HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

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

Protocol Title:	**A5320/V-HICS, Version 2.0, 1/29/15; Letter of Amendment 1, 8/26/16; Letter of Amendment 2, 5/28/18**: Viral Hepatitis C Infection Long-term Cohort Study (V-HICS) A DIVISION OF AIDS AIDS CLINICAL TRIALS GROUP (ACTG) 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:

This research study is called V-HICS. You are being asked to take part in this research study:

1. because you are or were infected with the hepatitis C virus (HCV)**;**
2. because you may be coinfected with HIV-1; and
3. because you have taken in the past a direct acting anti-viral (DAA) treatment for HCV infection. A DAA is an agent that disrupts the growth of viruses (that is, HCV/DAA treatment will interfere with the reproduction of HCV in your body).

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?

The study is being done to:

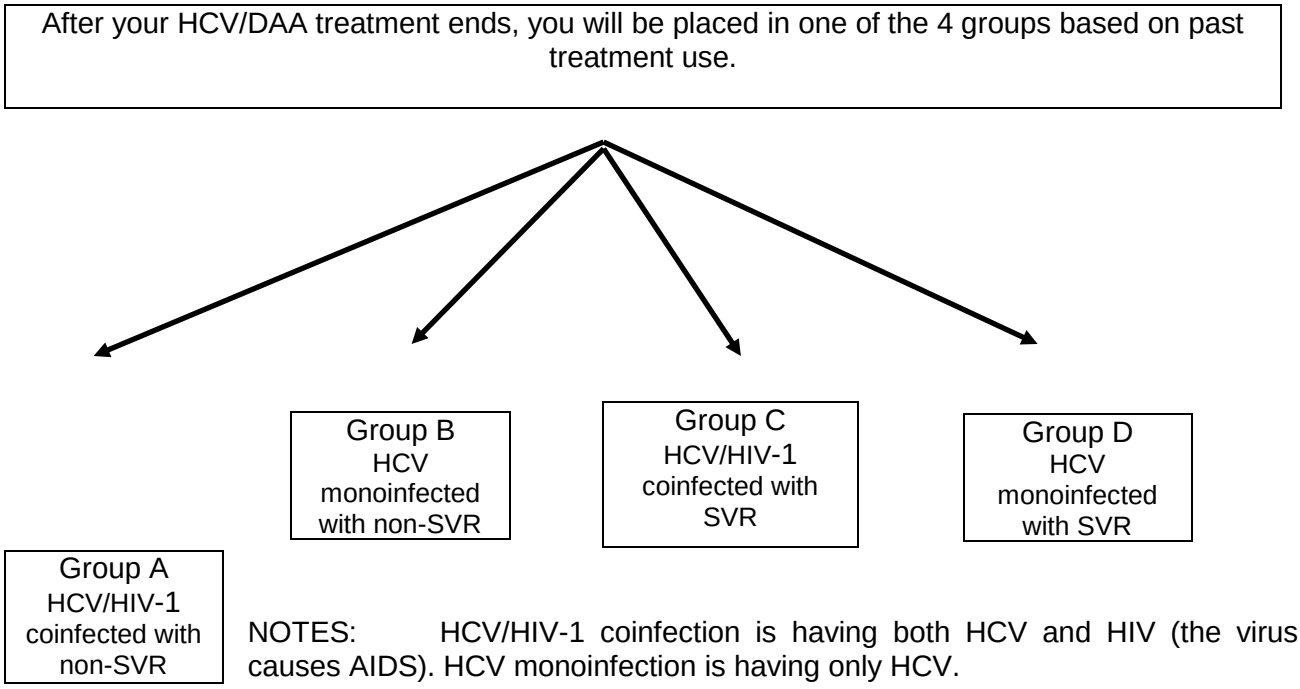
- find out how often HCV drug resistance occurs when the HCV treatment fails. Resistance tests look at the HCV in your blood to see which drugs might work best to lower the levels of the virus in the blood. HIV-1 resistance may also be tested.
- see how long HCV drug resistance remains detectable in your blood after treatment.
- see how successful or unsuccessful HCV/DAA treatment affects your health over 5 years.
- see how having or not having HIV-1 infection affects the impact of HCV infection treatment outcomes on a person's future health.

