Barts Health NHS
NHS Trust

PARTICIPANT INFORMATION SHEET – MAIN STUDY

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Study Sponsor:	Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404, USA
Protocol Title:	A Phase 3, Global, Multicenter, Randomized, Open-Label Study to Investigate the Safety and Efficacy of Sofosbuvir/Velpatasvir/ GS9857 Fixed-Dose Combination for 8 Weeks Compared to Sofosbuvir/Velpatasvir for 12 Weeks in Direct-Acting Antiviral-Naïve Subjects with Chronic HCV Infection
Protocol Number:	GS-US-367-1172

We would like to invite you to take part in a clinical research study. Before you decide if you want to take part, it is important for you to understand why the research is being done and what it would involve for you. Please take time to read the information in this Participant Information Sheet. Your study doctor or study nurse will go over this form with you and will answer all questions you have about this study. You will be given a copy of this Information Sheet and enough time to discuss with your GP, your family, or other people you choose, before you decide whether you should participate. If you agree to take part, you will be asked to sign and date this form. You will be given a signed and dated copy to keep. No one can force you to take part in this study.

PART 1 explains the purpose of this study and what will happen to you if you take part
PART 2 gives you more detailed information about the conduct of the study

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

PART 1 of the Information Sheet

1. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to compare two experimental medications, named SOF/VEL/GS-9857 FDC (Fixed-Dose Combination) and SOF/VEL FDC for the treatment of chronic hepatitis C virus (HCV) infection**.** An experimental medication is one that is currently being tested and has not been approved for use in the United Kingdom. Experimental medications may be tested in research studies such as this one.

This study will evaluate how effective, safe and tolerable SOF/VEL/GS-9857 is in comparison to SOF/VEL in patients infected with HCV. Information about any side effects that may occur will also be collected. SOF/VEL/GS-9857 FDC is a new combination of three medications (Sofosbuvir, Velpatasvir and GS-9857) that each work in a different way against the Hepatitis C virus. It is hoped that the combination of these three medications that have different actions against the HCV virus will be more effective than current treatments available.

2. WHY AM I BEING INVITED?

You are being invited to participate in this clinical research study because you are suffering from HCV infection. If you agree to take part in this study, you will be one of about 780 participants in this study. The study will take place at about 120 centres located in the United States, Canada, New Zealand, Australia, France, Germany, and the United Kingdom. Your study doctor will ask you to come to the clinic for a screening visit to see if you are able to take part.

3. DO I HAVE TO TAKE PART?

It is up to you to decide to join the study. We will describe the study and go through this Participant Information Sheet. If you agree to take part, we will then ask you to sign the Informed Consent Form below. You are free to withdraw at any time, without giving a reason. Choosing not to participate in the study or leaving the study will not affect the standard of care you receive.

4. WHAT WILL HAPPEN TO ME IF I TAKE PART?

This is a randomised, open-label study. Randomised means that the treatment you take will be chosen by chance, and open-label means you and your study doctor will know what study medication you will be taking.

Screening

You will be asked to attend a screening visit within 28 days of the start of the study treatment period. At this visit, you will have a number of procedures to check whether you are eligible to take part in this study. The table below shows what will happen each time you visit the clinic.

Assignment of Treatment Group

HCV has several different variations; these are called genotype 1, 2, 3, 4, 5, 6 (or indeterminate, which will include those that have genotype 6). Sometimes it is not possible to determine which genotype of HCV a patient has (indeterminate). At the screening visit, you will have a blood sample collected and this will be tested to check the type of HCV infection (variation) you have. The results of this test will determine whether you will be randomised and the treatment you receive as part of the study.

If your screening blood test results indicate that you have HCV genotype 1, 2, 3 or 4, you will be randomised to receive either SOF/VEL/GS-9857 for 8 weeks or SOF/VEL for 12 weeks. Randomised means the study treatment you take will be chosen by chance, like flipping a coin. You will have a 1 in 2 chance to receive SOF/VEL/GS-9857 for 8 weeks and a 1 in 2 chance to receive SOF/VEL for 12 weeks.

If your screening blood test results indicate that you have genotype 5 or indeterminate which will include those that have genotype 6, you will be enrolled to receive SOF/VEL/GS-9857 for 8 weeks.

If your screening lab results indicate that you have HCV genotype 3 and you also have cirrhosis, you will not take part in this study.

Tablets of SOF/VEL/GS-9857 (400/100/100 mg) FDC and SOF/VEL (400/100 mg) will be supplied by Gilead Sciences, Inc., which is also the Sponsor of this study.

How long will I be on the study?

If you are randomised to the group receiving SOF/VEL/GS-9857, your participation in this study will last about 32 weeks, not including the screening period. During this time, you will be required to visit the clinic at least 8 times.

If you are randomised to the group receiving SOF/VEL, your participation in this study will last about 36 weeks, not including the screening period. During this time, you will be required to visit the clinic at least 9 times.

Study Procedures

If you agree to take part in the study, no study-related procedures can start until the Informed Consent Form is signed and dated.

