you complete.

WHO IS FUNDING THIS STUDY?

The members of the NIH (National Institute of Health) National CTSA (Clinical and Translational Science Awards) Consortium is funding this research study. This means that University of Pennsylvania is receiving payments from NIH/CTSA to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NIH for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. 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 are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this 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.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities.
- The National Institutes of Health (NIH)
- The U.S. Food and Drug Administration
- The Institutional Review Board at Washington University in St. Louis (a committee that oversees the conduct of research involving human participants) and the Washington University Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- University of Pennsylvania Institutional Review Board.
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access 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.).
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- Public health agencies to complete public health reporting requirements
- Your primary care physician if a medical condition that needs urgent attention is discovered.

To help protect your confidentiality, we will keep all information in a locked area. The information you give us will be given a code number. A master list linking the code number and your identity will be

kept separate from the research data. Only the Principal Investigator at each site and people helping him will be able to see the list.

If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

Are there additional protections for my health information?

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 personal health information is collected and used in this study and might also be disclosed?
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
- Results of tests and procedures you will undergo during this research
- Social Security Number, Medical record number

Why is your personal contact and health information being used?
Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?
The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access 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.).

Who, outside of UPHS and the School of Medicine, might receive your personal health 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:

- Washington University in Saint Louis: Data for this study will be recorded on case report forms, keyed into a central database and electronically submitted. The data will be cleaned and stored at this facility until it is ready to be analyzed.
- Contract Research Organization : Monitors will visit the site to review data and correct mistakes before the data are sent to SDAC for analysis.
- Government Agencies: Data from this study will be made available to the Food and Drug Administration and to the National Institutes of Health/Division of AIDS (DAIDS)/National Institute for Allergy and Infectious Disease (NIAID), for them to evaluate the safety and efficacy of the treatments being used in this study.

Regulatory and safety oversight organizations

- The Office of Human Research Protections

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 UPHS and the School of Medicine be able to use or disclose your 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.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because if you have certain medical conditions like seizures, use of illegal drugs, or pregnancy or because in our judgment it would not be safe for you to continue, or because the funding for the research study has ended**.**

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. 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.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Washington University Human Research Protection Office, 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445 or email hrpo@wusm.wustl.edu. General information about being a research participant can be found by clicking "Participants" on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

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

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

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 07/20/17.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that he or she understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)