- see how your own genes and proteins respond to HCV/DAA treatment, either successfully or unsuccessfully.

How Many People Will Take Part in This Study?
About 625 people (men and women age 18 years and older) will take part in this study. About 70 people are expected to enroll at the University of Pennsylvania.

How Long Will I Be In This Study?
You will be in this study for a total of 5 years.

What Do I Have To Do If I Am In This Study?
If you decide to join this study, you will enroll within 1 year after completing an HCV/DAA treatment. NOTE: You may enter V-HICS when you have your HCV/DAA treatment outcome determination (sustained virologic response [SVR] or non-SVR) even if you stopped your HCV/DAA treatment early. You will be placed in one of the groups below. You will not be able to decide which of these groups you are in, but both you and your doctor will know which group you are in.



NOTES: HCV/HIV-1 coinfection is having both HCV and HIV (the virus that causes AIDS). HCV monoinfection is having only HCV.

Non-SVR is still having hepatitis C or having detectable HCV in your blood after treatment.

SVR is having undetectable (very low levels) HCV in your blood (gotten rid of virus, "cured").

You will enter the study and may have clinic visits up to 2 times a year for the next 5 years.

Most visits will last between 30 minutes to 1 hour. Some visits will require you to fast; this means you cannot have anything to eat or drink (except water) for 8 hours before your visit. The study staff will tell you when you need to fast and how you should take any medicines during this time.

I. Study Schedule

During the study, you will receive results from most of the tests (routine safety lab evaluations) that are done. The study staff can answer any questions you have about individual study visits, the evaluations that will occur, or how long each visit will be. The table below can be used as a quick reference for you, along with the explanations that follow.

Evaluation or procedure	Screen[1]	Entry[2]	Post-entry Visits[3]		HCV Re-treatment[4]	Early Discontinuation and Final Visit[5]
			Every 26 wks	Every 52 wks		
Consent	√					
Documentation of HCV and/or HIV treatment	√	√	√	√	√	√
Records of past results	√	√				
Clinical assessments		√		√	√	√
Blood collected	√	√	√	√	√	√
Fibrosis assessment/ Fibroscan		√		√		√
Questionnaire on Quality of Life		√		√		√
Questionnaire on behavioral risk factors				√		√

[1]Screening: After you have read and signed the consent form, you will be asked questions about your health and medications you are taking or have taken in the past to make sure that you qualify to join the study. You may have blood taken for HIV or hepatitis testing if needed to document your eligibility. It is possible that screening and entry can occur on the same day.

[2]Entry: You will have several tests, including blood being taken. You will be asked about your HIV treatment, if you are HIV-1 infected.

[3]Post-entry visits: After entering the study, you will be seen every 6 months through study completion.

At every visit, you will have blood taken for safety blood tests. Also, blood will be taken and stored for HIV and hepatitis tests that are required for this study. The study staff will tell you how long each visit will take. At the yearly visit, you will have a brief physical exam. If you are enrolled in Group C and Group D, you will have a Fibroscan done at entry and at the yearly visits.

[4]HCV Re-treatment Evaluations: If you are re-treated for HCV while on this study, you will be asked to complete a one-time re-treatment evaluation within 30 days of starting the HCV re-treatment. You will continue to be followed in this study as scheduled.

[5]Early Discontinuation and Final Visit: You will be asked to come to the clinic for an extra visit if you leave the study early or you are at the end of the study.

II. Explanation of Evaluations

Consent
After you read the consent form and have had a chance to ask questions about the study, you will be asked to sign the consent form if you want to continue to be evaluated for study participation.