The table below shows what will happen each time you visit the clinic. The procedures or tests are described after the table:

Study Procedures Table for Participants Randomised to SOF/VEL/GS-9857 for 8 Weeks

Procedure (what will happen)	Screening[a] (To see if you qualify)	Day 1	Week 1	Week 2	Week 4	Week 8/ EOT	ET	4 week FU	12 week FU	24 week FU
Informed Consent Process	X									
Review your health history	X									
Physical exam	X	X				X	X			
Height	X									
Weight	X	X				X	X			
Measure your vital signs (blood pressure, heart rate, breathing rate, and temperature)	X	X	X	X	X	X	X	X		
Electrocardiogram (ECG)	X	X	X			X	X			
Imaging test to make sure you don't have HCC (Hepatocellular Carcinoma)	X									
Review changes in your health (adverse events)	X	X	X	X	X	X	X	X		
Review medications you are taking	X	X	X	X	X	X	X	X		
Get study medication		X			X					
Bring back unused study medication and all containers since last visit			X	X	X	X	X			
Take blood samples for routine health tests	X	X	X	X	X	X	X	X		

Procedure (what will happen)	Screening[a] (To see if you qualify)	Day 1	Week 1	Week 2	Week 4	Week 8/ EOT	ET	4 week FU	12 week FU	24 week FU
Take blood samples for coagulation tests (to check the ability of your blood to clot)	X	X				X	X			
Take blood sample for viral infection test	X	X	X	X	X	X	X	X	X	X
Take blood sample for viral resistance test		X	X	X	X	X	X	X	X	X
Take a blood sample for pharmacokinetic test			X	X	X	X	X			
Take blood and/or urine samples for pregnancy test (for women who are able to have children)	X	X			X	X	X	X		
Urinalysis (Urine test for drugs and for general health checks)	X									
Take a blood sample to measure what HCV genotype you have and to test for the IL28B gene that you have	X									
Hepatitis B & C, and HIV Tests (to confirm your diagnosis and rule out all others)	X									

Procedure (what will happen)	Screening[a] (To see if you qualify)	Day 1	Week 1	Week 2	Week 4	Week 8/ EOT	ET	4 week FU	12 week FU	24 week FU
Complete four Health Related Quality of Life questionnaires		X			X	X	X	X	X	X
HbA1c (to measure your blood glucose), Fibrotest® (to measure the degree of liver damage)	X									
Potential Liver biopsy (this may be required to confirm the level of liver damage)	X									
Optional non-study test for future research		X				X	X			
Take a blood sample for Pharmacogenomic testing (optional)		X								
Approximate total amount of blood taken (tablespoons) (this does not include the additional/optional blood samples)	2	2	2	2	2	2	2	1.5	1.5	1.5

a. Screening information from another Gilead Sciences Phase 3 study with SOF/VEL/GS-9857 may be used to determine eligibility and fulfil screening visit assessments for this study.
EOT: End of Treatment, ET: Early Termination, FU: Follow Up

Study Procedures Table for Participants Randomized to SOF/VEL for 12 Weeks

Procedure (what will happen)	Screening[a] (To see if you qualify)	Day 1	Week 1	Week 2	Week 4	Week 8	Week 12/ EOT	ET	4 week FU	12 week FU	24 week FU
Informed Consent Process	X										
Review your health history	X										
Physical exam	X	X					X	X			
Height	X										
Weight	X	X					X	X			
Measure your vital signs (blood pressure, heart rate, breathing rate, and temperature)	X	X	X	X	X	X	X	X	X		
Electrocardiogram (ECG)	X	X	X				X	X			
Imaging test to make sure you don't have HCC (Hepatocellular Carcinoma)	X										
Review changes in your health (adverse events)	X	X	X	X	X	X	X	X	X		
Review medications you are taking	X	X	X	X	X	X	X	X	X		
Get study medication		X			X	X					
Bring back unused study medication and all containers since last visit			X	X	X	X	X	X			

Procedure (what will happen)	Screening[a] (To see if you qualify)	Day 1	Week 1	Week 2	Week 4	Week 8	Week 12/ EOT	ET	4 week FU	12 week FU	24 week FU
Take blood samples for routine health tests	X	X	X	X	X	X	X	X	X		
Take blood samples for coagulation tests (to check the ability of your blood to clot)	X	X					X	X			
Take blood sample for viral infection test	X	X	X	X	X	X	X	X	X	X	X
Take blood sample for viral resistance test		X	X	X	X	X	X	X	X	X	X
Take a blood sample for pharmacokinetic test			X	X	X	X	X	X			
Take blood and/ or urine samples for pregnancy test (for women who are able to have children)	X	X			X	X	X	X	X		
Urinalysis (Urine test for drugs and for general health checks)	X										
Take a blood sample to measure what HCV genotype you have and to test for the IL28B gene that you have	X										

Procedure (what will happen)	Screening[a] (To see if you qualify)	Day 1	Week 1	Week 2	Week 4	Week 8	Week 12/ EOT	ET	4 week FU	12 week FU	24 week FU
Hepatitis C & B, and HIV Tests (to confirm your diagnosis and rule out all others)	X										
Complete four Health Related Quality of Life questionnaires		X			X		X	X	X	X	X
HbA1c (to measure your blood glucose), Fibrotest® (to measure the degree of liver damage)	X										
Potential Liver biopsy (this may be required to confirm the level of liver damage)	X										
Optional non-study test for future research		X					X	X			
Take a blood sample for Pharmacogenomic testing (optional)		X									
Approximate total amount of blood taken (tablespoons) (this does not include the additional/ optional blood samples)	2	2	2	2	2	2	2	2	1.5	1.5	1.5

a. Screening information from another Gilead Sciences Phase 3 study with SOF/VEL/GS-9857 may be used to determine eligibility and fulfil screening visit assessments for this study.

