

**UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT FORM AND HIPAA AUTHORIZATION FORM**

Protocol Title:	LONG TERM FOLLOW-UP OF SUBJECTS EXPOSED TO RETROVIRAL-BASED GENE THERAPY PRODUCTS IN HIV STUDIES	
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Why am I being asked to volunteer?

You are being invited to participate in a research study because you have participated in a research study that requires the researchers to follow your health status for up to 15 years. 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. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this research study is to monitor your health status in accordance with the Food and Drug Administration guidelines. These guidelines require the research team to follow your health status for up to 15 years when subjects have participated research studies that have received cells that have been permanently modified by a gene therapy product (called gene transfer).

You are being asked to participate in this study because the previous study you were enrolled into a study that involved receiving your own cells that were changed using a retroviral vector. A retroviral vector is a virus that can insert genetic material into cells. When retroviral vectors enter a normal cell in the body, the deoxyribonucleic acid (DNA) of the vector inserts itself into the normal DNA in that cell. This process is called DNA integration. Most DNA integration is expected to cause no harm to the cell or to the patient. However, there is a chance that DNA integration might result in abnormal activity of other genes. In most cases, this effect will have no health consequences.

In some cases, abnormal activity of a normal gene may cause an uncontrolled growth of the cell that sometimes results in a cancer. This type of event has occurred in animal studies in which retroviral vector DNA integration appeared to cause cancers in mice and monkeys.

It is important that you know about some cancers that occurred in another gene therapy research study. The study, conducted in France, involved a disease called X-linked Severe Combined Immunodeficiency (SCID). Years after receiving cells that were modified by a retroviral vector, a significant number of the children in this small study developed a leukemia-like malignant disease (cancer). At least one child died from the cancer. A group of experts in this field studied the results from tests performed on these children's blood cells. They concluded that the leukemia-like malignancy was caused by the retroviral vector DNA. However, most of the children with X-linked SCID who have received experimental gene therapy have not been found to have a leukemia-like disease at this time. Although they appear healthy, we still do not know whether they, too, will develop a malignant growth.

We do not know if the retroviral vector used in this protocol might cause a new malignancy. However, you should be aware that the DNA contained in retroviral vectors will integrate into your DNA and that under some circumstances, this has been known to cause malignant (cancerous) growth months to years later. This is why we will follow you in this study for up to 15 years.

How long will I be in the study?

Active participation in this research study may be up to 15 years. The length of time of participation will depend on two things:

1. Length of follow up as outlined in the original study
2. Whether the gene therapy product continues to remain in your body

What am I being asked to do?

It is important that you notify your study team of any new problems you may be having with your health. You must provide your current address, email, and telephone number to the study doctor and must update this information throughout the research study so that he or his research staff will be able to contact you to give you any new information. It will be very important for you to keep follow up visits with the study doctor. You will be informed of all clinical test results and whether the gene therapy product is still in your body as they become available.

In addition, a letter will be sent to you and your doctor (primary care doctor, doctor treating your HIV) to inform your doctor that you have participated in a gene therapy protocol. This letter will request that you or your physician inform the study team if you have been diagnosed with any of the following:

1. Any type of cancer, including blood disorders such as leukemia or lymphoma.

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2. You develop loss of feeling in any part of your body, especially hands and feet; you develop a loss of control of any body part (arms, legs...); you have a seizure; you experience memory loss. In addition, if you experience a worsening of any of the symptoms listed, please contact your study nurse or doctor. These types of symptoms are called neurological disorders. If your primary doctor or specialist tells you that you have developed neurological symptoms, contact your study doctor or nurse.

3. You develop arthritis or autoimmune disease, or worsening of any previously experienced arthritis or autoimmune disease which you were experiencing prior to participation in the study. If you are experiencing symptoms of arthritis or have been told by your doctor that you have an autoimmune disease, contact your study doctor or nurse.

Below is a table that will summarize visits for the first 5 years. All visit time points refer to months after the last T cell infusion and the first visit will occur after participation in the T cell infusion protocol has completed.

