UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A Pilot Study for Collection of Anti-Zika Immune Plasma

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

Your contacts for this study at the Hospital of the University of Pennsylvania [HUP] are:

Principal Investigator:	Pablo Tebas, MD	(215) 349-8092
Coordinator:	Eileen Donaghy, MSN, CRNP	(215) 349-8092
Research Coordinator:	Soe Yu Naing	(215) 349-8092

24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

Introduction:

You are being asked to take part in this research study because you have participated in the Zika phase 1 trial study in which investigational vaccines targeting the ZIKA virus were administered to you. This vaccination prompts the immune system to make antibodies specific to the ZIKA virus. This current protocol will collect these antibodies from your plasma through an apheresis procedure. The doctor in charge of this study at this site is Pablo Tebas, MD. 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?

The Zika virus causes an acute, mostly mild illness characterized by fever, rash, joint pain and conjunctivitis. Symptoms can last for several days to a week. Many people are completely asymptomatic during the infection. Zika infection during pregnancy has been associated with birth defects, the most serious of which is microcephaly. Infection with Zika virus has also been associated with Guillen-Barre syndrome..

Our goal is to develop a possible new treatment for Zika which uses antibodies against the virus. Antibodies are natural proteins made by the body that attack influenza and other germs. These antibodies are found in plasma, the yellow clear part of the blood. The main goal of this study is to collect antibodies from participants that previously participated in the Phase 1 Zika vaccine study.

If we find out that you have high amounts of antibodies to the Zika virus, we would like to collect these antibodies by a procedure called apheresis. Apheresis is a type of blood donation, where we just collect the proteins and antibodies from your blood by separating out the blood cells from the liquid part of your blood called plasma. Volunteers in this protocol are asked to undergo 1 or 2 sessions of apheresis. Each session must be at least 7 days apart. We will use your plasma to do research studies that will explore if the use of antibodies is a potential strategy in treating Zika patients or prevention of the infection. This might include using your plasma in animal studies of Zika infection.

How Many People Will Take Part in This Study?

12 people are eligible to participate in this study at the University of Pennsylvania.

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

Screening Visit #1

If you agree to join this study, you will be asked to sign this consent form. After you have signed this form, you will be asked some questions and will undergo some tests at the first screening visit to see if you can take part in this study. The screening visit will take about 30-45 minutes.

At the screening visit, we will go over with you the criteria to take part in this study.

- We will ask you about your health and any medicines you are taking.
- You will have a complete physical examination where the site staff will check your vital signs such as weight, height, temperature, blood pressure, breathing, and pulse.
- We will take about 4 tablespoons of blood for routine safety blood tests and for your blood counts, chemistries, protein levels and overall antibody levels. We may also test for HIV, HTLV (diseases in the blood), hepatitis (B and C), and syphilis (a sexually transmitted disease).
- If you are female, we will take a urine sample for a pregnancy test.

As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will not be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report newly diagnosed HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.

After your visit, the blood work will tell us if you are able to have apheresis (if you meet the standard criteria for blood donation).

If you are not qualified to participate in the apheresis, we will call you and tell you the reason why. In this case, this will be the end of your participation in this study.

If you qualify to have apheresis, we will talk to you about scheduling these procedures. Apheresis is a type of blood donation. The apheresis procedure involves sticking a needle in your arm, withdrawing blood, and separating the blood cells from the antibodies and protein. We will collect the antibodies and protein, and return your blood cells into your vein. The procedure is common in blood banks, and the procedure in this study is identical to those performed in blood banks to collect plasma. For this study, we plan to collect 250-300 ml plasma per collection

On-study evaluations

As part of this study, you will participate in 1 or 2 apheresis sessions. There must be at least 7 days between sessions. The apheresis procedure will take about 60 minutes.

When you go for apheresis, a donor-screen interview will occur before the first procedure and a donor questionnaire will be completed before each of the procedures afterwards. You will have a brief physical exam, an assessment to check that you do not have an infection and a fingerstick hemoglobin test. If you are female, we will perform a urine pregnancy test. The test must be negative to proceed with the apheresis procedure.

When you are finished with the procedure, we may test your plasma for a number of infectious diseases that can be transmitted (passed to others) through blood, including HIV, hepatitis B, hepatitis C, and syphilis. All of these can be transmitted in blood. If you test positive for the above reportable infectious diseases for which testing will be performed specifically for research, by law we have to report the positive test results to the City of Philadelphia Health Department and/or the PA

Department of Health. Personal identifiers such as name, sex, date of birth, address, and phone number will be reported. For more information about the requirements reporting infectious diseases to the City of Philadelphia Health Department, please visit https://hip.phila.gov/ReportDisease. For more information about the requirements reporting infectious diseases to the PA Health Department, please visit: http://www.health.pa.gov/Your-Department-ofHealth/Offices%20and%20Bureaus/epidemiology/Pages/Reportable-Diseases.aspx#.V620aZ3D9eU.

You may be contacted by the local or state health department if you have a confirmed syphilis diagnosis.
Protein levels will be measured at each donation if plasma donations are more frequent than every 28 days.

We will contact you within 3 days of your apheresis to make sure you did not have any problems from the procedure.