EOT: End of Treatment, ET: Early Termination, FU: Follow Up

Procedure or Test	Description
Electrocardiogram (ECG)	You will lie down and have adhesive patches (similar to Elastoplasts®) placed on your chest, arms, and legs. In some areas, it may be necessary to shave a small spot of body hair so the adhesive patches can be properly placed on your body. Wires from the machine are then attached to the adhesive patches. These wires record your heart's electrical activity. The ECG test will take approximately 5 minutes.
Imaging for Hepatocellular Carcinoma (HCC)	If you have cirrhosis, an Ultrasound scan may need to be done to rule out hepatocellular carcinoma (HCC) which is the most common primary disease of the liver. This will not be required if you have had imaging (e.g. MRI scan, CT scan or ultrasound scan) of your liver in the 6 months prior to the study. You will be asked about any findings if you have another test conducted as part of your standard of care.

Lab Tests and Biologic Sample Collection	Description
Pregnancy test	If you are a woman who can get pregnant, a sample of your blood or urine will be taken to test for pregnancy. To take part in this study, the pregnancy test must be negative.
Routine health test	Samples of your blood will be collected and tested to check your health.
Urine tests	A sample of your urine will be tested for general health checks and also to test whether you have used certain recreational drugs
Potential liver biopsy	Liver biopsy is a common test used to confirm the diagnosis for hepatitis. A liver biopsy may be required to confirm the level of liver cirrhosis (liver damage). This will not be required for all participants
Viral infection test for HCV	Blood samples will be collected to see how much virus is in your blood
Viral infection test for HBV and HIV	Blood samples will be collected to check you do not have Hepatitis B Virus (HBV) or Human Immunodeficiency Virus (HIV).
Viral resistance test (Viral Sequencing/Phenotyping)	Blood samples will be collected to see if there are any mutations that may cause resistance to medications. A small piece of your DNA will be analysed to check your IL28B gene.
Pharmacokinetic test	Samples of your blood will be tested to see how much study medication is in your body.

Optional Pharmacogenomics Test	If you agree, extra blood sample will be collected for future testing. If you do not agree, you can still take part in the main study. More information is below.
Optional non-study test for future research	If you agree, extra blood samples may be collected and archived for future testing. If you do not agree, you can still take part in the main study. More information is below.
Optional non-study test for future research	If you agree, leftover blood samples collected during the study may be used to help answer questions that are not part of the main study. If you do not agree, you can still take part in the main study. More information is below.

Study Medication	**Description**
Get study medication	At the visits marked on the table, you will be given study medication to take home with you. Store your study medication at room temperature (25ºC).
Take study medication	If you are randomised to the group receiving SOF/VEL/ GS-9857, take your study medication one time per day **with food**. If you are randomised to the group receiving SOF/VEL, take your study medication one time per day without regards to food. On the Day 1 visit, your study medication will be administered at the clinic.
Bring back study medication and containers	Bring back all unused study medication and all study medication containers (even if they are empty or used). Your study doctor or study nurse will count how many doses you have taken. Your study doctor or study nurse will ask about any doses you did not take or if you took any extra doses.

Once you have completed the screening evaluations, your study doctor will review the results of these tests to determine if you qualify for this study. If you do not qualify for this study, there may be another Gilead Sciences Phase 3 study with SOF/VEL/GS-9857 that you may be asked to participate in. You would be asked to sign a different consent form for participation in that study.

Study Food/Drink Restrictions
There are no known food and/ or beverages restricted during this study.

5. WHAT WILL I HAVE TO DO?

If you decide to be in this study, there are some rules you must follow. Some of the rules are listed below. There could be other rules that the study doctor will review with you.

- You must not get pregnant or get someone pregnant during this study.
- If you are a woman that can have children and are sexually active, you and your partner must use effective birth control from screening until 30 days following the last dose of study medication. Please see the Pregnancy and Breast-Feeding section below for more information.

- Male participants with female partners of childbearing potential must agree to consistently and correctly use a condom during treatment and until 30 days after the last dose of study medication.
- It is very important that you tell your study doctors all of the information you know about your health and medications you are taking now or start taking while in the study. This includes vitamins, minerals, and medications that do not require a doctor's prescription. Some medications are not allowed. Your study doctor will discuss these with you in detail. If you do not tell the study doctor everything you know, you may be putting your health at risk.
- You are not allowed to take the following medications while in this study. Your study doctor will go through this information with you:

Type of Medications	**Medications Not Allowed**
Antibiotics	Clarithromycin, Erythromycin
Acid Reducing Agents	Proton-Pump Inhibitors
Anticonvulsants	Phenobarbital, Phenytoin, Carbamazepine, Oxcarbazepine
Antimycobacterials	Rifabutin, Rifapentine, Rifampin
Cardiac Medications	Amiodarone, Bosentan, Digoxin, Diltiazem, Dronedarone, Olmesartan, Quinidine, Ranolazine, Telmisartan, Valsartan, Verapamil
Herbal/Natural Supplements	St. John's Wort, Echinacea, Milk thistle (i.e., silymarin), Chinese herb sho-saiko-to (or Xiao-Shai-Hu-Tang)
HMG-CoA Reductase Inhibitors	Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin
Other	Modafinil, Methotrexate, Sulfasalazine

- You must ask your study doctor before you take any new medications during the study.
- If you decide to take part in this study, it is very important that you attend all visits as scheduled, including all of the follow-up visits.
- You should take the study medication exactly as you are told.
- If you are randomised to the group receiving SOF/VEL/GS-9857, you must take every dose of study medication with food.
- If you are randomised to the group receiving SOF/VEL, you must take study medication once daily either with or without food.
- Only you should take the study medication. It must be kept out of the reach of children. Please also keep the study medication away from people who may not be able to read or understand the label.
- You must return all of the used and unused study medication materials (including empty medication bottles).
- You must follow all instructions given to you while you are participating in this study. If you do not, you may no longer be able to take part in the study. If you are unsure about what you are supposed to do, ask the study doctor.
- Some insurance companies require people who are renewing a policy or getting a new policy to tell them about participating in a clinical study. You should check with your insurer to determine if taking part in this study will affect your existing insurance policy.

If you cannot follow these restrictions, you should not be in this study.

6. WHAT WILL HAPPEN TO ANY SAMPLES THAT I GIVE?

Some of your leftover blood taken at the study visits will be frozen and stored for future research. You will be asked to sign a specific consent section at the end of the Informed Consent Form below. You do not have to consent to the collection of these samples for future research in order to take part in the main study. Your stored samples and the information collected about you during the study may be used by the Study Sponsor or its research partners to help answer study questions about the medication or HCV. At the end of this study, these samples may be held in storage by Gilead Sciences, Inc. for up to 10 years. You may request that your stored samples be destroyed at any time by writing to the study doctor at the address listed in this form.

Samples collected as part of the main study and also the sub-studies (including those for future research) will be collected at the study site on the scheduled visits. These samples may be stored for up to 10 years at the central laboratory based in Switzerland.

Viral Infections
Some of your blood drawn at the study visits will be frozen and stored. Your stored samples and the information collected about you during the study may be used by the Study Sponsor or its research partners for additional testing. Additional testing may be to test the amount of HCV in your samples as part of the main study, medication levels in your samples, or medical care laboratory data. No additional human genetic testing will be done without your separate written consent. However, as part of the main study, a blood sample will be collected at the screening visit in order to test your DNA for a specific gene called the IL28B gene; you will not be able to participate in the study if you do not consent to this test.

At the end of this study, these samples may be held in storage by Gilead Sciences, Inc. for up to 10 years. You may request that your stored samples be destroyed at any time by writing to the study doctor at the address listed in this form.

Viral mutation testing finds changes or “mutations” in parts of the virus being studied. Some mutations can prevent certain medications or medication treatments from reducing the amount of HCV in your blood. Some of the blood samples you provide throughout the study may be tested for ‘viral mutations’ to see if the HCV virus you have is becoming resistant to the study medications. Please see section 8 ‘What are the Side Effects of the Study Medication’ for more information under the ‘Viral Resistance’ section.

These tests for mutations may be experimental and may not have been approved in the United Kingdom. The results of these tests are “for research use only”, and the understanding of the test results may not have direct benefit to you.

7. WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?

Blood Samples

Collecting a blood sample from a vein may cause pain, bruising, light-headedness, fainting, and very rarely, infection at the site of the needle stick.

Electrocardiogram (ECG)
After you have an ECG, you may have mild irritation, slight redness, and itching on your skin where the recording patches are attached. You may have your chest shaved for this procedure.

Questionnaires
Some of the questions may seem personal and may make you feel uncomfortable. If you have any questions or concerns while answering these questions, please talk to your study doctor.

Fibroscan®
There are no known risks associated with FibroScan® at this time. FibroScan® uses ultrasound technology to assess the liver. It is a non-invasive procedure that takes only a few minutes to perform. Since this is a new technology, not all doctors' offices will have access to FibroScan® equipment.

Ultrasound
For standard diagnostic ultrasounds there are no known harmful effects on humans.

Liver Biopsy Risks
Liver biopsy is a common test used to confirm the diagnosis for hepatitis. Many doctors also do a liver biopsy to help confirm the extent of liver damage. Risks and complications of liver biopsy may include:

- Pain and discomfort located at or near the puncture site and radiating upwards toward the right shoulder region
- Bleeding at the biopsy site
- Possible internal bleeding for up to a few hours after the procedure
- Infections at the biopsy site or internal organs
- Puncture of internal organs (gall bladder, lung, intestine or kidney)
- Allergic reaction to the anaesthetic

8. WHAT ARE THE SIDE EFFECTS OF THE STUDY MEDICATIONS?

Common Side Effects for SOF/VEL/GS-9857

Safety information about common side effects for the active treatment medication (SOF/VEL/GS-9857) is based on the safety information from three other clinical studies in which SOF/VEL was given together with GS-9857 to over 420 participants with HCV. In these studies, SOF/VEL and GS-9857 were given for 4 to 12 weeks. Most of the side effects were considered to be mild. The most common side effects (≥ 10%) reported were:

- Headache (23%)
- Nausea (17%)
- Fatigue (tiredness) (17%)
- Diarrhoea (15%)

Three participants decided on their own to stop taking the medication SOF/VEL + GS-9857 because of side effects. One participant stopped treatment because of moderate tiredness (fatigue). The second participant stopped treatment because of moderate diarrhoea and moderate vomiting which caused the participant to have mild water loss from the body (dehydration) and moderate feelings of weakness (asthenia). The third participant stopped treatment due to moderate stomach irritation (gastritis).