Visit	That will be done at each visit
3 months	<ul style="list-style-type: none"> • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body. This visit is only for subjects who enroll into this LTFU study less than 3 months after receiving T cells.
6 months	<ul style="list-style-type: none"> • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body. This visit is only for subjects who enroll into this LTFU study less than 6 months after receiving T cells.
9 months	<ul style="list-style-type: none"> • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body. This visit is only for subjects who enroll into this LTFU study less than 9 months after receiving T cells.
12 month visit	<ul style="list-style-type: none"> • Medical history, Physical exam, list of medications • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.
1.5 years	<ul style="list-style-type: none"> • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.
2 year	<ul style="list-style-type: none"> • Medical history, Physical exam, list of medications • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.
2.5 years	<ul style="list-style-type: none"> • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.
3 years	<ul style="list-style-type: none"> • Medical history, Physical exam, list of medications • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.
3.5 years	<ul style="list-style-type: none"> • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.

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Visit	That will be done at each visit
4 years	<ul style="list-style-type: none"> • Medical history, Physical exam, list of medications • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.
4.5 years	<ul style="list-style-type: none"> • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.
5 years	<ul style="list-style-type: none"> • Medical history, Physical exam, list of medications • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the study drug is in your body.

If there is no sign of gene therapy products at the 5 year visit, you will be contacted annually for up to 15 years after your first infusion of the gene therapy product. Contact may occur by mail, phone, email or through your physician. At each contact, you will be asked to complete a short survey regarding your health.

If the gene therapy product continues to be detected in your body, then you will continue to come in to see the study doctor and have blood drawn once a year for a maximum of 15 years. Once there is no gene therapy product detected in your blood, you will be contacted by the study team once a year. The study team may “bank” (store) some of your blood samples throughout your participation in this study. These samples will be kept frozen and will not identify you by name. The blood samples will only be used by the study team to go back and do testing on your blood if an unexpected event occurs.

Below is a table that will summarize visits for the next 10 years.

Visit	That will be done at each visit
Yearly visits years 6-15 when gene therapy product is found in your blood	<ul style="list-style-type: none"> • Medical history, Physical exam, list of medications • Blood Tests (2 tablespoons): to evaluate your health status and to determine if the gene therapy product is in your body. • Yearly visits until there is no gene therapy product found in your blood.
Yearly contact for years 6-15 once there is no gene therapy product found in your blood	<ul style="list-style-type: none"> • You will be contacted annually for up to 15 years after your first infusion of the gene therapy product. • Contact may occur by mail, phone, email or through your physician. At each contact, you will be asked to complete a short survey regarding your health.

Additional Blood Collection: In the event something unexpected occurs to you during your participation in the protocol, the research team may request an additional blood draw be performed to collect additional blood samples for research analysis. This is being done with the intention of evaluating the likely effects from the investigational product you have received. The total amount of extra blood that will be collected from you will be 3 tablespoons of blood (not to exceed a maximum blood draw of 3 tablespoons total in an 8 week period). The

potential risks from drawing this extra blood is unchanged from the risks listed below in “risks associated with blood draws”.

What are the possible risks or discomforts?

Below are the possible risks associated with participation in this long term follow up study:

Risks associated with blood draws: Drawing blood involves a small puncture in your skin. Risks associated with this procedure are minimal, but blood drawing may cause bruising, pain, or infection at the site. Rarely, inflammation or irritation of the vein may occur (also known as phlebitis).

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You are not expected to get any benefit from being in this research study.

What other choices do I have if I do not participate?

The alternative is to not participate in the research

Will I be paid for being in this study?

You may receive a total of \$250.00 for completing visits up to year 5 and \$250 for completing visits from year 6 to year 15 required to come in for these time points. The study payments are to reimburse you partially for your time and effort. Please note that if you receive more than \$600.00 in compensation in one year for participation in research studies at the University of Pennsylvania, you must report this as income to the federal government for tax purposes. The payment schedule is as follows:

1. After 6 month visit:	\$ 25
2. After 12 month visit:	\$ 25
3. After 1.5 year visit:	\$ 25
4. After 2 year visit:	\$ 25
5. After 2.5 year visit:	\$ 25
6. After 3 year visit:	\$ 25
7. After 3.5 year visit	\$ 25
8. After 4 year visit	\$ 25
9. After 4.5 year visit	\$ 25
10. After 5 year visit:	\$ 25
11. After 6-15 year visit:	<u>\$250</u>
Total compensation for the trial:	\$500

Will I have to pay for anything?