Documentation of HCV and/or HIV treatment
You will be asked about any therapy or drugs you are receiving or have received to treat HCV and/or HIV infection. NOTE: If available, any HCV viral load results obtained outside of V-HICS will be recorded.

Records of past results
You will be asked whether you have documented results of HIV-1 infection, hepatitis B infection, and prior HCV resistance results.

If available, the results from any past liver scans will be obtained and recorded.

Clinical Assessments
You will be asked to report any changes you may have had since the last study visit such as medications/medical treatment, contact information, and co-enrollment in other studies. You will have the following clinical evaluations in this study:

Physical examination
You will have a physical exam. The study staff will check your vital signs such as temperature, blood pressure, and respiratory rate. You will be asked questions about your health and about any medicines you have taken or are taking now. You will also have a targeted physical exam that includes an examination of the head, mouth, neck, chest, abdomen, and lower legs.

Alcohol and substance use and smoking status
You will be asked whether you drink alcohol-containing beverages, use other substances (e.g., recreational drugs), and smoke tobacco-containing products (e.g., cigarettes)

Dialysis status
You will be asked if you are undergoing dialysis treatment for kidney failure.

Blood collection
Blood will be collected from you for various tests during the study. Approximately 5 tablespoons of blood will be collected during any study visit. These may include: routine safety lab tests, HIV-1 antibody testing (a test that looks for HIV antibodies in your blood) if you are HIV-1 negative, CD4 count (a test that shows how many infection-fighting cells you have in your blood), a test for hepatitis B surface antigen (a test that looks for early signs of hepatitis B infection) if you do not have earlier results available, prothrombin time and international normalized ratio (tests that check for bleeding or clotting problems), a test to measure alpha-fetoprotein levels, insulin sensitivity test, and resistance tests. Routine laboratory results will be given to you when they become available.

You will be asked to fast before some of the visits. This means that you should not eat or drink anything except prescription drugs and water for at least 8 hours before the visit.

Resistance testing
Your blood will be tested to check for HCV drug resistance. Your blood may also be checked for the presence of HIV-1 drug resistance. Resistance results may become available after the end of the study.

Genetic testing
Some of your blood will be tested to see whether the 'cure' of the HCV infection or development of resistance to the DAA therapy is associated with different genes related to interferon use. (An interferon is a type of protein that is released by the cells in the body during an infection**.**) You will not receive the results of these studies because they will be done in the future.

Fibrosis Assessment
There are different types of tests that can be done on the liver to check for a build-up of scar tissue such as taking a sample of your liver (a biopsy) and looking at it under a microscope; or by taking special pictures of your liver; or by blood tests. If you have had any of these tests done at any time in the past or as part of routine clinical care, we will use those results in the study. The study will use some of your blood test results for fibrosis testing. At entry and at the yearly visits, a FibroScan will be done on SVR participants (Groups C and D only). A FibroScan is an easy, simple, and safe ultrasound procedure that measures the stiffness of the liver by placing a small probe over the area of the liver while you lie on your back. The scan will be conducted at Presbyterian Medical Center, Infectious Disease clinic at 3910 Powelton Avenue.

Questionnaires
QOL Measure
You will be asked to complete a brief questionnaire on QOL. If you missed a scheduled visit, you may be contacted by the study staff to complete the QOL questionnaire.

HCV Risk Factors Measure
You will be asked to complete a brief questionnaire on risk factors for HCV re-infection. If you missed a scheduled visit, you may be contacted by the study staff to complete the HCV risk factors questionnaire.

If you do not enroll into the study
After signing this consent form, 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 the eligibility visit, some demographic (for example, age, gender, race), clinical (for example, disease condition, diagnosis), and laboratory (if applicable) 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.

Genetic Testing
If you agree, some of your blood will be saved and tested in the future to see how your own genes and proteins respond to HCV/DAA treatment, either successfully or unsuccessfully. You will not receive the results of these studies because they will be done in the future.