There were no serious medication-related side effects reported by participants taking SOF/VEL and GS-9857. However, one participant experienced a serious side effect (atrial fibrillation - abnormal heart rhythm) 1 day after completing 3 days of GS-9857 alone.

For people that are lactose intolerant, please note that combined SOF/VEL/GS-9857 tablets contain small amounts (less than 400 milligrams per tablet) of lactose. It is unknown whether this amount of lactose may lead to symptoms of lactose intolerance. For comparison, one cup (about 235 mL) of low-fat milk contains over 30x this amount of lactose.

Common Side Effects for SOF/VEL
Safety information about common side effects for the study medication SOF/VEL is based on the combined safety information from three other Phase 3 clinical studies. In these studies,

1035 participants with HCV took the fixed dose combination of SOF/VEL (400mg/100 mg) for 12 weeks.

Most side effects reported by participant were mild. The most common side effects (≥ 10%) reported were:

- Headache (29%)
- Fatigue (25%)
- Nausea (14%)
- Nasopharyngitis (a cold), or cold symptoms (12%)

Only two of the participants taking SOF/VEL stopped treatment because of side effects in these studies. There were no serious medication-related side effects reported in any of the participants.

It is not expected that you will have any of these side effects. Other side effects may occur that are not listed here or were not seen before. Please speak to your study doctor for more information. Side effects are usually temporary and can often be treated. However, it is very important that you report all side effects to your study doctor as it is possible that side effects may suggest a serious or fatal health problem.

Viral Resistance
Treatment with medications that directly inhibit the hepatitis C virus has been shown to lead to development of hepatitis C virus that is resistant to that medication and other medications with the same type of action. These resistance mutations have been observed in the body as late as 4 to 5 years after treatment has ended. It is unknown whether having these resistance mutations might reduce the chance of treatment success with future medications with the same type of action or with different types of action. It is possible that if you are treated with the medications in this study and treatment doesn't work, you might have resistance mutations that would make future treatment less successful.

Hepatitis B and HIV Testing Risks
As part of the screening procedure you will be tested for Hepatitis B and HIV virus infection. If either test is positive local laws may require that the test results be reported to local health authorities.

Allergic Reaction
Allergic reaction is always possible with a medication you have not taken before. Serious allergic reactions that can be life-threatening may occur. Some things that happen during any allergic reaction to any type of medication are:

- rash
- difficulty breathing
- wheezing when you breathe
- sudden drop in blood pressure
- swelling around the mouth, throat, or eyes
- fast pulse
- sweating

Unknown/Unexpected Risks and Discomforts

There are adverse events that are not known or happen rarely when participants take these study medications. You will be told of any new information that might cause you to change your mind about continuing to take part in this study.

As with any new medication, extra care has to be taken to monitor the side effects that are not always obvious. If you feel any side effects or unusual symptoms, please notify your study doctor as soon as possible at the phone number listed in this form.

9. HARM TO THE UNBORN CHILD

The risks of these medications to an unborn baby or nursing child are unknown and may be hazardous. If you are a woman who is pregnant or intend to become pregnant, you cannot be in this study. You should be aware that on rare occasions in early pregnancy, the pregnancy test may be falsely negative and that a negative test result does not prevent pregnancy. If you think that you have become pregnant during the study or within 30 days of taking the last dose of study medication, you must tell the study doctor immediately. If you do become pregnant during the study, you will be removed from the study and the study doctor will refer you to seek obstetrical care and request to track your pregnancy and report the outcome including that of your infant to the Sponsor and the Ethics Committee. Neither the study Sponsor, <insert study site address>, or its Investigators will be responsible for providing routine medical care relating to your pregnancy.

If you are currently nursing (breastfeeding), you must discontinue nursing before starting study medication. Female participants must also refrain from egg donation and in vitro fertilisation during treatment and until at least 30 days after the last dose of study medication.

You must protect yourself or your partner from becoming pregnant before, during, and after the study. Women, and men with female partners capable of becoming pregnant, must use effective methods of birth control as described below. Your study doctor will need to document what type(s) of birth control you are using. You must also not rely on hormone-containing contraceptives as a form of birth control during this study.

Women only:

Women who can get pregnant should not take study medication unless they and their partner do not engage in intercourse or are using one of the following methods of birth control from screening and for 30 days after last dose of the study medication, or longer as directed by your study doctor.