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay.

What happens if I am injured or hurt during the study?

If you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event that you are hurt or injured as a result of participation in this research study, please contact the investigator listed on page one of this form.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise offered from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

When is the study over? Can I leave the study before it ends?

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, the study Sponsor, or the Food and Drug Administration (FDA) 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 have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. If this study is

being overseen by the Food and Drug Administration (FDA), they may review your research records.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

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.

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.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

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 information about me may be collected, used or shared with others?

- Name, address, telephone number, date of birth, email address
- Information from a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- Results of tests and procedures you will undergo during this research study as described in the informed consent form
- Personal and family medical history
- Current and past medications or therapies
- Prior or current medical information from any hospitalization, physician, radiology, laboratory results and any other facility you have been to that would aid in obtaining an accurate medical history, medical status while participating in this study.

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right.

Who may use and share information about me?

- *The investigator for the study and the study team*
- *Other authorized personnel at Penn (e.g., committees charged with overseeing research on human subjects)*

Who, outside of the School of Medicine, might receive my information?

- *Oversight organizations*
The Food and Drug Administration
The Office of Human Research Protections
The study data and safety monitoring board
- *Company Collaborators*
VIRxSYS Corporation
Adaptimmune Ltd.
- *Subject's HIV doctor, Oncologist or Primary Care Physician.*

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

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 my 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 do this by sending written notice to the investigator 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.

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

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 to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania 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.

Name of Subject *Signature of Subject* *Date*

Name of Person Obtaining Consent *Signature of Person Obtaining Consent* *Date*

About Using Blood and Tissue for Research

The storage of blood and tissue for future research is optional. In addition to the study and the analysis of blood and tissue outlined above, researchers are also interested in using blood and any excess tissue/fluid specimens (tissue or fluid specimens collected during a clinical procedure that would normally be discarded) that may be obtained from you during the study for other investigations. These research tests may be developed during the time you are on study or, in some cases, years later. We ask that you give approval for these tests to be performed using these specimens. Because it is not possible for you or the researchers conducting this study to know what will be discovered in the future and what additional tests may be appropriate at that time, we ask that you give your permission for such studies without being contacted for permission for each test. These tests may provide additional information that will be helpful in understanding your disease or response to treatment, but it is unlikely that what we learn from these studies will have a direct benefit for you. These studies may benefit subjects in the future.

In addition, blood/tissue/fluid obtained from you may be used to establish products that could be patented or licensed. There are no plans to provide financial compensation to you should this occur. These tests will not involve the study of cancer genes that can be inherited. If studies of genes that might cause cancer are proposed, and you give permission to be contacted, we would contact you and ask for your permission to conduct such tests at that time.

You have the right to withdraw your sample from further use by contacting Dr. Pablo Tebas at (215) 215-349-8901.

Samples will be stored indefinitely. Researchers involved in this study at the Abramson Cancer Center and the University of Pennsylvania will have access to the specimens. These specimens may be used to conduct pilot (new) studies regarding your disease or regarding your response to the kind of treatment you received. Samples may be sent to other researchers for collaborative studies, including researchers at for-profit agencies. However, prior to shipment, all subject identifiers (i.e. initials, medical record numbers) will be removed.

Subjects will not be given results of these pilot studies. Study data from banked blood/tissue/fluid will not be placed in the subject's medical record.

You agree that your blood/tissue/fluid may be kept for use in research to learn about, prevent, treat, or cure cancer or other diseases.

Check	Initial	
<input type="checkbox"/>		I AGREE to my blood/tissue/fluid being kept for use in research to learn about, prevent, treat, or cure cancer or other diseases.
<input type="checkbox"/>		I DO NOT AGREE to my blood /tissue/fluid being kept for use in research to learn about, prevent, treat, or cure cancer or other diseases.

Name of Subject

Signature of Subject

Date

Name of Person Obtaining Consent

Signature of Person Obtaining Consent

Date