If you have a high antibody titer from your first collection, we will invite you to have a second plasma apheresis. It is up to you if you want to undergo another collection.

Stored Samples and Future Research
Some of the blood and plasma that we collect may be stored for future research. This plasma will be used for additional research laboratory testing only. We will use your plasma to study how your body's immune system has responded to the Zika vaccine. No genetic testing will be done.

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, 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.

What Are The Risks Of The Study?

Risk of Blood Draw
You may feel some pain at the needle entry site. There is a slight risk of bleeding around the site. This is not dangerous, but it could result in a bruise. Some people feel lightheaded or dizzy after having blood drawn. To reduce the risk of injury because of a fall, you will be closely monitored and asked about these symptoms before you are allowed to stand up. There is also the possibility of infection at the site where the needle went in, but this rarely happens.

Risk of Apheresis
Apheresis involves the same risks as donating blood, including pain and bruising at the needle site, developing an upset stomach, throwing up, having chills, feeling lightheaded, and fainting. People undergoing apheresis sometimes have mild symptoms of low blood calcium, which is caused by the

chemical (citrate) used to prevent the blood from clotting. These symptoms may include tingling around the lips and fingers and mild trembling or muscle cramping in the hands. The symptoms can be treated by slowing down the speed of the apheresis and by eating calcium-containing antacid tablets or drinking milk. Allergic reactions, including eye tearing, coughing, sneezing, itching, flushing, difficulty breathing, and hives may occur during apheresis and are caused by the chemicals used to sterilize the plastic collection kits. If you experience these symptoms, the apheresis staff will give antihistamines (a drug to reduce allergic reactions) to you. In rare cases of apheresis the device malfunctions, it may not be possible to return the blood in the machine to you, and you could lose as much as 1 pint of blood (or the amount of blood usually given in a routine blood-bank donation). If this happens, we will ask you not to donate any blood products (in our study or at any blood bank) for 2 months. Other rare side effects can include developing an infection at the site where the needle was inserted, increased bleeding tendency, abdominal cramps, difficulty breathing, and chest pain.

There can also be changes in the chemistries in your blood such as the protein level, hemoglobin (red blood cell count), and IgG levels (proteins that fight infection) that may cause postponement (delay or rescheduling at a later time) or removal from the study. In addition, there may be other risks from the procedure or the protocol that we do not know about at this time.

Are There Benefits to Taking Part in This Study?

You will not receive any direct benefit for participating in this study. What we learn from this study may allow us to further develop new treatment for Zika.

What Other Choices Do I Have Besides This Study?

The alternative is not to participate in this study.

What About Confidentiality?

The greatest risk is that someone may take information from your medical records without your permission. The chances of this happening are very low. If this information becomes available, you may face discrimination when you apply for insurance or a job. You may also have similar problems if you share the information yourself or let us release your medical records.

Confidentiality and Labeling of Plasma

We will label your plasma with a code that only the study team can link to you. We will keep any information that can be traced back to you private to the extent permitted by law.

Information about you (such as your name, address, and telephone number) will be kept separate from the results of research tests we perform. Research information will be kept in a password-protected computer file that only the study investigators can view. If we learn anything of importance to our research from this testing, we may publish the results in a medical journal. However, you will not be identified in such an article.

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?

- Name, address, telephone number, email
- Current and past medications or therapies.

address, dates directly related to you such as date of birth and clinic visits, social security number, medical record number.
- Personal and family medical history
- Results of tests and procedures you will undergo during this research study

Why is my information being used?
Your information is important for 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
- to evaluate and manage research functions

Who may use and share information about me?
The following individuals may use or share your information for this research study:
- The Principal Investigator and the Investigator's study team
- Other authorized personnel at Penn, including offices that support research operations.
- Greenphire, as ClinCard will be used to provide compensation for the study.

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 is not a treatment study and no outside agencies will receive your information.

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 vaccine 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 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 repository (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 to do so
- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

Will you be able to access your records?
During your participation in this study, you might not be able to access some or all of your medical records. For example, access to portions of your medical records may be denied in studies where your knowledge of study results included in such records could affect the reliability of the study. You will have access to your medical record information when the study is over or earlier, if possible. The Principal Investigator is not required to release research information to you that is not part of your medical record.

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.

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.

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).

Will I Receive Any Payment?
You will receive payment for the time and inconvenience of participating in this study, and it will be based on the number of clinic visits and apheresis sessions you complete. For completing screening visit you will receive $50. If you qualify for apheresis procedures, you will be compensated $150 for each donation. All compensation will be provided on a ClinCard (a debit card).

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?
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 or the National Institutes of Health 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.

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?

For questions about this study or a research-related injury, contact:

- Pablo Tebas, MD (215-349-8092)
- Clinical Trials Unit (215 349-8092)

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

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.

The purpose, details of each study visit, less than minimal risk procedures, confidentiality, compensation, contact information were discussed with the participant.

Name of Subject (Please Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date

The study drug risks and/or greater than minimal risk procedures, alternatives and benefits of the study were discussed with the participant.

Name of Subject (Please Print)	Signature of Subject	Date

PABLO TEBAS, MD

Name of Physician Obtaining Consent (Please Print)	Signature	Date

IRB APPROVAL FROM: 09/18/2018 TO: 09/17/2018