UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Gilead Sciences, Inc. GS-US-334-0123, Amendment 1, 7-AUG-2012
A Phase 3, Open-label Study to Investigate the Efficacy and Safety of GS-7977 plus Ribavirin in Chronic Genotype 1, 2 and 3 Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) Co-infected Subjects

CONSENT TO PARTICIPATE IN OPTIONAL PHARMACOGENOMIC RESEARCH SUB-STUDY

Your contacts for this study are:

Site address: 502 Johnson Pavilion, Philadelphia, PA 19104

Principal Investigator:	Pablo Tebas, MD	(215) 349-8092
Investigators:	Jay Kostman, MD	
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Manager:	Joseph Quinn, RN, BSN	(215) 349-8092
Study Nurses:	Yan Jiang, RN, BSN	(215) 349-8092

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

You are invited to participate in this optional substudy because you have already agreed to volunteer for a research study, GS-US-334-0123, involving study drug (investigational) GS-7977 with ribavirin for the treatment of chronic Hepatitis C virus (HCV) co-infected with Human Immunodeficiency Virus (HIV). Investigational means this study drug is not approved for the treatment of HCV or HIV.

This consent form details the optional pharmacogenomic (PG) substudy which will be conducted in subjects enrolled in the GS-US-334-0123 study. Additional procedures will be performed on you if you agree to participate in this substudy. By signing this informed consent form and checking the applicable box, you agree to participate in this substudy. This consent form is in addition to the main study consent form for the GS-US-334-0123 study that you have already signed. You must have reviewed and signed the main study consent before you review this consent. This consent is not meant to replace the main study consent, and the contents of the main study consent apply to this substudy.

Your study doctor or study staff will go over this with you and answer any questions you may have regarding this substudy. This consent form may contain words you do not understand. Please ask the study doctor or study staff to explain any words or information you do not clearly understand before agreeing to volunteer for this substudy.

Before you agree to volunteer, you must understand the purpose of this substudy, how your participation may help you, any potential risks to you, and what is expected of you during this substudy. Even if you agree to take part in any of this substudy now, you are free to change your mind and stop at any time without penalty or loss of benefits which you would otherwise have.

If you agree to take part, you will be asked to sign and date this consent form. You will be given a copy of the signed and dated consent form to keep. No one can force you to take part in this substudy and if you agree to participate now, you can change your mind at anytime and still continue in the GS-US-334-0123 study. If you do not agree to participate in this substudy, you can still continue to participate in the GS-US-334-0123 study.

What will happen to your blood sample?
Your sample(s) will be labeled with the same subject number used for identifying all of your other blood samples obtained on this research study. Although your name will not be attached to the sample,

information that characterized you (for example, gender {male or female}, age, height and weight) will be associated with the subject number. The sample will be prepared and stored in a freezer for future genetic testing up to a maximum for 10 years. After 10 years, the sample will be destroyed.

I. PURPOSE OF THE PHARMACOGENOMIC (PG) SUBSTUDY

All subjects already enrolled in GS-US-334-0123 will be asked to take part in PG substudy.

Genetic testing is performed to determine, for example, if a specific genetic make-up or predisposition will predict how responsive an individual might be to a particular treatment, or whether they may have particular side effects from a treatment.

Genes are found in chromosomes, which are in every human cell and store and transmit hereditary information. For example, some genes control the color of a person's hair or eyes. Some genes may increase a person's chances of suffering from a particular disease and may also affect the way an individual responds to a particular drug. Genes are made up of pieces of deoxyribonucleic acid (DNA).

This document will refer to DNA samples and other gene products as "genetic material" and to research on these genetic materials as "genetic testing" or "genetic research".

Genetic testing can be done by testing individual genes, or groups of genes, or all of the body's genes. In this consent form, when genetic testing is described, it includes the possibility that any of these methods might be used, as appropriate for the scientific questions related to HCV and HIV coinfection, treatment response and side effects, that are being asked.

The purpose of this research substudy is to study your whole DNA (genetic testing) to find small pieces of DNA, called genetic markers, that could be related to how well GS-7977 with ribavirin, work to cure HCV infection, or how likely you are to have a particular side effect. In addition, Gilead may test your DNA to try to find a small piece of DNA (genetic markers) that may help predict how your body will fight the HCV infection and how the HCV infection will attack your body over time. This is separate from the genetic sample for IL28 testing that was explained to you in the informed consent form for the main study.