- Intrauterine device (IUD)
- Tubal sterilisation
- Bilateral tubal occlusion
- Vasectomy in the male partner (provided that the partner is the sole sexual partner and has received medical assessment of the surgical success)
- Female barrier method (diaphragm or cervical cap) with spermicide (where locally available)

A condom must also be used in addition to one of the above methods. Unacceptable birth control methods include periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea method (LAM).

You must tell your study doctor immediately if you become pregnant while in this study and through the follow up period, or for as long as you have been directed by your study doctor to use contraception. The study doctor will tell you about the possible risks to your unborn child and options available to you.

In the event of a positive urine pregnancy result, you will be instructed to stop study medication immediately and return to the study clinic as soon as possible for a serum (blood) pregnancy test. The pregnancy will be followed to its completion and the outcome, including any premature termination, must be reported to the Sponsor. You should be counselled and monitored by your own doctor. As the risk to the unborn baby is unknown, it is recommended you seek medical supervision from your own doctor during the pregnancy and for the baby after it is born. Neither the study Sponsor nor the study doctor will be responsible for providing routine medical care relating to the pregnancy.

Men only:
Male participants with female partners of childbearing potential must agree to consistently and correctly use a condom during treatment and until 30 days after the last dose of study medication. If their female partner is of childbearing potential, their female partner must use 1 of the methods of birth control listed above from the date of screening until 30 days after the last dose of study medication.

Male participants must also not donate sperm during treatment and for at least 30 days after the last dose of study medication.

10. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

You may not benefit from taking part in this study. Studies are a way for doctors to see if a medication is useful in fighting a disease.

Your taking part in this study may help people with HCV understand more about the treatment of your disease. By taking part in this study, your health will be monitored closely at study visits.

11. WHAT ARE THE ALTERNATIVES?

Your study doctor will discuss appropriate treatment options and the risks and benefits with you. You can discuss if you want to have any treatment or if you want to choose another treatment for your disease.

12. EXPENSES AND PAYMENTS

There will be no cost to you for taking part in this study. You will not be paid to take part in this study. You will, however, be reimbursed for any reasonable expenses (parking and travel) related to your study visits. You will need to provide original tickets, receipts or other documents to the study staff in order to receive this reimbursement.

13. WHAT IF THERE IS A PROBLEM?

Any complain about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

14. WILL MY TAKING PART BE KEPT CONFIDENTIAL?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1.

If the information in Part 1 was interesting to you and you are considering your participation, please read the additional information in Part 2 before making a decision.

PART 2 of the Information Sheet

1. WHAT IF NEW INFORMATION BECOMES AVAILABLE?

During the course of this study, important new information may become available which could affect your decision to stay in the study. You will be informed in a timely manner, both verbally and in writing of any new information, findings or changes to the way the research will be done that might influence your willingness to continue to take part in this study. We will also update this Participant Information Sheet and Informed Consent Form and give you a copy which you will need to sign if you wish to continue to participate.

2. WHAT WILL HAPPEN IF I DON'T WANT TO CARRY ON WITH THE STUDY?

Your decision to take part in this study is voluntary. You can refuse to take part or stop taking part at any time without giving a reason. If you decide to stop the study at any time, your exit from this study will not affect medical care which you otherwise may receive.

Your participation in this study may be stopped at any time by your study doctor, Gilead Sciences, Inc., or other Regulatory Authorities.

Your study doctor may decide for your medical safety to stop your study medication or take you off the study. You may be taken off the study if your study doctor learns you did not give a correct medical history or did not follow instructions for the study. If you are taken off the study, you will no longer receive the study medication. If your study medication is stopped, your study doctor will closely monitor your overall health.

Once the research study stops, your care will be continued under the management of your treating doctor according to the current standard of care. The study medication SOF/VEL/ GS-9857 FDC nor SOF/VEL FDC will not be available to you after the end of the study.

3. WILL ANY GENETICS TESTING BE DONE?

At the screening visit, a blood sample will be collected in order to test your DNA for a specific gene called the IL28B gene. This gene is linked to how well your body is able to clear the HCV infection from your body so it is important for the researchers to be able to check this. If you do not allow this particular genetic test (IL28B genotype) to be done, you cannot participate in this study**.** You will not be told of the result of this test and it will in no way affect your future medical care.

You will also have the opportunity to participate in additional research of genetic analysis of your blood called the Pharmacogenomic Research Study. This will involve the collection of one additional blood sample at the Day 1 visit in order to test for certain biomarkers in your blood. You will be asked to sign a separate section of the Informed Consent Form below if you are willing to participate with the genetic part of this research study. If you do not wish to participate in this additional research, your participation in this main research study will not be affected.

4. WHAT IF THERE IS A PROBLEM?

If you are injured or become sick as a direct result of taking part in the study, medical treatment will be offered to you by Barts Health NHS Trust. The sponsor, Gilead Sciences, Inc. will reimburse you or [institution] for the reasonable costs of any medical treatment of a study-related injury or illness provided that you have followed the instructions of the study doctors.