Other Testing
If you agree, any leftover blood after all required study testing is done may be stored (with no information that will identify you) and used for future ACTG-approved research. These blood samples may be stored for an unknown period of time. Results of testing done on these samples may not be given to you.

Why Would The Doctor Take Me Off This Study Early?

The study doctor may need to take you off the study early without your permission if:
- The study is stopped or cancelled.
- Your study doctor believes that remaining on the study is no longer what is best for you.
- The team recommends that the study be stopped early.

- The site investigator thinks that you are at significant risk of failing to comply with the requirements of the protocol.

What Are The Risks Of The Study?
Since there is no specific treatment or intervention in this study, no major risk is anticipated. However, taking blood may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting or infection.

Although the study site will make every effort to protect your privacy and confidentiality, it is possible that other people could find out that you are in a study and this could cause problems for you. For example, other people might figure out that you are infected with HIV. If this happens, you could be treated unfairly or you could have problems being accepted by other family members, friends, and/or the community.

Are There Benefits to Taking Part in This Study?
It is possible that being in this study will be of no direct benefit to you. It is possible that your being in this study will provide information that will help others with HCV when the drugs they have been taking stop working for them.

What Other Choices Do I Have Besides This Study?
Laboratory tests to monitor how you are doing and quality medical care may or may not be available to you outside the study. The clinic staff will discuss other choices available to you and the risks and the benefits of all the choices.

What About Confidentiality?
We will do everything we can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have obtained a Certificate of Confidentiality from the U.S. 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, any publication of this study will not use your name or identify you personally.

The following people might review your records: the University of Pennsylvania institutional review board (IRB) a group that makes sure that your rights and safety are protected while in the study, US National Institutes of Health (NIH), Office for Human Research Protections, AIDS Clinical Trials Group (ACTG), study staff, study monitors, and US, local, and international regulatory entities supporting this study. Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.

Your personal information may be given out if required by law. Positive for HIV or Hepatitis C or if a CD4 or viral load is done at a study visit, by law we have to report the result to the City of Philadelphia Health Department/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#.620aZ3D9eU.

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 and 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
- Questionnaires
- Results of tests and procedures you will undergo during this research
- Social Security Number, Medical record number

Why is my 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.

Who may use or share information about me?
The following individuals may use or disclose your personal health 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.
- 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.
- 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 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.

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, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

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.

Will I Receive Any Payment?

You will be compensated $50 for the required 12 study visits (screen, entry, and then twice yearly for 5 years) you attend. In addition, you will be compensated $50 at visits when you have a Fibroscan procedure. Compensation for the screen visit will be given as cash, compensation for all other visits will be given on a Clincard (a debit card). For the routine study visits the total compensation is $600; the total compensation for the Fibroscans will depend on where you are in the study when you sign this consent form. There is no other form of compensation available such as reimbursements for parking, tokens or child care. 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.

What Happens If I Am Injured?

If you are injured as a result of being in this study, you will be given immediate treatment for your injuries. The cost for this treatment will be charged to you or your insurance company. There is no program for compensation either through this institution or the National Institutes of Health. You will not be giving up any of your legal rights by signing this 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

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.

Genetic Testing

On page 5 of this form we told you about using your blood for genetic testing. You may change your mind at any time and your samples will be destroyed. . Please write your initials or make your mark in the box next to the option you choose.

☐ I am willing to have some of my blood stored for genetic testing

OR

☐ I am NOT willing to have my blood stored for genetic testing

Use of Leftover samples

On page 5 of this form we told you about storing your leftover blood (with no information that will identify you) and using it for future ACTG-approved research. These samples may be stored for an indefinite period of time. Results of testing done on these samples may not be given to you because they will be done in the future. Please write your initials or make your mark in the box next to the option you choose.

☐ I allow my leftover samples to be stored and used for other studies related to HIV.

OR

☐ I do not allow my leftover samples to be used in any other studies.

If you decide now that your samples can be stored, 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 leftover samples.

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

IRB Approved: 17-Jul-2018 To: 01-Nov-2018