PROCEDURES

I. <u>Pharmacogenomic Substudy</u>

A single blood sample will be collected at the Baseline/Day 1 visit or at any visit afterwards. You will have an extra 6 mL (approximately 1 teaspoon) of blood collected.

RISKS AND BENEFITS

Please refer to the Risks and Benefits section in the main consent form for the complete risks and benefits associated with this study. Since you will be giving a large amount of blood, if you participate in the optional PG substudy the risks associated with blood draws are listed below.

<u>Blood Draws</u>

In addition to risks associated with the study drug(s), drawing blood from a vein may cause local pain, bruising, occasional lightheadedness, fainting, and very rarely, infection at the site of the blood draw. You will have an additional 6 mL (about 1 teaspoon) of blood drawn for the optional PG substudy.

Possible Benefits of the Substudy

You will not receive personal benefit from participating in this substudy. However, clinical research studies such as this are a way for doctors to determine if a drug is useful in fighting a disease. By participating in this substudy, you and the Sponsor, Gilead Sciences, Inc. may benefit if GS-7977 with ribavirin is effective in treating Hepatitis C and HIV coinfection**.** Your participation in this study may benefit the community, scientists and doctors who work with Hepatitis C and HIV coinfection by providing increased knowledge and information about the treatment of your disease. In addition, during your participation you will have close medical monitoring of your health condition by blood tests and other evaluations during clinic visits.

WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE

If you withdraw from the study or if you revoke your authorization for the collection and use of information about you, your participation in the study will end, and the study personnel will stop collecting information from you. The Sponsor will need to keep and use any research results, and may need to keep and use any samples, that have already been collected. The Sponsor must do this to comply with its legal obligations and to maintain the scientific integrity of the study.

COMMERCIAL ISSUES

Pablo Tebas, MD receives compensation from the sponsor, Gilead Sciences, Inc., for enrolling patients in this research study. You should also know that Gilead Sciences, Inc. and other researchers who study your genetic and medical information have an economic interest in developing new drugs and medical tests. The results of this genetic research may lead to a commercial product for the diagnosis, cure, mitigation, treatment, or prevention of disease. You understand and agree that by signing this consent form you are releasing to Gilead Sciences, Inc., your blood sample, by-products of the sample, and any products developed from the sample. Gilead Sciences, Inc. or other researchers or research companies may patent or sell discoveries that result from this research. Neither Gilead Sciences, Inc. nor the Study Doctor(s) will compensate you if this happens.

COMPENSATION FOR STUDY-RELATED INJURY

If you become sick or injured as a direct result of taking the study drug and/or following the study procedures, the University of Pennsylvania will provide you with medical treatment. The Sponsor, Gilead Sciences, Inc., will reimburse you or the University of Pennsylvania for the reasonable and necessary costs of such medical treatment. No other form of reimbursement for study-related injury or illness is offered by the Sponsor. You do not give up any legal rights by signing this form. You should immediately contact your Study Doctor at the contact information shown below in the event you experience any study-related illness or injury.

If you receive Medicare benefits, the Sponsor, Gilead Sciences, Inc., is required by law to report payments made to you for treatment, complications, and injuries that arise from this Study. Information that you are taking part in the Study, medical treatments received, Medicare claims, and other personal information about you such as your name, social security number, and date of birth, will be provided to the Centers of Medicare and Medicaid Services and its agents and/or contractors for this purpose.

STATEMENT OF PRIVACY

Records identifying you will be kept confidential and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available. In the event of any publication regarding the substudy, your identity will remain confidential.

Representatives from government agencies, including the U.S. Food and Drug Administration ("FDA"), institutional review boards, the Sponsor and/or the Sponsor's authorized representatives may need access to your original medical records and substudy records for the purpose of checking data collected for the substudy. By signing this consent form, you authorize this access.

Your coded substudy information and samples may also be used for additional unanticipated medical and/or scientific research projects in the future relating to HCV and HIV coinfection or the development of the study drug (but at all times in compliance with applicable law and regulation).