The sponsor will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

In accordance with the ABPI Guidelines, the sponsor will pay compensation where the injury probably resulted from:

- A drug being tested or administered as part of the trial protocol
- Any test or procedure you received as part of the trial

Any payment would be without legal commitment. (Please ask if you wish more information on this.)
In accordance with the ABPI Guidelines, the sponsor would not be bound to pay compensation where:

- The injury resulted from a drug or procedure outside the trial protocol
- The protocol was not followed.
- for temporary pain or discomfort or less serious or curable complaints
- for injury that has arisen through the wrongful act or default of a third party
- for injury that has arisen through your contributory negligence, including your failure to answer any question put to you as accurately as you are able

By agreeing to participate in this study, you do not give up any legal rights to other remedies that may be available to you in connection with an injury or illness caused by the study drug or study procedures.

If you experience any health problems during your participation in this study, you must contact your study doctor immediately.

5. WILL MY PARTICIPATION BE KEPT CONFIDENTIAL?

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

The information collected about you, will be held by Barts Health NHS Trust, Sponsor and Sponsor's authorized representatives. These records will be kept securely by the study doctor at the study site for two years after the last marketing application approval and until there are no pending marketing applications, or if no application is filed then for two years after the study discontinues (or clinical development of the study medication discontinues) and regulatory authorities are notified. 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 Sponsor or Sponsor's authorized representatives. Instead, you will only be identified by your year of birth and a code. The code is used so that your doctor can identify you if necessary.

Sponsor and its authorized representatives will analyse and use the coded information they receive for the purposes of this study. Such purposes include:

- checking your suitability to take part in the study,
- 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, Sponsor may communicate information to affiliates of Sponsor, people and companies with whom Sponsor works, and regulatory or other governmental agencies. These people, companies, and agencies may be located in your country, other countries of the European Economic Area (EEA), the United States, and other countries that are outside of the EEA. Some non-EEA countries may not offer the same level of privacy protection as you are used to in your country. However, Sponsor will keep any information it receives as confidential as possible within the limits of the law. The Sponsor, either alone or together with other researchers, may publish or present the results of the study based on your records and the records of all subjects in this study; however, you will not be identified personally in any publication or presentation.

Representatives from government agencies, the local ethics committee, and Sponsor or its authorized representatives, may also need access to your medical records and study records for the purpose of checking data collected for the study. By signing the consent form, you authorise this access.

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

You have certain rights to gain access and to correct any inaccuracies in information about you. By signing the consent form you agree that you will not be able to have access to your personal health information related to this study until the study is over. This is done to maintain the scientific integrity of the study. After the study is concluded, you can obtain access to your information through your Study Doctor.

As indicated above, your participation in this study is voluntary and you may withdraw from the study at any time by informing your Study Doctor. If you do so, your participation in the study will end and the study personnel will stop collecting information from you, but Sponsor needs to retain and use any research results that have already been collected. Sponsor must do this to comply with its legal obligations and to maintain the scientific integrity of the study.

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

6. WHO HAS REVIEWED THE STUDY?

All research in the National Health Service (NHS) is looked at by an independent group of people called a Research Ethics Committee. This is done to protect your safety, rights, wellbeing and dignity. The East of Scotland Research Ethics Service REC2, which has responsibility for scrutinizing all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of medical ethics.

It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from Gilead Sciences, Inc., and Barts Health NHS Trust, whose role is to check that the research is properly conducted and the interests of those taking part are adequately protected.

7. WILL MY GP BE INFORMED?

With your consent, your family doctor (General Practitioner) will be informed about your participation in this study. We would do so to ensure that we and your GP can best manage your overall healthcare. This can be done by providing information, for instance, about medications that should not be prescribed to you while you are on the study. If you do not consent to this, you cannot participate in this study.

8. WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

A final report will be written at the end of the study and your study doctor will be able to share and explain the results of the study with you in lay terms once the report is available. You will not be identified in any report/ publication.

A description of this clinical study will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

9. WHO IS ORGANISING AND FUNDING THE RESEARCH?

The study is being funded by Gilead Sciences, Inc. Your study doctor is not being paid directly by Gilead Sciences, Inc. A payment will be made to the Barts Health NHS Trust for including you in this study and to cover the costs of the study tests and the services provided by your study doctor and study staff.

10. FURTHER INFORMATION AND CONTACT DETAILS

While on this study, you will be under the care of Prof. Graham Foster. If at any time you feel that your symptoms are causing you problems or you have experienced a study-related injury, please contact your study doctor. The telephone number to reach your study doctor or other study personnel is:

Study Doctor: Prof. Graham Foster
Study Coordinator: James Hand
Site telephone number: 020 3594 6773 / 020 7377 7457

24 HOUR PHONE NUMBER: 020 7377 7000 (Trust Switchboard) and ask for the Hepatology Registrar "on-call"

Barts Health NHS
NHS Trust

INFORMED CONSENT FORM – MAIN STUDY

A Phase 3, Global, Multicenter, Randomized, Open-Label Study to Investigate the Safety and Efficacy of Sofosbuvir/Velpatasvir/GS9857 Fixed-Dose Combination for 8 Weeks Compared to Sofosbuvir/Velpatasvir for 12 Weeks in Direct-Acting Antiviral-Naïve Subjects with Chronic HCV Infection

Site Number: 03078

Protocol Number: GS-US-367-1172

Participant Identification Number: _____

Participant's Name: _____
(Full name in BLOCK CAPITALS)

Name of study doctor: _____
(Full name in BLOCK CAPITALS)

Your Consent	**Please initial box**
1. I confirm that I have carefully read and that I understand the information sheet dated and version 25-Nov-2015, version 2.2 for the above study. The purpose and procedures of this research study have been fully explained to me. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. I have received a signed and dated copy of this Informed Consent Form.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. I agree that the Sponsor can continue to use the information about my health collected during the study to preserve the integrity of the study, even if I withdraw from the study. The possible effect on my health, if any, of stopping the study early has been explained to me.	
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from Gilead Sciences, Inc., and its contractors, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4. I agree to my GP being informed of my participation on this study.	
5. I agree to the use of my medical data as described in this form.	