During the substudy, your Study Doctor, nurses and other study staff will record information about you, your health and your participation in the substudy on forms provided by the Sponsor. These forms are known as case report forms. You will not be able to participate in the substudy if you do not consent to the collection of this information about you.

The information collected about you, will be held by study staff, the Sponsor and the Sponsor's authorized representatives. To ensure that your personal information is kept confidential, your name and any other information that allows you to be identified directly will not be entered on the case report forms or included in any records or samples your doctor provides to the Sponsor or the Sponsor's authorized representatives. Instead, you will only be identified by your initials and a code. The code is used so that your doctor can identify you if necessary.

The Sponsor and its authorized representatives will analyze and use the coded information they receive for the purposes of the substudy. Such purposes include:

- checking your suitability to take part in the substudy,
- monitoring your treatment with the study drug,
- comparing and pooling your treatment results with those of other subjects in clinical studies,
- establishing whether the study drug meets the appropriate standards of safety set by the authorities,
- establishing whether the study drug is effective,
- supporting the development of the study drug,
- supporting the licensing application for regulatory approval of the study drug anywhere in the world,
- supporting the marketing, distribution, sale and use of the study drug anywhere in the world, and/or
- as otherwise required or authorized by law.

If necessary for these purposes, the Sponsor may share your information with its affiliates, people and companies with whom the Sponsor works, and regulatory or other governmental agencies. Although efforts will be made to protect your privacy, absolute confidentiality of your records cannot be guaranteed. Your medical information and records may be re-disclosed and no longer protected by federal privacy law.

As explained in this consent form, your participation in this substudy is voluntary and you may withdraw from the substudy at any time by informing your Study Doctor. By signing this consent, you authorize the collection and use of information about you as described in this consent. You may revoke (take back) this authorization for the collection and use of information about you by informing your Study Doctor in writing. If you withdraw from the substudy or if you revoke your authorization for the collection and use of information about you, your participation in the substudy will end and the substudy personnel will stop collecting information from you. The Sponsor will need to keep and use any research results, and may need to keep and use any samples, that have already been collected. The Sponsor must do this to comply with its legal obligations and to maintain the scientific integrity of the substudy. Your decision to withdraw from the substudy or to revoke your authorization for the collection and use of information about you will not result in any penalty or loss of access to treatment or other benefits to which you are entitled. This authorization has no expiration date, unless and until you revoke it.

There is risk associated with the loss of privacy or confidentiality. For example, if your identity as a participant in this genetic research substudy or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your genetic information.

This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that the sponsor will get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that the sponsor will get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans and all employers with 15 or more people must follow this law.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance or long-term care insurance.

A recent federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The loaw does not include other types of misuse by life insurance or longterm care insurance. If you want to learn more about the GINA law, you can find information about it on the internet or ask the study staff.

If you have any questions about the collection and use of information about you, you should ask your study doctor.

WHO CAN I CALL WITH QUESTIONS, COMPLAINTS OR IF I'M CONCERNED ABOUT MY RIGHTS AS A

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

GS 334-0123: **PHARMACOGENOMIC RESEARCH SUB-STUDY**

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.

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.

This consent form contains important information to help you decide if you want to be in this substudy. If you have questions that are not answered in this form, please ask one of the study staff.

Please indicate your willingness to participate in the substudy by initialing the yes (will participate) or no (will not participate) columns. Please date each time you enter your initials.

	YES	**NO**	**DATE**
I agree to participate in the **Pharmacogenomic (PG)** substudy.			

CONSENT STATEMENT

I have read this consent form and its contents were explained. I agree to be in this research substudy for the purposes listed above. All of my questions have been answered. I will receive a signed and dated copy of this consent form for my records.

I am not giving up any of my legal rights by signing this form. Nothing in this form is intended to change applicable Federal, State, or local laws.

_____ ____/____/____

Signature of Research Subject Date

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UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

GS 334-0123: **PHARMACOGENOMIC RESEARCH SUB-STUDY**

Printed Name of Research Subject

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the subject the nature and purpose of this consent form. There has been an opportunity for the subject to ask questions about this consent form. I have been available to answer any questions that the subject has about this consent form.

_____ ____/____/____
Signature of Person Explaining Consent Date

_____
Printed Name of Person Explaining Consent