6. I agree that my anonymised personal data may be transferred worldwide and submitted to Regulatory Authorities where the medication may be considered for marketing or used for legitimate scientific purposes, including use in future medical and pharmaceutical research.	
7. I understand that data and samples will be transferred outside the EEA and that data protection laws may not be as stringent as the Data Protection Act in the UK, but the sponsor will take all reasonable steps to protect my privacy.	
8. I confirm I have been informed of the parts of the program that are experimental and of the possible discomforts, symptoms, adverse events and risks that I might reasonably expect, and the possible complications, if any, that I might reasonably experience from both known and unknown causes as a result of my participation.	
9. I have read the information below regarding 'Future Research Consent' and have provided my consent to these future research sub-studies below if applicable	
10. I agree to take part in this study.	

Participant

_____

Participant Printed Name Signature Date

_____

<Description of Legal Representative's Authority (e.g., parent or legal guardian)>

Person Obtaining Consent

_____

Printed Name & Title Signature Date

Witness (if applicable)*

Witness Printed Name Signature Date

*A witness is not required unless the participant is unable to read (e.g., blind or illiterate) or unless indicated in the protocol. If a witness is present, however, the witness must observe the entire informed consent process.

When completed, one for participant; one for study doctor site file; one (original) to be kept in medical notes.

Future Research Consent

We would like your consent to use your donated human tissue/blood samples for future research. If you decide to not allow this future research, you can still take part in the main study.

This research may help scientists to better understand:

- How your disease and related diseases work
- The effect of the study medication and/or other medications on the body
- How the study medication is processed by the body
- Who could benefit from the study medication
- Why some people have adverse events

The results of the tests done on your blood samples (also called biologic sample(s)) will not be given to you or your study doctor. Information from these tests may be printed in a medical journal or presented at scientific meetings. Only a summary of data from all participants will be used.

The results of this research may lead to an approved product for the treatment, prevention, or confirmation of disease. You understand and agree that by consenting to the storage and testing of your samples for possible future research, you authorise the use of your sample, the by-products of the sample, and any products developed from the sample as described by this form. The Study Sponsor, other researchers, or companies may patent or sell discoveries that result from this research. You will not be paid any money if this happens.

You may choose to take part in **none, some, or all** of the future research, listed below.

If you decide you no longer want to take part in this future testing of your biologic sample(s), your unused sample(s) will be destroyed. The Study Sponsor may continue to use and disclose the results from samples that were tested before you withdrew your consent.

If you decide to no longer take part in the main study or are taken off the main study by your study doctor, the biologic samples you provided for future research will still be kept and may be used for future testing. If you decide you no longer want to take part in this future testing, then your unused sample(s) will be destroyed.

For this study, you are being asked to let the Study Sponsor store and use the samples listed below for future testing. Any samples you provide for future research will be stored for up to 10 years at a central laboratory based in Switzerland.

Carefully read the sentences below and think about your choice(s).
Check the 'Yes' or 'No' box and initial next to your choice.

1) Store and use your leftover blood samples collected during this study for future research outside of the main study. Your samples may be stored and used for up to 10 years after the end of the study.

I agree to allow my leftover biologic samples to be stored after the main study testing is complete and used for future research outside of the main study.

Yes _____ *(initial)* No _____ *(initial)*

2) Collect, store and use additional blood samples for future research outside of the main study. This optional sample will be collected at Day 1 and End of Treatment or Early Termination. Your samples may be stored and used for up to 10 years after the end of the study.

I agree to provide additional biologic samples for future research.

Yes _____ *(initial)* No _____ *(initial)*

Future Pharmacogenomics Research Consent

3) Collect, store, and use additional blood samples for future research outside of the main study to do pharmacogenomic testing. Pharmacogenomics is the study of how genes affect a person's response to medication. This optional sample will be collected at Day 1. Your samples may be stored and used for this research for up to 10 years after the end of the study. You will not be informed of the results of these genetic tests.

I agree to provide additional blood samples to be used for pharmacogenomics testing outside of the main study.

Yes _____ *(initial)* No _____ *(initial)*

Participant

_____

Participant Printed Name Signature Date

_____

<Description of Legal Representative's Authority (e.g., parent or legal guardian)>

Person Obtaining Consent

_____

Printed Name & Title Signature Date

Witness (if applicable)*

_____

Witness Printed Name Signature Date

*A witness is not required unless the participant is unable to read (e.g., blind or illiterate) or unless indicated in the protocol. If a witness is present, however, the witness must observe the entire informed consent process.

When completed, one for participant; one for study doctor site file; one (original) to be kept in medical notes.